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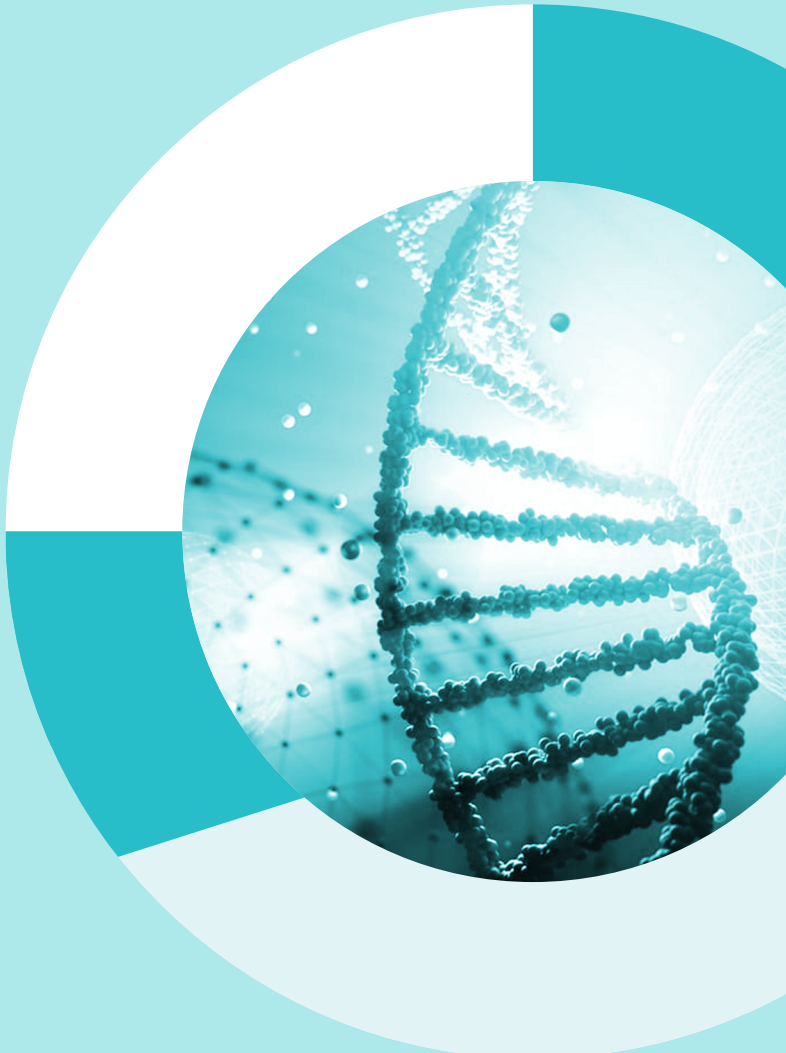

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CONTENTS

REVIEW

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The Use of Artificial Intelligence in Different Dental Applications

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Abstract

In response to technological breakthroughs, artificial intelligence (AI) applications are being extensively studied and developed in the fields of medicine and dentistry. AI applications significantly contribute to healthcare services and enhance efficiency by reducing the workload of healthcare professionals. The capacity of machines to exhibit human-like thinking and learning will significantly enhance the early detection and prevention of diseases. Although currently regarded as a supplementary component in dental diagnosis and treatment, it is expected that its significance will further advance in the coming years. This study aims to discuss the current use of AI technology in different branches of dentistry.

Keywords: Artificial intelligence, dentistry, deep learning

INTRODUCTION

Artificial intelligence (AI) involves developing systems that simulate human-like thinking processes in computers.[1] Developments in AI first began in 1943 with Allan Turing's question, "Can machines think?", and John McCarthy first used the term "AI" at a conference in 1956.[2] AI is a general term that encompasses the use of machines and technology to assist in performing tasks that are typically done by humans.[3] Machines can create algorithms based on what they learn from data; thus, they can solve problems without human assistance.[2]

To understand AI, it is necessary to first know its subsets such as machine learning (ML), neural networks (NN), and deep learning (DL) (Figure 1). The process of extracting the required data from internet data pools is called ML. ML involves algorithms that identify patterns and predict outcomes directly from existing datasets, operating autonomously without human guidance.[4]

NN are specialized ML algorithms designed to mimic the structure and functioning of the human brain. They consist of interconnected layers of artificial neurons (perceptrons) to replicate human neural processes. These networks enable computers to simulate human cognitive abilities such as learning, reasoning, and problem-solving.[2]

On the other hand, DL, a subset of ML, enables computers to learn how to process data on their own. DL extends the concept of NN by using multiple interconnected layers, forming complex architectures known as Deep NN.[2,5,6] The depth of these networks refers to the numerous algorithmic layers that work together, each contributing incrementally to interpreting data, but lacking significance individually.

Within DL, models such as artificial NN (ANN) and convolutional NN (CNN) play pivotal roles, especially in fields like dentistry. CNNs, particularly proficient in analyzing visual data, are widely utilized in dental research for tasks such as classifying, segmenting, and detecting features

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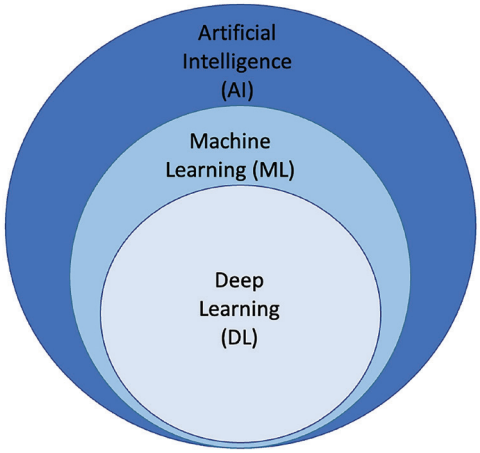

Figure 1. Subsets of artificial intelligence.

in dental radiographs. Conversely, ANNs, which feature multilayered architectures capable of refining and interpreting data progressively, excel at identifying intricate patterns-much like a dentist enhances radiograph images to discern different dental structures clearly.

Overall, the advanced NN structures of DL position it as a more powerful and effective tool for addressing complex problems compared to traditional ML approaches.

With advances in technology, AI has begun to modernize the traditional aspects of dentistry.[7] AI can perform many simple procedures in dental clinics with higher precision, using less personnel, and fewer errors compared to human performance. With the increase in digitalization, AI is used in many areas, from scheduling and coordinating regular appointments to assisting in clinical diagnosis and treatment planning and from designing prostheses to improving education. Integrating AI technology into dentistry reduces human-induced errors and saves time and money.[8] The purpose of this review is to examine the role and usage possibilities of AI as an auxiliary element in different departments of modern dentistry.

Table 1 summarizes the application of AI in different fields of dentistry.

Artificial Intelligence Applications in Oral, Dental and Maxillofacial Radiology

Radiographic evaluations are used for two basic purposes in dentistry. The first of these purposes, "analysis and differentiation of radiological features of normal and pathological formations in tissues", can be performed automatically using AI applications nowadays. The second purpose, "determination of preliminary and differential diagnoses, by evaluating data together with clinical examination findings", cannot yet be fully achieved with AI applications.[9,10] AI applications are most appropriate for identifying a potential abnormality and also assist the clinician in the final decision, but should not be the decision maker.[11] Therefore, AI applications can be used as a supportive tool in the field of oral, dental and maxillofacial radiology.

Putra et al.[12] discovered that the number of AI studies in the radiology field has been consistently increasing each year, with a significant increase beginning in 2020. Two-dimensional radiographs, including periapical, panoramic, and cephalometric radiographs, were the first used in the field of radiological studies.[10] After Flores et al.[13] proposed the AI-supported cone beam computed tomography (CBCT) model to differentiate periapical cysts from granulomas in 2009, 3-dimensional images have become more prevalent in the studies. The DL method was found to be the most frequently used AI technique, accounting for 59% of radiograph analyses, followed by ML, and other computer imaging methods in 26% of cases.[12]

Hung et al.[14] published a review in 2020 that focuses on four primary topics related to the use of AI in the fields of oral, dental, and maxillofacial radiology. These topics are automatic localization of cephalometric landmarks, diagnosis of osteoporosis, classification and segmentation of maxillofacial cysts and tumors, and identification of periodontal and periapical diseases.[14] In addition to these, AI applications are also used in areas such as numbering of teeth, detection of caries, extra roots and supernumerary teeth, evaluation of root morphology and determination of vertical root fractures, diagnosis of osteoporosis, and Sjögren syndrome.[15-18]

Table 1. Application of AI in different fields of dentistry.

Oral, dental and maxillofacial radiology	Automated interpretation of radiographs Segmentation of dental and bone structures Detection of pathological formations Detection and numbering of teeth
Oral, dental and maxillofacial surgery	3D image analysis for surgical planning Integration of robotic surgical systems Prediction of complication risks Diagnosis of cysts and tumors Localization of anatomic landmarks
Periodontology	Early diagnosis of periodontal diseases Detection of bone loss and gingival recession Monitoring treatment progress and prognosis prediction Detection of plaque accumulation
Endodontics	Analysis of root canal morphology in radiographs Assessment of root canal filling quality Detection of apical lesions Measuring working length Predicting treatment success and prognosis
Restorative dentistry	Detection of dental pathologies and treatments in radiographs and photographs Detection of vertical fractures in CBCT Predict prognosis of restorations
Prosthodontics	Digital prosthesis design using CAD/CAM systems Optimization of 3D printing processes Personalized prosthetic planning Assessing tooth color
Pedodontics	Tracking dental development stages in children Caries risk analysis Behavioral analysis for treatment planning
Orthodontics	Automated cephalometric analyses Simulation of tooth movements Individualized treatment planning Detect crowding and malocclusion from photographs

CBCT: Cone beam computed tomography, CAD: Computer-aided design, CAM: Computer-aided manufacturing.

Chen et al.[19] achieved an accuracy value of over 90% in their AI study on periapical radiographs for the detection and numbering of teeth. According to the results of the studies on AI use in detecting periapical pathologies, it has been reported that the accuracy rate of AI applications can aid clinicians in diagnosis.[15,20] In their study, Fukuda et al.[21] found the accuracy of AI in detecting vertical root fractures on panoramic radiographs to be 93%. Kise et al.[22] and Ariji et al.[23] conducted studies on Sjögren syndrome and the detection of lymph node metastases on computed tomography, and reported that AI models had high diagnostic accuracy. According to the study conducted by Lee et al.[24,25] on the diagnosis of osteoporosis using panoramic radiographs, AI applications showed an accuracy rate of 98.5%, a rate compatible with that of maxillofacial radiologists.

Artificial Intelligence Applications in Oral, Dental and Maxillofacial Surgery

In the field of oral, dental, and maxillofacial surgery, AI applications are used to perform several tasks such as radiographic image quality improvement, diagnosis of cysts and tumors, and localization of anatomic landmarks for improved surgical planning, precision, and patient outcomes. With the support of AI software, the aim is to determine enhanced and personalized treatment planning, while surgeons can also benefit from AI's real-time assistance and feedback during intraoperative decision-making, which increases surgical accuracy and decreases complications.[26]

Vinayahalingam et al.[27] evaluated the relationship of the third molar teeth with the inferior alveolar nerve using AI software in their study. They reported that the AI software was successful in preventing possible surgical complications, but the algorithm and accuracy rates should be increased for its use in clinical routine. Zhang et al.[28] in a study evaluating postoperative edema after extraction of mandibular impacted third molars, reported that AI applications showed 98% accuracy. According to the results of this study, AI applications are important in predicting the prognosis of the surgical procedure.[28]

Another area where AI can be used in maxillofacial surgery is implantology. Park et al.[29] scompared in 2023 compared the identification of various implant systems from radiographic images by an AI program and by dentists. They reported that the pre-trained and modified AI program gave statistically-significantly higher rates of correct answers in a shorter time compared to experienced and inexperienced clinicians.[29] Kurt Bayrakdar et al.[30] evaluated the success of the AI software in implant planning using CBCT in their 2021 study. According to the results of the study, the AI software was found to be more successful in determining bone height and width than manual methods. It has been reported that incorporating these systems in implant planning would simplify the work of clinicians. However, further comprehensive research about the evaluation of environmental anatomical structures using AI systems is required.

AI applications can also be used to scan and classify lesions in the oral mucosa and detect suspicious areas. The early diagnosis of malignant tumors in the oral region, especially in areas where health services are limited, with the help of AI-supported software programs is thought to affect morbidity and mortality rates.[31] Studies have reported that AI applications are also promising in the diagnosis of head and neck cancers.[32,33]

Artificial Intelligence Applications in Periodontology

In the field of periodontology, AI is used for various purposes such as detecting plaque accumulation and gingivitis, measuring pocket depth during probing, assessing alveolar bone loss, early identification of periodontitis through radiographic analysis, detecting changes in bone density, and diagnosing peri-implantitis and halitosis.[34-43] AI can also be used to identify individuals at a high risk of developing periodontal diseases. This approach enables the implementation of preventive interventions, which can decrease the severity and frequency of the disease. Several retrospective studies specifically designed for periodontal diseases and based on extensive electronic dental information have been conducted to assess the impact of AI algorithms.[44-46] These studies suggest that the probability of having periodontal disease can be determined by examining demographic factors, general health indicators, behaviors, blood values, medical history, dental hygiene, and periodontal parameters.[47] Shimpi et al.[44] developed a predictive model for periodontal disease using supervised ML techniques. Decision trees and ANNs were more accurate in classifying patients as having low or high risk of periodontitis compared to other models (sensitivity =87.08% and specificity =93.5%). Another retrospective study reported that ANNs performed well in terms of accuracy (90.0% - 98.1%), specificity (89.4% - 97.9%), and sensitivity (91.1% - 98.6%) in classifying patients as having aggressive or chronic periodontitis.[44]

Uzun Saylan et al.[48], in their study evaluated the effectiveness of AI models in identifying alveolar bone loss as present or absent across different regions. They found that regional bone loss detection was more successful than general bone loss detection in panoramic radiographs.[48] Shankarapillai et al.[49] used 230 textual topics for effective periodontitis risk prediction. However, the actual reliability of these innovative prediction methods for periodontitis has not yet been verified.

It should be noted that providing more standardization and methodology development in this area is needed. The decrease in the number of participants due to retrospective analysis and division of patients into subgroups leads to changes in the results of the studies. AI can significantly improve the diagnosis and treatment of periodontal diseases. Evaluating the amount of bone loss alone is not sufficient to determine the severity and extent of periodontal disease. Clinical attachment loss and tooth loss should also be evaluated. Factors such as general health status, number of cigarettes smoked per day, psychological state, and family history, also determine diagnosis and prognosis. Therefore, in future research, it is necessary to use an AI model in which information regarding these parameters is defined and organized to create modern AI applications. After the necessary development, AI can play an important role in the diagnosis of long-term periodontal diseases.

Artificial Intelligence Applications in Endodontics

The use of AI applications in endodontics is increasing in all the stages such as diagnosis, treatment planning, and follow-up.[50] The use of AI applications in many areas such as determining pulpal status[51,52], measuring working length[53,54] , detecting periapical lesions[20,53,55-57], or root fractures[20,58-60], evaluating root anatomy[61-63], evaluating the difficulty of the case[64], and predicting treatment success and prognosis[65-67] has been investigated in studies. In addition, AI programs are applied to explaining the working principles of endodontic devices and are also used in clinical education.[68-70]

Although AI cannot replace clinical examination for the assessment of the pulpal condition, it can be used as a supportive instrument to enhance diagnostic accuracy. Tumbelaka et al.[51] demonstrated the ability of an ANN trained using periapical radiographs to differentiate between healthy pulp, necrotic pulp, and pulpitis. Similarly, Zheng et al.[52] demonstrated that the accuracy of diagnosing deep caries and pulpitis was greatly improved by training CNNs using periapical radiographs combined with clinical parameters. While AI has the potential to identify different pulpal conditions using radiographs, it is essential to acknowledge its limitations. Radiographic assessments should be complemented by clinical examinations and other diagnostic tools, such as pulp and periapical tests, to ensure a thorough and accurate diagnosis in clinical practice.

In root canal treatment, success is mainly related to the correct determination of the working length, since the termination of the instruments within the apical region affects the prognosis of the treatment. Saghiri et al.[53] first introduced the use of AI in determining the working length. In their study, they evaluated the effectiveness of AI and showed that the AI program determined the location of the minor apical constriction with higher accuracy compared to professional endodontists.[54]

One of the applications of AI in endodontics is the radiological diagnosis of apical periodontitis, which is often performed using periapical and panoramic radiographs or CBCT.[56,57] Setzer et al.[56] reported that the rate of detecting periapical lesions correctly from CBCT images with a DL model was 93%. Similarly, Orhan et al.[20] tried to detect periapical lesions in CBCT images using CNN in their study. The results of the study indicated that CNN achieved 92.8% accuracy, and this rate was similar to the results obtained by experienced dentists.[20]

The use of AI systems has also been evaluated in the detection of vertical root fractures, which is a difficult clinical condition to diagnose. The AI systems have been found to provide very high accuracy in the determination of fracture lines.[20,58,59]

It has been stated that AI systems can provide a clear clinical picture of root canal morphology and a 3D modification that can be used as a guide for clinicians in challenging cases.[71] In the studies conducted[61-63], the use of DL models and CNN for the detection and classification of C-shaped canals was evaluated. The results indicate that AI can be a helpful technique in overcoming complex diagnostic difficulties.[61-63]

A new approach developed by Mallishery et al.[64] tested an automated system using AI to assess case difficulty and support referral decisions. The system used the American Association of Endodontists' Endodontic Case Difficulty Assessment Form and 500 clinical cases. The results of the study showed that AI has the potential for automation in assessing the complexity of endodontic cases.[64]

Campo et al.[65] used AI software to assess whether a case required endodontic treatment and stated that the application provided valuable contributions to the treatment decision-making process. Similarly, Herbst et al.[66] evaluated the use of AI techniques to predict endodontic treatment failure and concluded that AI applications can assist clinicians in determining the factors associated with failure. Another study conducted by Hasan et al.[67] in 2023 evaluated root canal filling success using AI system. This study successfully classified filling errors and demonstrated the effectiveness of these algorithms in evaluating endodontic treatment outcomes.[67]

Artificial Intelligence Applications in Restorative Dentistry

In restorative dentistry, clinical examinations and radiographs, are commonly used to diagnose, and plan treatment for patients' teeth and existing restorations. Considering the latest developments in medicine and dentistry focused on automating diagnosis, AI may have a substantial impact on the detection and classification of dental pathologies in the future.[8,72] The use of AI models to diagnose dental caries and vertical fractures, detect tooth margins, and predict restoration failure has increased significantly since 2019.[73] It has been emphasized that AI systems can have an important place in the field of restorative dentistry by improving clinical decision-making diagnosis, treatment planning, and predicting prognosis.[74] A systematic review reported that non-specialist dentists can obtain diagnostic assistance from DL systems.[8]

DL has been shown to detect dental pathologies or treatments on bitewing radiographs[75,76], periapical radiographs[52,77,78], panoramic images[79,80], or infrared light transillumination images.[81] In restorative dentistry, AI models are frequently used on periapical radiographs.[77] It has been shown that AI can be used for caries diagnosis and can detect both enamel and dentin caries (with a sensitivity of 60% for enamel caries and 97% for dentin caries). AI has shown nearly 100% success in detecting caries in cavities up to 0.6 mm deep.[73] A study conducted with bitewing radiographs reported that computer-aided tools for caries detection facilitate the diagnosis and classification of dental caries and help in appropriate treatment planning and monitoring of disease progression. In another study, the defect matching of the AI-aided computer program was found to be 96% on average for "no caries", 21% for score 1 (outer enamel defect), 23% for score 2 (inner enamel defect), 35% for score 3 (outer dentin defect) and 41% for score 4 (inner dentin defect).[82]

In addition, AI is used in the detection of tooth fractures and cracks. It has been reported that when AI models are used together with tomography in fracture detection, they provide more accurate and specific diagnostic results.[20] In a study using intraoral photographs, it was reported that ceramic, metal, amalgam or composite restorations compatible with tooth color in posterior teeth are can be automatically categorized with an accuracy rate of over 90% using DL-based AI. Researchers have shown that such AI-based methods can support dentists in the future.[83] In another study using intraoral photographs of patients with fissure sealants, the AI system categorized the restorations as "sound," "adequate," and "inadequate" with a diagnostic accuracy of approximately 90%.[85]

AI can also be used for treatment planning, and process. For example, it has been reported that AI programs can accurately predict the depth and type of finish line to be used for a specific tooth preparation and has an accuracy of 90.6 to 97.4% in this regard.[73] It is thought that AI programs can analyze images of tooth preparations predict areas of debonding in resin composite restorations comment on the prognosis of composite restorations, and enhance long-term success.[85]

AI applications are also used to compare the accuracy and repeatability of intraoral scanners or computer-aided design/computer-aided manufacturing (CAD/CAM) systems, as well as to articulate models obtained using scanners, both of which are essential components of digital restorative dentistry. It has been shown that AI can eliminate errors that may arise during data transfer.[86] Three-dimensional models of prepared teeth can be created, dental restorations can be designed, and these designed restorations can be milled or printed with CAD/CAM systems. In this context, AI models can be used to automate the design of dental restorations through customized reconstruction.[87]

Artificial Intelligence Applications in Prosthodontics

In prosthetic dentistry, the incorporation of CAD/CAM technologies into the treatment procedures has emerged as a significant advancement, enhancing the efficacy of therapies. Mangano et al.[88], in their study with 25 patients, found that 40 monolithic zirconia crowns, which were designed with the assistance of AI and a fully digital process, had a survival rate of 97.5% and an overall success rate of 92.4%.

In CAD/CAM systems, AI is now being used in the initial stages of work, specifically the impression phase as well as the design phase. AI support is utilized in modern devices to enhance the precision of scanning in impressions captured by intraoral scanners, and to offer users a more convenient scanning experience.[89] These devices improve the clinician's experience and enhance treatment comfort by shortening scanning time and ensuring that any missing parts may be filled with the software. This is achieved by excluding tissues like the cheek and tongue from the image during scanning. Furthermore, AI enables operations like the automatic drawing of preparation margins, making clinician-laboratory communication more efficient. AI is also used in manufacturing processes such as modeling, determining the most appropriate restoration type, and designing restorative morphology.[90] Revilla-León et al.[86] demonstrated that AI-assisted interjaw relationship recording using intraoral scanners is more accurate than recordings made without AI support.

There are some situations in prosthetic applications that require advanced experience. It has been reported that AI applications are used in some special situations, such as determining the tissue emergence profile in implant-supported prostheses, as well as planning the new crown to be made by taking into account the patient's tooth wear.[91,92] Lerner et al.[93] reported the 3-year survival and success rates of 99% and 91.3% for 106 implant-supported monolithic zirconia crowns they applied to 90 patients. This result is quite important because the researchers used AI support in all stages of their studies such as determining the emergence profile, designing the personal abutment and temporary prosthesis, and designing the margin line of the permanent crown.

Apart from these, AI applications are also used in prosthetic dental treatment applications like assessing tooth color, creating designs for removable prostheses, and predicting potential facial alterations caused by the use of these prostheses in patients.[94]

Artificial Intelligence Applications in Pedodontics

AI applications in pediatric dentistry provide assistance in preventive and therapeutic oral care until adulthood.[95] Research has demonstrated that AI systems can assist clinicians in utilizing behavioral guidance approaches, which are crucial in the field of pedodontics. Additionally, AI may assist in the early identification of plaque accumulation in primary teeth, early childhood caries (ECC), and dental anomalies.[95,96]

In their study, You et al.[36] reported that the DL model exhibited comparable efficacy to an experienced pedodontist in identifying plaque accumulation in primary teeth. The researchers stated that the advancement of the system would enable the utilization of AI not only by clinicians to manage children's everyday dental hygiene, but also by parents. Furthermore, the incorporation of ML in dentistry has been found to enhance precision and expedite outcomes. Consequently, this facilitates comprehension of the necessity for dental therapy and enables the evaluation of oral health by dentists, parents, and even children.[97,98]

Many general dentists may lack specific qualifications to diagnose mixed dentition in children. For this reason, the use of AI in pedodontics has also been evaluated to enhance radiographic imaging in detecting abnormal tooth eruptions and optimizing the identification of dental anomalies.[99-101] Ahn et al.[100] and Ha et al.[101] reported in their studies that the DL model provided a more accurate, faster, and clinically acceptable diagnosis than clinicians in detecting mesiodens across all dentition groups. Studies have indicated that with the support of AI in the detection of missing or excess teeth, clinicians can save time and energy while reaching more accurate treatment alternatives.[102,103]

In addition to environmental and behavioral factors, biological factors such as genetics also play a role in the formation of ECC.[104,105] In studies conducted; AI support has been used in the evaluation of the factors in the formation of ECC[105-107] and in the detection of ECC.[104,108] Research suggests that the advancement of these systems can have a positive impact on children's oral health by promoting early caries prevention strategies and encouraging parents to adopt healthier nutritional habits. Additionally, these systems can serve as a valuable tool for assessing the risk of caries.

Ensuring the elimination of child's fear and anxiety is crucial in pediatric dentistry. Hence, the child's behavior should serve as the basis for a effective and efficient therapy approach and a successful treatment outcome. AI-powered technologies like virtual reality and augmented reality enhance dental operations by providing immersive and engaging experiences that reduce fear and anxiety in children.[109] Research indicates that virtual reality decreases the average levels of anxiety and behavioral issues in children.[96,110,111] Nevertheless, it has been stated that AI functions mostly as an auxiliary instrument, due to the lacking ability to precisely respond the changing emotions and needs

of children in the same manner as a clinician and may be insufficient in non-verbal communication. Therefore, it has been emphasized that AI should be regarded as a tool that enhances the skills of dentists and should be utilized while maintaining interaction with patients focused on human needs.

Artificial Intelligence Applications in Orthodontics

AI applications in orthodontics have a wide range of uses in the fields of diagnosis, treatment planning, and clinical practice. A satisfactory orthodontic diagnosis relies on a series of analyses, like cephalometric analysis, dental analysis for molar relationships, tooth crowding, dental arch width, overjet and overbite, facial analysis, skeletal maturation determination, and upper airway obstruction assessment, to comprehensively evaluate patients' overall profile.[112] Visual configurations are crucial tools in the diagnostic and evaluative stages since they provide guidance for treatment and enhance patients' motivation for it. However, analyzing these visual configurations, like lateral cephalograms, intraoral and facial photographs manually is time-consuming and need intensive labor. Detecting the anatomical landmarks on lateral cephalograms is especially experience-dependent and may be inconsistent within and across orthodontists.[113] In recent years, with the advancements in AI technology, these analyses can be generated using AI-assisted software, which can utilize pictures, lateral and anteroposterior cephalograms or 3D models created by intraoral scanners.[114-116] CNN models are another instance where AI support is utilized in the diagnostic phase. The utilization of AI models has demonstrated the ability to detect crowding and malocclusion, that necessitates orthodontic treatment from intraoral photographs.[117,118] AI is also used for tooth detection in cleft lip and palate patients, and it demonstrated high overall sensitivity (0.98±0.03) and precision (0.96±0.04). It was found that the AI system is effective in detecting and numbering teeth in cleft lip and palate cases, but further refinement is required for improved accuracy, especially in the cleft region.[119]

Furthermore, there have been reported cases where AI programs have been used to assess the need for extraction treatment. Research has demonstrated that AI applications are highly capable and achieve exceptional accuracy when determining the need for tooth extraction.[114,115] AI has also made some progress in orthognathic surgery decision making; however, there is still a need for further improvement for more comprehensive and borderline cases.[113] Hence, it has been asserted that AI can serve as a supplementary instrument in clinical decision-making, and its potential in this area needs to be improved.

Study Limitations

AI has the potential to transform both daily life and professional activities, and its influence is growing across various industries, including dentistry.[120] Today, AI applications are widely used as supportive tools in different areas of dentistry. However, it presently lacks the ability to establish associations similar to the human brain and is only partially capable of making intricate decisions in a healthcare environment.[121] In uncertain situations, advanced information derived from a dentist's experience is crucial; these scenarios include performing physical examinations, integrating medical histories, evaluating aesthetic results, and facilitating discussions.[21,122] Effective patient-dentist communication requires a non-verbal evaluation of the patient's desires, concerns, and anticipations. This holds true despite ongoing discussions over the necessity of programming empathy into the algorithms that allow affective robots to replicate human emotions.[121,122]

Besides these, the adoption of new technologies often faces resistance. Dentists need to acquire specific skills to use AI safely and effectively in dental treatments, as the potential risks and challenges associated with AI must be carefully managed. Ethical, legal, and practical concerns, such as data privacy, algorithm transparency, and liability, present significant challenges that must be addressed to ensure the responsible and ethical implementation of AI in dentistry.[123] Continuous research in this field allows AI algorithms to be trained and refined over time. Despite these advancements, successfully integrating AI into everyday dental practice remains challenging due to limited data availability, a lack of rigorous scientific studies, and practical concerns about the value and application of these technologies.[119]

CONCLUSION

AI cannot yet replace clinical expertise, but its role in supporting traditional diagnostic and treatment methods is growing. Ongoing advancements, supported by collaboration and thorough validation, will further improve AI and ensure its safe and effective use in everyday dental practice.

MAIN POINTS

- Artificial intelligence (AI) enhances diagnostic accuracy and clinical outcomes in various dental specialties.
- Convolutional neural networks outperform traditional methods in analyzing dental radiographs.
- AI supports personalized treatment in prosthodontics, endodontics, pedodontics, periodontology, orthodontics, and oral surgery.
- Despite rapid progress, AI currently remains an adjunctive tool in dentistry.
- Integration of AI into routine dental practice requires further clinical studies and interdisciplinary collaboration.

Footnotes

Authorship Contributions

Design: S.E., Y.E.Ö., İ.Ö., Data Collection and/or Processing: S.E., Y.E.Ö., İ.Ö., B.D.K., B.B., Z.Ö.K., Literature Search: S.E., Y.E.Ö., İ.Ö., B.D.K., B.B., Writing: S.E., Y.E.Ö., İ.Ö., B.D.K., B.B., Z.Ö.K.

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REVIEW

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Ensuring Effective Communication with Patients Receiving Mechanical Ventilation Support in Intensive Care Units: Current Communication Materials

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Abstract

In recent years, with the reduction in sedation use among mechanically ventilated patients, research indicates that a considerable number of patients stay conscious yet are incapable of verbal communication. The presence of an endotracheal tube or tracheostomy cannula, necessary for mechanical ventilation, disrupts or even prevents communication in these patients. As a result, communication challenges pose a major problem for patients receiving mechanical ventilation in intensive care units (ICUs), as well as their families and healthcare providers. These patients face considerable challenges in communication, as they are unable to convey verbal messages or respond to communication attempts. Only a small percentage of the messages conveyed by mechanically ventilated patients are received and understood by healthcare providers, indicating communication difficulties compounded by comprehension challenges. Effective communication with awake and responsive patients during mechanical ventilation facilitates early extubation and reduces ICU stay durations. Nurses must be well-versed in and must apply appropriate communication methods. Additionally, the use of various communication tools, such as low-tech communication boards, high-tech tablet computers, and communication cards, with great awareness is crucial for effective communication with this patient group. The aim of this review is to examine the effects of communication tools used with patients undergoing mechanical ventilation in ICUs on the communication between patients and health workers.

Keywords: Communication, communication tools, mechanical ventilators, intensive care units

INTRODUCTION

When examining sedation strategies applied to patients in intensive care during the last three decades, a transition has occurred from deep sedation practices to lighter sedation in terms of duration and intensity.[1-3] It is an established fact that a significant number of patients remain conscious and responsive during mechanical ventilation, yet are unable to speak due to the use of artificial airways.[2,4,5] Approximately 40% of intensive care unit (ICU) patients require endotracheal intubation or tracheostomy, which can impair their verbal communication.[5] During this process, the inability to speak among a considerable number of patients is frequently coupled with physical weakness, resulting in the incapacity to use gestures.[6] Consequently, there are challenges in receiving and understanding the messages conveyed by mechanically ventilated patients. Only about 5% of the messages patients attempt to convey are correctly perceived and understood by healthcare providers. This indicates that communication difficulties reported by 50% of mechanically ventilated patients are compounded by comprehension and perception challenges.[5,7]

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Communication difficulties pose significant challenges for mechanically ventilated patients in ICUs, their families, and healthcare providers.[8] Literature reviews reveal that various communication methods have been created and implemented in clinical settings to address communication issues with mechanically ventilated patients.[1,2,5,9-14] There are limited comprehensive studies in the current literature that cover all communication tools used in intubated patients. Considering the clinical impacts and benefits, along with the current gaps in the literature, this study seeks to elucidate the barriers to communication with mechanically ventilated ICU patients. Additionally, it seeks to evaluate and improve the effectiveness of communication, and develop new communication strategies by discussing the benefits of different communication tools and offering a perspective on existing deficiencies. In this context, addressing communication with conscious mechanically ventilated patients; the challenges of communication; the techniques used; and the materials employed for communication, along with their benefits, is believed to significantly enhance and facilitate nurse-patient communication.

Communication Methods and Tools Used in Patients Who Cannot Communicate Verbally

In ICUs, both verbal and non-verbal communication methods are used with mechanically ventilated patients, considering their health status and communication abilities. Different communication techniques can be employed simultaneously with the same patient.[15]

Common non-verbal communication methods used in ICUs include hand, eye, and head movements, gestures, eye-letter coding, writing yes-no questions, and lip reading.[7,9,14,16,17] However, the lack of lip-reading skills among healthcare providers often leads to misunderstandings. Additionally, these time-consuming methods can drain patients' energy, leaving them unable to communicate effectively.[2,7,18]

To overcome these challenges, various communication tools have been developed for non-verbal patients.[14] These tools typically include expressions related to physical needs (e.g., thirst, toilet needs), emotional states (e.g., anger, anxiety), requests (e.g., massage, turning lights on/off), hygiene needs (e.g., oral care), titles of healthcare providers (e.g., doctor, nurse), and pain assessment scales.[7,14]

Augmentative and alternative communication (AAC) methods, which include both aided and unaided techniques, have been developed to address communication deficits. Unaided techniques involve non-verbal communication methods (e.g., facial expressions, body posture, gestures), while aided techniques include low-tech and high-tech interfaces.[1,5] Low-tech AAC materials include writing tools, communication boards, and pain charts, whereas high-tech AAC materials encompass computer-based communication applications, tablet computers, eye-tracking devices, and speech-generating devices.[2,5,12,13] High-tech communication methods and communication boards are considered more user-friendly than other methods.[5,10,11,19] However, a consensus has yet to be reached regarding the most appropriate communication tool for ICUs, and more comparative research is needed.[20]

A Look at Studies Examining the Effectiveness of Communication Tools in Mechanically Ventilated Patients

It is evident that effective communication is of paramount importance in determining the course and outcome of patient treatment. Therefore, addressing communication problems in mechanically ventilated patients is of utmost importance.[21] In healthcare settings where services are meticulously provided, patient-centered communication enhances patient satisfaction, improves health outcomes, and increases care quality. However, patients who cannot communicate verbally due to illness or treatment processes often struggle to convey their needs to nurses or other healthcare providers.[22] In this context, examining the communication tools used with mechanically ventilated patients is crucial (Table 1).

An examination of studies conducted over the last ten years (2014-2023) reveals that low-tech communication tools developed for conscious patients in ICUs in our country include "pictorial communication materials"[7], "pictorial communication cards"[9], and "visual communication guides"[16]. High-tech communication tools include "computer-based communication tools" and "AAC systems (AACS) prototypes"[14]. Studies indicate that communication boards, a low-tech communication tool, are highly beneficial and effective in facilitating communication among patients, their families, and nurses.[2,10,11,21,23-26] Examples of communication boards are provided in Figures 1,2.[23]

Additionally, studies have utilized tablet computers[6,27], eye-tracking communication devices[28,29], voice-activated systems[30,31], and advanced support systems such as speech-generating devices[32,33] among the high-tech communication tools in the literature. Studies examining the effectiveness of communication tools used with mechanically ventilated patients are summarized in Table 2.

CONCLUSION

Communication difficulties between healthcare providers and mechanically ventilated patients in ICUs are common. The findings of the studies reviewed in this article suggest that both low-tech and high-tech communication tools used in ICUs can be effective in improving communication between ICU patients and healthcare providers. The use of low-tech and high-tech communication tools can enhance communication and improve patient-centered outcomes. A combination of methods is recommended. However, the implementation of advanced eye-tracking-based communication devices in ICU practices can significantly contribute to patient-centered care by improving communication in mechanically ventilated patients. Furthermore, integrating technological advancements into care will enhance the satisfaction of both patients and healthcare providers in this group, as well as improve nursing care outcomes.

Table 1. Communication tools used in mechanically ventilated patients

Communication tools used	
Low-tech communication tools	Pictorial communication materials
	Pictorial communication cards
	Visual communication guides
	Communication boards
High-tech communication tools	Computer-based communication tools
	Augmentative and alternative communication system (AACS) prototype
	Tablet computers
	Eye-tracking communication devices
	Voice-activated and speech-generating devices

Figure 1. Sample communication board.[23]

Figure 2. Sample communication board.[23]

Table 2. Studies investigating the effectiveness of communication materials used in patients receiving mechanical ventilator support

Author/year	Country	Type of research/sample	Measurement tool	Research findings
Kuruppu et al.[2]	Sri Lanka	Qualitative research n=17 (nurses: 9, patients: 8)	Communication board	It was determined that communication practices in the ICUs where the research took place included head nodding, gestures, lip reading, eye blinking, and the use of paper and pen, but communication boards had not been used previously. After the implementation, both patients and nurses participating in the research expressed that the use of communication boards was acceptable and appropriate for effective communication. However, nurses indicated that during busy times, they might use communication boards less. The study concluded that communication boards are highly important for identifying patient needs, improving nurse-patient communication, and ensuring patient-centered care in intensive care units.
Szymkowicz et al.[5]	Belgium	Randomized crossover comparison n=44 (patients)	Communication card eye-tracking system (ET)	This study compared the use of low-tech communication cards and high-tech eye-tracking devices to enhance the effectiveness of interactions with mechanically ventilated patients in ICUs. The results revealed that the eye-tracking device quantitatively and qualitatively improved communication effectiveness compared to conventional communication cards. Additionally, the study concluded that the use of advanced eye-tracking-based communication devices in ICU practices can improve communication in mechanically ventilated patients, thereby contributing to patient-centered care.
Bhardwaj and George[10]	India	Quantitative research n=50 (patients)	Post-test communication board	This research sought to evaluate the efficacy of communication boards in terms of satisfaction among patients receiving mechanical ventilation in ICUs. The communication board was implemented in the experimental group throughout the weaning process. The results showed a significant difference in communication satisfaction scores between the experimental and control groups, suggesting that the implementation of communication boards effectively increased satisfaction among mechanically ventilated patients.
Ull et al.[29]	Germany	Experimental research n=11 (patients)	Richmond Agitation-Sedation Scale Eye-tracking system (ET)	In this study, the ET system was observed over a 4-week period in patients undergoing mechanical ventilation through oral intubation or tracheostomy. The results showed that all patients preferred the gaze fixation technique over blink control to operate the eye-tracking system. The study concluded that eye-tracking systems can be easily used to express patients' basic needs and fears, monitor complications during rehabilitation, and respond to assessment scales related to pain, quality of life, and self-esteem.
Yırtık et al.[14]	Türkiye	Qualitative research n=7 (healthcare workers: 5, patients: 2)	High-tech augmentative and alternative communication system (AACS) prototype	In this study, a high-tech prototype was created to address the communication requirements of non-verbal individuals in intensive care, based on data obtained from qualitative research interviews. The prototype was designed to facilitate communication among patients by dividing it into submenus. In addition to the existing touchscreen, the prototype's pointing feature further simplified communication. Along with the development of pre-defined cards as the primary communication tool, the prototype included modules such as "pain modüle", "drawing module", "writing module, and text-to-speech module" to address patients' communication needs. It was noted that the prototype could be preferred in situations where other communication methods are insufficient for non-verbal patients.
Divani et al.[11]	Iran	Randomized controlled trial n=60 (patients)	Communication board	In this study, after nurses were trained on the use of communication boards, notable differences were observed in serum cortisol levels among patients, who communicated using the boards and those who used routine communication methods. Additionally, significant reductions in hemodynamic parameters, including heart rate and blood pressure, were noted following the use of communication boards. At the beginning of the study, patients with high cortisol levels were found to be anxious. However, the use of communication boards effectively reduced both cortisol levels and anxiety.

Table 2. Continued

Author/year	Country	Type of research/sample	Measurement tool	Research findings
Ull et al.[28]	Germany	Prospective descriptive study n=64 (patients)	Survey form Behavioral Pain Scale (BPS) Eye-tracking system (ET)	At the beginning of the research, calibration was performed by having each patient follow a cursor on a monitor with their gaze, reaching a total of 9 consecutive points. Subsequently, all patients were introduced to the eye-tracking system by playing simple games for 10 minutes. After completing the training phase, a yes-no questionnaire was projected onto the monitor and was designed to be read aloud using the eye-tracking system. Patients read the question on the monitor and selected "yes" or "no" by fixing their gaze on the corresponding answer. The study concluded that the use of these devices, which can convert text and symbols into clear speech and provide access to computers, phones, and control of Windows or home environments, led to improvements in family support and quality of life for patients.
Kuyler and Johnson[25]	South Africa	Qualitative research n=40 (nurses: 30, patients: 10)	Vidatak EZ board	In the study conducted to identify the content of the communication board, patients and nurses suggested 111 common words that should be included on the board. Of these, 104 words were included in the communication board employed in the research, and the final selection of words was based on patient preferences. While evaluating the words, the patient and nurse participants recommended that certain phrases be adapted for South African use. For example, "I love you" should be changed to "I appreciate you," "light-headed" to "dizzy," "physical therapist" to "physiotherapist," and "respiratory therapist" to "respiratory care practitioner." They also suggested removing some phrases from the board as they were not linguistically or culturally appropriate for South Africa. Additionally, they proposed adding words such as "catheter," "place, date, month, and time," "please," "okay/good," "good morning or hello," "move, get up, or walk," "speech therapist," "psychologist," "bed up or down," and "head up or down. The study concluded that the Vidatak EZ Board communication board is valuable for patient communication in intensive care units and that a portion of its content is applicable in South Africa. However, the study emphasized that word selection, linguistic, spiritual, and cultural diversity should be thoroughly evaluated when designing such boards.
Al-Yahyai et al.[22]	Oman	Descriptive-cross-sectional study n=194 (nurses)	Survey form	This study found that very few nurses used alphabet, picture, writing or drawing boards, or modern electronic assistive devices, while the majority relied on traditional methods such as lip reading and using gestures/body language. It was observed that nurses did not adopt assistive communication tools and lacked standardized, evidence-based communication methods. Therefore, the study concluded that policies should improve patient outcomes in intensive care units, and healthcare workers urgently require training in this area.
Vignesh et al.[34]	India	Quantitative research n=60 (patients)	Post-test Patient Satisfaction Scale High-tech Communication board	This research was carried out to assess the effects of implementing a high-tech communication board on patients' responses and satisfaction levels. In contrast to the group of patients who did not utilize the communication board, the group using the high-tech communication board showed significant improvements and increased satisfaction in their responses.
Albayram and Yava[9]	Türkiye	Descriptive study n=47 (patients)	Survey form pictorial communication cards	This research sought to examine the effects of pictorial communication cards, developed for communicating with intubated patients who had undergone open-heart surgery, on patient communication and satisfaction. The majority of patients reported that the pictorial communication cards assisted their communication. Additionally, it was observed that visual communication cards could be used for patients of all age groups, regardless of education level or gender, facilitating communication. However, it was concluded that these cards could not completely eliminate communication challenges.
Pandian et al.[33]	United States of America	Randomized controlled trial n=44 (patients)	Quality of life (QOL-MV) Voice-related quality of life (V-RQOL) Speech ıntelligibility test (SIT) Blue line ultra suctionaid (BLUSA) Speaking tracheostomy tube	This study, conducted with awake, mechanically ventilated patients attempting to communicate who could not endure a one-way speaking valve, assessed the quality of life through the use of the BLUSA speaking tracheostomy tube. The results showed that the BLUSA speaking tracheostomy tube significantly improved the quality of life for mechanically ventilated patients with tracheostomies who were unable to tolerate cuff deflation.

Table 2. Continued

Author/year	Country	Type of research/sample	Measurement tool	Research findings
Erturk Yavuz and Gursoy[16]	Türkiye	Mixed-methods research n=34 (healthcare workers: 20, patients: 14)	Visual communication guide	In this study, the implementation of a visual communication guide developed for patients who underwent partial laryngectomy in Türkiye showed that patients found the guide helpful and practical for expressing themselves. It was reported that the guide could be effective in preventing misunderstandings in communication and providing faster solutions to patient problems and requests. However, while 50% of the patients deemed the images insufficient, healthcare workers and other patients considered the images in the guide to be clear, comprehensible, and suitable in terms of color, size, and font. Healthcare workers stated that the guide was practical and efficient in saving time during communication but fell short in addressing patients' psychological concerns.
Hosseini et al.[21]	Iran	Quasi-experimental study n=30 (patients)	Hospital Anxiety and Depression Scale (HADS) Ease of Communication Scale (ECS) Communication board	This research sought to evaluate the impact of communication boards on communication and anxiety levels in conscious, mechanically ventilated patients in ICUs. The findings revealed that the implementation of communication boards facilitated communication and reduced anxiety. Additionally, it was noted that communication with conscious, mechanically ventilated patients is challenging. In the control group, where no assistive communication tools were used, difficulties persisted for a while but decreased over time. Traditional means such as body language and eye contact were identified as effective factors in communication.
Ertürk Yavuz and Gürsoy[35]	Türkiye	Experimental study n=90 (patients)	Survey form Glasgow Coma Scale Perianesthesia Comfort Scale State Anxiety Scale Computer-based communication tool (CBCT)	In this study conducted with mechanically ventilated patients in ICUs, after open-heart surgery, a CBCT which vocalizes patients' requests, needs, and problems in Turkish was used. The results revealed that 82.2% of patients in the control group and 20.0% of those in the experimental group experienced difficulties in communication. The experimental group had higher perianesthesia comfort scores and lower state anxiety scores compared with the control group. Although 93.3% of the experimental group patients, who were studied alongside CBCT, 43.3% of the control group patients reported that hand-arm movements were the best communication method, all patients in the experimental group found the communication tool easy and learnable. It was concluded that the developed CBCT assisted patients in communication, increased their comfort levels, and reduced their anxiety. It was emphasized that this tool is the first voice-enabled, pictorial, and easily applicable application developed in Türkiye for non-verbal patients to communicate with their surroundings.
El-Soussi et al.[23]	Egypt	Randomized controlled trial n=60 (patients)	Communication board	In this research, most patients in the intervention group found communication boards easier and more beneficial compared to using paper and pen for communication. Additionally, their mechanical ventilation and ICU stay duration decreased. On the other hand, most patients in the control group expressed dissatisfaction. The results showed that communication boards increased patient satisfaction levels and were an effective intervention in reducing patient distress.
Rathi and Baskaran[26]	India	Quasi-experimental study n=30 (patients)	Survey form Communication board	This study evaluated the impact of communication boards on the satisfaction levels of mechanically ventilated patients. The results revealed that the satisfaction levels of the experimental group, using the communication board, were notably higher compared with the control group, which used a routine whiteboard for communication. The study concluded that communication boards improved interpersonal relationships between nurses and patients, reduced communication errors, increased the time allocated for care, and enhanced patient comfort. It was emphasized that communication boards can be used to improve communication satisfaction in mechanically ventilated patients.

ICU: Intensive care unit

MAIN POINTS

- **Shift in sedation strategies and communication challenges**: Over the past thirty years, there has been a transition from deep sedation to lighter sedation practices in intensive care units (ICUs). This has resulted in some mechanically ventilated patients remaining conscious but unable to speak, leading to communication difficulties. Only about 5% of patients' messages are correctly understood, exacerbating communication challenges.
- **Non-verbal communication methods and tools**: In ICUs, non-verbal methods such as hand, eye, and head movements, writing, and yes-no questions are used to communicate with mechanically ventilated patients. However, these methods can be time-consuming and exhausting for patients. As a result, low-tech (communication boards, pictorial cards) and high-tech (eye-tracking systems, tablet computers, speech-generating devices) communication tools have been developed.
- **Effectiveness of communication tools**: Studies have shown that tools such as communication boards and eye-tracking systems are effective in helping patients express their needs, reducing anxiety, and facilitating nurse-patient communication. High-tech tools, in particular, provide more effective communication compared to traditional methods.
- **Cultural and linguistic adaptation**: The design of communication tools must take into account cultural, linguistic, and individual differences. For example, adapting the expressions on communication boards to local culture enhances patients' ability to use these tools effectively.
- **Role of technological advancements**: High-tech solutions such as eye-tracking systems, speech-generating devices, and computer-based communication tools have significant potential in meeting the communication needs of mechanically ventilated patients. These technologies support patient-centered care and improve satisfaction for both patients and healthcare providers. However, further research is needed to standardize and widely implement these tools.

Footnotes

Authorship Contributions

Concept: C.Ç., K.ÖY., Design: C.Ç., K.ÖY., Data Collection and/or Processing: C.Ç., K.ÖY., Analysis and/or Interpretation: C.Ç., K.ÖY., Literature Search: C.Ç., K.ÖY., Writing: C.Ç., K.ÖY.

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RESEARCH ARTICLE

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Mitigating Cisplatin-Induced Nephrotoxicity in Rats: A Comparative Study of Ambroxol and Coenzyme Q10 Effects

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Abstract

BACKGROUND/AIMS: Cisplatin (Cis), used in the treatment of various types of cancer, causes serious kidney damage. In this study, the protective effects of ambroxol (Amb) and coenzyme Q10 (CoQ10) were examined to reduce the toxic effect of Cis on the kidneys.

MATERIALS AND METHODS: Adult female rats were divided into 6 groups; control, Cis, Amb, CoQ10, Cis + Amb and Cis + CoQ10. The rats were sacrificed at the end of the 7-day experimental period. Blood and tissue samples were taken for biochemical and histomorphological examinations. Biochemically, urea and creatinine were analyzed from serum, and TNF-α and malondialdehyde (MDA) analyses were performed from serum and tissues. Histologically, H&E and immunohistochemical caspase-3 staining analyses were performed.

RESULTS: Serum urea, creatinine, TNF-α, and MDA (both serum and tissue values) were quite high in the Cis group, and there was a significant difference between them and all other groups ($p<0.05$). As a result of biochemical analyses, no significant difference was detected between Cis + Amb and Cis + CoQ10 ($p>0.05$). Under light microscopy, the Cis group showed the most damage. It was observed that Cis + Amb and Cis + CoQ10 groups reduced kidney damage. There was a significant difference between the Cis-only group and the Cis + Amb group in terms of glomerular and tubular damage ($p<0.05$). In the Cis group, caspase-3 expression was significantly increased compared to the other groups, and a statistical difference in caspase-3 expression was found between the Cis + Amb and Cis + CoQ10 groups ($p<0.05$).

CONCLUSION: Ambroxol and coenzyme Q10 were found to be effective in reducing kidney damage caused by cisplatin.

Keywords: Cisplatin, kidney, urea, TNF-α, caspase-3

INTRODUCTION

Cisplatin (Cis), an anticancer agent, is a platinum-based metal-binding agent. It is used therapeutically in most types of cancer, such as lung, testicular, ovarian, and breast cancer.[1] The major factors limiting the use of Cis include nausea, vomiting, nephrotoxicity, hepatotoxicity, neurotoxicity, and ototoxicity.[2] Acute kidney injury due to nephrotoxicity is seen in 20-30% of patients.[3] These toxic effects caused by Cis may occur due to inflammation, oxidative stress, and apoptosis.[1,2] When Cis is taken into the cell, it becomes positively charged and it binds to DNA, RNA, and proteins. By binding to purine bases, it prevents DNA replication and transcription by causing structural defects in the form of single, intra-chain cross-links and inter-chain cross-links. The cell cycle is arrested in the G2 phase and apoptosis occurs.[4] Cell and tissue damage caused by increased reactive oxygen species (ROS) due to Cis can be reduced by substances with high antioxidant potential, such as silymarin, gallic acid, selenium, and vitamin E.[5-7] Since Cis is

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excreted through the kidneys, the structural changes in the kidneys due to the drug are evident. Studies have shown kidney damage such as tubular damage, cytoplasmic vacuole formation, cell degeneration, and mononuclear cell infiltration after Cis injection.[8,9]

Ambroxol (Amb) is an agent used in mucus-related respiratory diseases with a mucolytic effect. Surfactant facilitates mucus outflow by regulating protein production and increasing ciliary movement.[10] It has also been reported to have antioxidant and anti-inflammatory effects.[11,12] Bishr et al.[13] demonstrated the positive effect of ambroxol on the kidneys in Cis nephrotoxicity. Liu et al.[14] demonstrated that Amb alleviated kidney damage caused by cardiopulmonary bypass.

Coenzyme Q10 (CoQ10), also known as ubiquinone, is a lipid-soluble molecule that is primarily produced within the human body. It participates in the transfer of electrons and protons within the mitochondrial respiratory chain. Alongside Amb, it possesses antioxidant and anti-inflammatory qualities, shielding biomolecules interacting with reactive oxygen radicals and lipoperoxides.[15] Some studies suggest that CoQ10 may be effective in kidney damage caused by Cis.[16,17]

Although there are many studies on the effects of Cis on the kidney, there are few studies showing the protective effects of Amb and CoQ10.[13,15,16] In this study, the aim was to examine the possible protective effects of Amb and CoQ10 against the toxic effects of Cis on the kidneys, light microscopically, immunohistochemically, and biochemically.

MATERIALS AND METHODS

This study was approved by the Near East University Local Ethics Committee for Animal Experiments (approval number: 2020/11, date: 27.11.2020). Animals were kept in plastic cages at optimal temperature (22±1 °C) and in a 12-hour light, 12-hour dark environment. They were provided with water and feed ad libitum throughout the experiment.

Drugs

In the study, a cytotoxic drug containing 50 mg/100 mL Cis (Koçak-İstanbul), a mucolytic and expectorant drug containing 30 mg/5 mL Amb hydrochloric acid with the trade name Sekrol, and CoQ10 capsules containing 30 mg of active ingredient with the trade name Webber Naturals were used. We determined the doses of 50 mg/kg Amb and 10 mg/kg CoQ10 administered to the rats based on doses used in previous studies. In a study investigating Amb against Cis-induced hepatorenal toxicity, it was reported that doses of 35 and 70 mg/kg Amb reduced toxicity.[13] In another study, a protective effect of 50 mg/kg Amb was observed against acetaminophen-induced hepatotoxicity.[18]

The ameliorative effect of 10 mg/kg CoQ10 in reducing Cis-induced damage in various organs has been reported in numerous studies.[19] Taking these references into account, we used a 50 mg/kg dose of Amb and a 10 mg/kg dose of CoQ10 in our study.[20]

Animals and Experimental Design

Thirty-six female Wistar albino rats, each weighing approximately 250-300 grams, were used in the experiment. The investigation was conducted at a single center, utilizing a randomized, controlled, single-blind design (analyst remained blinded of the treatments assigned to the rats). The rats were divided into six groups; each containing six rats. Chemical agents were applied to the rats as shown in Table 1, and at the end of the 7th day, the rats were euthanized under anesthesia.

Collection of Blood and Tissue Samples

At the end of the experiment, all rats were sacrificed. Kidney tissue was taken from the subjects through an incision in their abdomen, for both biochemical and histopathological examinations. After samples were taken for biochemical analysis, erythrocytes were removed by perfusion with cold physiological saline (0.9% NaCl).[21] Subsequently, it was dried with filter paper and divided into two separate parts. Then, the specimen to be used for biochemical analyses was placed in sample containers filled with 50 mM phosphate buffer (pH 7.4).[22] Tissue pieces to be used for histological examination were fixed with 10% formaldehyde.

Measurement of TNF-α, an Inflammation Marker

TNF-α analysis, one of the pro-inflammatory cytokines, was measured with rat-specific ELISA test kits (ElabScience, Cat. No: EEL-R0019, Lot No: UQC179VSYP) using blood samples and tissue homogenates. The manufacturers' instructions were followed to perform the assay. MW-12A Microplate Washer and MR-96 Microplate Reader (Mindray, Shenzhen, China) were used during assay procedures. The results were given as pg/mL in plasma and pg/mg protein in tissues.

Determination of Lipid Peroxidation Level

Malondialdehyde (MDA), the most stable lipid peroxidation product, was measured in blood samples and tissue homogenates. Cayman brand test kit (Cat. No: 10009055, Lot No: 613569) was used for MDA analysis. The test was performed using the spectrophotometric method

Table 1. The timeline illustrates the schedule of drug administrations and the sacrifice day across all groups during the 7-day experimental period

Day	0	1	2	3	4	5	6	7
Control (C)	Saline i.p.	-	-	-	-	-	-	-
Cisplatin (Cis)	-	Cis i.p. (7 mg/kg)	-	-		-	-	-
Ambroxol (Amb)	-	Amb p.o. (50 mg/kg, BID)	Amb p.o. BID	Amb p.o. BID	Amb p.o. BID	Amb p.o. BID	Amb p.o. BID	Amb p.o. BID
Coenzyme Q10 (CoQ10)	-	CoQ10 p.o. (10 mg/kg, BID)	CoQ10 p.o. BID	CoQ10 p.o. BID	CoQ10 p.o. BID	CoQ10 p.o. BID	CoQ10 p.o. BID	CoQ10 p.o. BID
Cis + Amb	-	Cis i.p. + Amb p.o. (50 mg/kg, BID)	Amb p.o. BID	Amb p.o. BID	Amb p.o. BID	Amb p.o. BID	Amb p.o. BID	Amb p.o. BID
Cis + CoQ10	-	Cis i.p. + CoQ10 p.o. (10 mg/kg, BID)	CoQ10 p.o. BID	CoQ10 p.o. BID	CoQ10 p.o. BID	CoQ10 p.o. BID	CoQ10 p.o. BID	CoQ10 p.o. BID
Sacrifice								Day 7

i.p.: Intraperitoneal injection, p.o.: Oral gavage, BID: Twice daily administration

based on the reaction with thiobarbituric acid at 100 °C in an acidic environment and measuring the absorbance of the reaction mixture at 530-540 nm.[23] The results were given as nmol/mL in plasma and nmol/mg protein in tissues.

Histological Procedures

The fixed tissues were passed through a tissue tracking device (Leica TP1020, Leica Biosystems Nussloch GmbH, Germany) and embedded in paraffin (Leica EG1150 H).[5] µm thick sections were taken with a microtome device (Leica RM2255), and H&E (Bancroft and Gamble 2008) staining was performed. Histomorphological examination of the sections was performed with a light microscope (Leica DM500) coupled with the Leica Microsystem Framework integrated digital imaging analysis system (Leica Application Suite version 3.0 Series 38132019 Leica ICC50 HD). Kidney tissue sections were evaluated in terms of glomerular damage, tubular damage, and mononuclear cell infiltration criteria. For each criterion, 10 different areas were scored as none (0), mild (1), moderate (2), and severe (3).[24] A mouse and rabbit-specific HRP/DAB (ABC) Detection IHC kit (ab64264) and a primary antibody, caspase-3 (ab4051), diluted 1:100, were used for immunohistochemical staining. Caspase-3 positivity in kidney tissue was evaluated using the ImageJ program.

Statistical Analysis

SPSS (IBM SPSS statistical version 26.0) software (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. Data groups were compared using Kruskal-Wallis analysis followed by Mann-Whitney U tests. A $p<0.05$ difference was considered statistically significant.

RESULTS

Biochemical Results

The values of kidney serum urea, creatinine, TNF-α, and MDA, along with kidney tissue TNF-α and MDA, are presented in Tables 2-4.

Urea and creatinine levels, which indicate kidney function, were at normal levels in the control groups. When the values in Table 2 were examined, it was evident that the urea level in the group given only Amb was lower than that of the control group ($p<0.05$). Creatinine values were similar in the control, Amb, and CoQ10 groups. The Cis group experienced the most kidney damage. Urea and creatinine values were significantly higher than those of the other groups ($p<0.05$). Urea and creatinine levels decreased in the cis + Amb group. Although no decrease comparable to that caused by Amb was observed in the Cis + CoQ10 group, urea and creatinine values were observed to decrease.

When the serum MDA levels in Table 3 are examined to evaluate the lipid peroxidation levels of the experimental groups, the control groups are observed to have the lowest MDA values. The Cis group had the highest MDA value, and a statistical difference was observed between this group and all other groups ($p<0.05$). It has been determined that the antioxidant effects of Amb and CoQ10 compound reduce the level of MDA, which is a product of oxidative damage. Serum TNF-α values, one of the inflammation markers, were observed at lower levels in the control groups than in the Cis group ($p<0.05$). The Cis group had the highest TNF-α value. TNF-α value in the Cis + Amb and Cis + CoQ10 groups was lower compared to the Cis group ($p<0.05$). Amb and CoQ10 reduced Cis-induced inflammation (Table 3). Although no significant difference was detected between the Cis + Amb and Cis + CoQ10 groups, as seen in Table 3 ($p>0.05$), Amb was descriptively more effective in reducing TNF-α serum levels than CoQ10.

In terms of TNF-α levels measured in kidney tissue, the group with the highest TNF-α value among all groups was the Cis group. Statistical

Table 2. The rat blood sample parameters that reflect kidney damages. Results are represented as mean ± SD (n=6)

Mean ± SD	Biochemistry Parameters	
	Urea (mg/dL)	Creatinine (mg/dL)
Control	47.50±7.12^{a}	0.538±0.061^{h}
Ambroxol	31.83±3.25^{b,c,d}	0.551±0.047^{i}
Coenzyme Q10	42.66±6.28^{e}	0.550±0.037^{j}
Cisplatin	586.83±135.62^{a,b,e,f,g}	6.608±1.27^{h,i,j,k,l}
Cis + Amb	71.83±49.04^{c,f}	0.850±0.513^{k}
Cis + CoQ10	100.50±81.93^{d,g}	1.001±0.689^{l}
p values	0.000***	0.002**

The letters used in the table indicate statistically significant differences between groups. Groups not sharing the same letter have a significant difference at the p<0.05 level. Differences among control groups are excluded from this evaluation.
SD: Standard deviation, Cis: Cisplatin, Amb: Ambroxol, CoQ10: Coenzyme Q10.

Table 3. The rat blood sample parameters that reflect kidney damages. Results are represented as mean ± SD (n=6)

Mean ± SD	Serum TNF-α and MDA parameters	
	Serum TNF-α (pg/mL)	Serum MDA (nmol/mL)
Control	1253.60±234.42^{a}	41.41±17.61^{h,i,j}
Ambroxol	1265.90±377.91^{b}	39.41±19.18^{k,l,m}
Coenzyme Q10	1038.03±222.98^{c,d,e}	50.38±22.26^{n,o,p}
Cisplatin	3124.01±441.71^{a,b,c,f,g}	240.77±22.16^{h,k,n,r,s}
Cis + Amb	1633.03±437.04^{d,f}	185±22.26^{i,l,o,r}
Cis + CoQ10	1877.41±6^{e,g}	181.79±33.67^{j,m,p,s}
p values	0.001**	0.000***

The letters used in the table indicate statistically significant differences between groups. Groups sharing the same letter have a significant difference at the $p < 0.05$ level. Differences among control groups are excluded from this evaluation.
SD: Standard deviation, Cis: Cisplatin, Amb: Ambroxol, CoQ10: Coenzyme Q10, MDA: Malondialdehyde.

Table 4. The rat tissue sample parameters that reflect kidney damages. Results are represented as mean ± SD (n=6)

Mean ± SD	TNF-α and MDA parameters	
	Kidney TNF-α (pg/mg)	Kidney MDA (nmol/mg)
Control	20.14±16.73^{a,b,c}	2.15±1.05^{i,j,k}
Ambroxol	38.97±19.47^{d,e}	4.03±2.06^{l,m,n}
Coenzyme Q10	45.23±40.09^{f}	4.52±2.86^{o,p,r}
Cis	207.95±67.33^{a,d,f,g,h}	18.45±5.00^{i,l,o,s,t}
Cis + Amb	86.33±34.40^{b,e,g}	10.08±3.80^{j,m,p,s}
Cis + CoQ10	59.20±31.98^{c,h}	11.24±4.73^{k,n,r,t}
p values	0.000***	0.002**

The letters used in the table indicate statistically significant differences between groups. Groups sharing the same letter have a significant difference at the p<0.05 level. Differences among control groups are excluded from this evaluation.
SD: Standard deviation, Cis: Cisplatin, Amb: Ambroxol, CoQ10: Coenzyme Q10, MDA: Malondialdehyde.

significance was observed between the Cis group and all other groups ($p<0.05$). According to the data in Table 4, no statistical difference was observed between the Cis + CoQ10 group and the cis+amb group ($p>0.05$). However, the TNF-α value decreased more in the Cis + CoQ10 group compared to Cis + Amb. The MDA value, in Table 4, which shows lipid peroxidation in kidney tissue, was again detected at the highest level in the Cis group. The MDA value statistically significantly decreased in the Amb and CoQ10 treatment group compared to the Cis group ($p<0.05$).

Histomorphological Results

Kidney tissues from all experimental groups were evaluated under light microscopy, and the histological scoring results are summarized in Table 5.

When the histomorphological scoring data in Table 5 are examined, it is evident that the renal tissues in the Cis group exhibit higher levels of tubular necrosis, glomerular damage, and mononuclear cell infiltration. A statistically significant difference was observed between the Cis group and the control group ($p<0.05$). Cis + Amb or Cis + CoQ10 reduced the extent of renal damage compared to the Cis group. According to the data in Table 5, the Cis + Amb group significantly decreased tubular necrosis, and glomerular damage relative to the Cis group ($p<0.05$).

Under light microscopy, the control groups had a normal structure (Figure 1A). Vacuolization and degeneration in tubule cells, and intertubular and interglomerular hemorrhage foci were observed in the kidney tissue of the Cis group (Figure 1B). In some regions, it was found that the glomerulus spaces in the corpusculum renis completely disappeared (Figure 1C), and mononuclear cell infiltration was observed around the corpusculum renis (Figure 1D). It was determined that hemorrhage foci continued to be present in the tissue sections of the Cis + Amb and Cis + CoQ10 groups, but their amount decreased compared to the Cis group (Figures 1E, F).

Table 5. Scores of kidney histomorphological measurements in the rat groups. Results are represented as mean ± SD (n=6)

Mean ± SD	Histomorphological scoring criteria of the kidney		
	Tubular necrosis	Glomerular damage	Mononuclear cell infiltration
Control	$0.033\pm0.051^{a,b,c}$	$0.033\pm0.051^{k,l}$	$0.167\pm0.0408^{s,t,u}$
Ambrokxol	$0.050\pm0.054^{d,e,f}$	$0.000\pm0.000^{m,n,o}$	$0.050\pm0.054^{v,w,x}$
Coenzyme Q10	$0.066\pm0.051^{g,h,ı}$	0.083 ± 0.075^{p}	$0.050\pm0.083^{y,z,a}$
Cisplatin	$0.783\pm0.440^{a,d,g,j}$	$0.633\pm0.294^{k,m,p,r}$	$0.366\pm0.242^{s,v,y}$
Cis + Amb	$0.266\pm0.136^{b,e,h,j}$	$0.200\pm0.178^{n,r}$	$0.316\pm0.213^{t,w,z}$
Cis + CoQ10	$0.500\pm0.340^{c,f,ı}$	$0.283\pm0.306^{l,o}$	$0.333\pm0.081^{u,x,a}$
p values	0.000***	0.000***	0.000***

The letters used in the table indicate statistically significant differences between groups. Groups sharing the same letter have a significant difference at the $p<0.05$ level. Differences among control groups are excluded from this evaluation.
SD: Standard deviation, Cis: Cisplatin, Amb: Ambroxol, CoQ10: Coenzyme Q10.

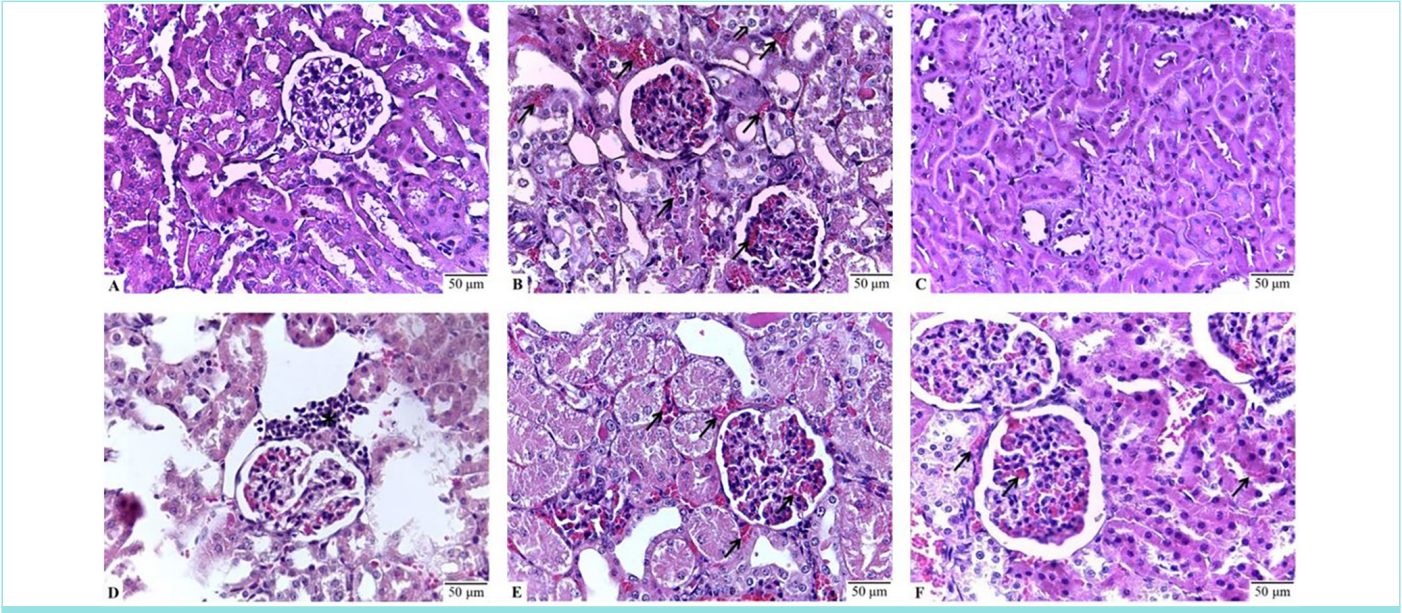

Figure 1. H&E stained light microscopic images of the experimental groups. Normal kidney tissue from the control group (Figure 1A) can be observed. In the cisplatin group, intertubular and interglomerular hemorrhage (➔), vacuolization of tubule epithelial cells (⇒) (Figure 1B), disappearance of the space between Bowman's capsule and glomeruli (Figure 1C), and mononuclear cell infiltration (*) (Figure 1D) are observed. It is observed that intertubular and interglomerular hemorrhage decreased in the Cis + Amb (Figure 1E) and Cis + CoQ10 (Figure 1F) groups.

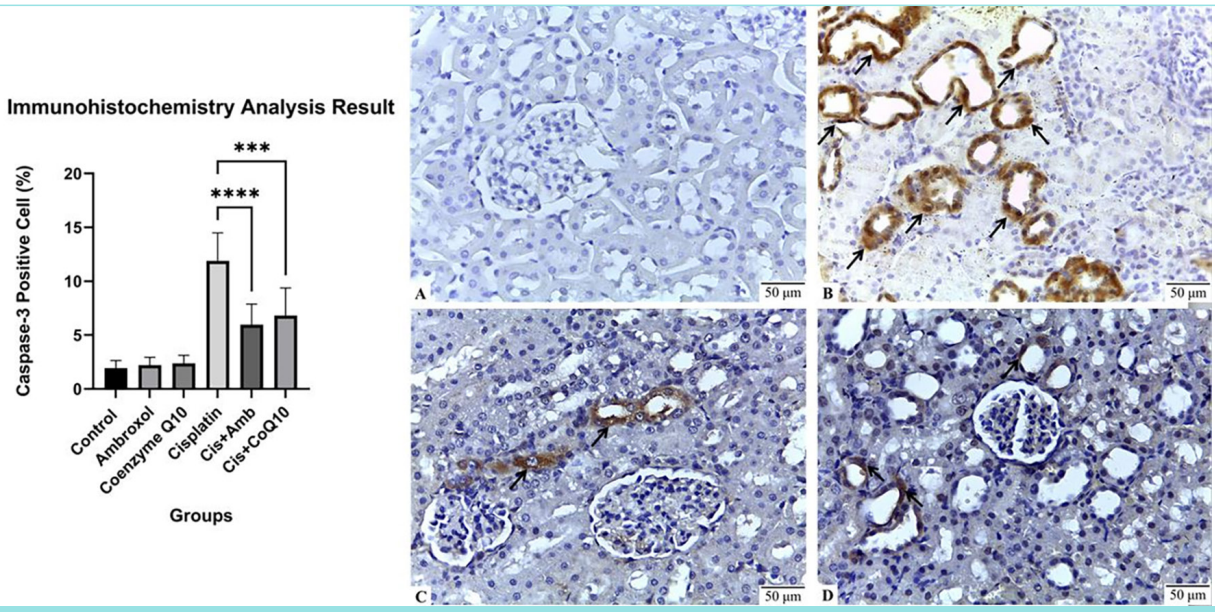

Figure 2. Evaluated by measuring stained area percentage on image J software. Light microscopic images of the experimental groups stained with caspase-3 are also shown. Cas-3 expression is not observed in the control (Figure 2A) group. It is observed that caspase-3 expression is increased in tubule epithelial cells in the cisplatin group (➔) (Figure 2B), while it is decreased in the Cis + Amb, (Figure 1C), and Cis + CoQ10 (Figure 2D) groups.

In the immunohistochemical caspase-3 staining performed for apoptotic cell evaluation, the highest expression was observed in the Cis group (Figure 2B). A statistical difference was detected between the Cis group and the other groups ($p<0.05$). Cas-3 expression was significantly reduced in the groups treated with Cis + Amb and Cis + CoQ10 compared to Cis (Figure 2C, D). There was no statistically significant difference between "Cis + Amb" and "Cis + CoQ10" in reducing the number of caspase-3 positive cells, although Amb showed a numerically greater effect than CoQ10 ($p>0.05$) (Figure 2).

DISCUSSION

Cis remains one of the most widely used anticancer drugs today, even though it has considerable side effects that endanger the patient's life.[5] The kidneys are particularly affected by Cis, resulting in inhibition of their functions and serious tissue damage. Ongoing investigations seek to prevent and mitigate Cis's toxic effects.[25,26] This study evaluated the histomorphological and biochemical protective effects of Amb and CoQ10 against Cis toxicity in kidney tissue. The protective effects were quantified and analysed. Cis administered as a single intraperitoneal dose of 7 mg/kg caused kidney damage in rats. It has been shown that kidney damage can be reduced by giving twice daily Amb at 50 mg/kg and CoQ10 at 10 mg/kg. Amb, one of the drugs we tested in the study, is an agent used as a mucolytic. In the studies, its antioxidant properties and protective effects on tissue have been shown. Recently, the presence of a protective effect on renal tissue has been suggested in both experimental and clinical studies. In a clinical study conducted in China, it was emphasized, that the administration of Amb before cardiopulmonary bypass reduced renal damage in children.[14] The protective effect of Amb in rats with renal ischaemia-reperfusion injury was suggested both biochemically and histopathologically.[27] CoQ10 is also known to have a protective effect on kidney tissue in both experimental and clinical studies.[28,29]

Cis hinders the mitochondrial respiratory complex, leading to elevated ROS. Elevated levels of ROS inhibit the antioxidant system, leading to oxidative stress, lipid peroxidation, alterations in cell fluidity and permeability, and disruptions in gene expression, consequently inducing cell death.[30,31] Cis initially increases serum urea and creatinine levels in kidney tissue.[32,33] Consistent with prior research, our study identified a marked elevation in urea and creatinine concentrations in the Cis-treated group, indicative of impaired kidney function. Amb and CoQ10 were effective in reducing increased urea and creatinine values. Bishr et al.[13] administered Amb intraperitoneally to rats at two different doses (35 and 75 mg/kg), Fouad et al.[16] administered CoQ10 to mice intraperitoneally at a dose of 10 mg/kg. In this study, Amb was administered at a dose of 50 mg/kg and CoQ10 at a dose of 10 mg/kg, via oral gavage.

Cellular damage caused by Cis is associated with an increase in inflammation due to the secretion of TNF-α.[34] TNF-α, a pro-inflammatory cytokine, ensures the mobilization and activation of further leukocytes.[35] In our study, inflammation caused by Cis was evidenced by measuring TNF-α from both serum and tissue. Amb and CoQ10, administered to counteract the effects of Cis on inflammation, mitigated acute kidney injury by reducing TNF-α levels. Dupre et al.[36] and Deng et al.[37] demonstrated the positive effects of anti-inflammatory agents against the kidney toxicity of Cis. Gültekin et al.[27] showed that Amb was effective in reducing the TNF-α level in the ischemia reperfusion model created in kidney tissue. Mirmalek et al.[38] reported that CoQ10 reduced inflammation in experimental acute pancreatitis.

MDA is an indicator of lipid peroxidation, disrupts membrane permeability in the cell, causes protein denaturation, and leads to the destruction of important antioxidant enzymes such as catalase. Cis increases MDA levels by causing lipid peroxidation in cells.[39] In this study in which Cis toxicity was established, it was observed that the MDA level in serum and kidney tissue increased significantly, and that Amb

and CoQ10 were effective in reducing lipid peroxidation in the groups treated with Amb and CoQ10. In a study in which hepatic ischemia and reperfusion were performed, it was reported that Amb reduced MDA levels.[40] In another study, Hossain et al.[41] reported that CoQ10 reduced the MDA increase caused by carbofuran.

Cis activates TNF-α in the kidneys, increasing inflammation and attracting leukocytes to the area. In the light microscopic examination results of our study, it was observed that Cis increased the number of inflammatory cells and that Bowman spaces narrowed. Intertubular congestion increased, and there was degeneration and epithelial shedding in tubule cells in some places. Amb and CoQ10 reduced mononuclear cell infiltration, although they did not completely prevent tubular and glomerular damage. Several studies corroborate our findings.[16,27,37]

Apoptosis is observed in tubule cells as a result of the toxic effect of Cis on the kidney.36 Cis binds to apoptotic protease activating factor-1 after cytochrome C passes into the cytosol in cells. This resulting complex activates procaspase-9. Caspase-9 also activates other caspases (3, 6, 7).[32] Caspase-3 is an enzyme that completely destroys cells by causing the proteins that form the cytoskeleton and the DNA to break down.[31] Bish et al.[13] biochemically demonstrated that Amb reduced the caspase-3 increase caused by Cis. In this study, the effect of Cis on the increase in caspase-3 expression was demonstrated by immunohistochemical staining. It was observed that Cis increased apoptosis, especially in kidney tubule epithelial cells, and CoQ10 decreased it. In a study on CoQ10 against the acute liver toxicity of acetaminophen, CoQ10 was found to be effective in reducing the amount of caspase-3.19 The reducing effect of CoQ10 on caspase-3 has been reported in acute nephrotoxicity caused by Cis in mice.[16]

Study Limitations

In this study, some markers of inflammation could not be examined immunohistochemically. In addition, the gene expression of these molecules could not be examined and compared.

CONCLUSION

The present study aimed to investigate the potential of Amb and CoQ10 to mitigate experimentally induced Cis nephrotoxicity. Results showed elevated levels of urea and creatinine, indicative of impaired renal function, as well as heightened values of TNF-α and MDA, markers of inflammation and lipid peroxidation, in Cis-administered rats. In addition, light microscopy revealed tubular degeneration, congestion-hemorrhage, and increased apoptotic cell death. Cis toxicity was reduced in groups treated with Amb and CoQ10, but was not entirely prevented. Biochemical and histomorphological analysis indicates that Amb is more effective at reducing damage than CoQ10. Further investigation into the effects of various doses and durations of Amb and CoQ10 on Cis toxicity at the molecular level will yield more detailed information.

MAIN POINTS

- Cisplatin (Cis) treatment causes significant kidney damage, leading to increased inflammation and oxidative stress markers (TNF-α, malondialdehyde) in serum and tissue.
- Ambroxol (Amb) and coenzyme Q10 (CoQ10) significantly reduce Cis-induced kidney injury both biochemically and histologically.
- Caspase-3 expression, an indicator of apoptotic cell death, is decreased in groups treated with Amb and CoQ10, contributing to kidney tissue protection.

ETHICS

Ethics Committee Approval: This study was approved by the Near East University Local Ethics Committee for Animal Experiments (approval number: 2020/11, date: 27.11.2020).

Informed Consent: Since the study was conducted on animals, informed consent is not required.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.Ş., N.G., S.S., A.Ö.Ş., A.K., Concept: H.Ş., N.G., S.S., A.Ö.Ş., A.K., Design: H.Ş., N.G., S.S., A.Ö.Ş., A.K., Data Collection and/or Processing: H.Ş., N.G., S.S., A.Ö.Ş., A.K., Analysis and/or Interpretation: H.Ş., N.G., S.S., A.Ö.Ş., A.K., Literature Search: H.Ş., Writing: H.Ş.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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RESEARCH ARTICLE

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Awareness of Asthma and COPD Among Healthcare and Support Staff in Hospitals in TRNC

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Abstract

BACKGROUND/AIMS: With the increasing prevalence of chronic respiratory diseases worldwide, the likelihood of healthcare personnel encountering these patients has also risen. The purpose of this study is to determine the awareness of chronic obstructive pulmonary disease (COPD) and asthma among staff working in hospitals in North Cyprus.

MATERIALS AND METHODS: A survey was administered to staff in 4 hospitals. In addition to demographic data, the survey consisted of 22 questions related to COPD and asthma, which were part of the GARD-Türkiye Project established by the Turkish Ministry of Health in 2013. The data were analyzed using appropriate statistical methods.

RESULTS: A total of 316 personnel from 4 hospitals participated in the study. The age range was 18-59 years (36±9.82 years), and the average duration of work was 11.35±9.53 years. The group with more than 10 years of work experience had a lower awareness that COPD is seen in individuals over 40 years of age compared to other groups (p=0.008). Additionally, this group had a stronger belief that asthma medications cause addiction (p=0.035). When examining doctors, nurses, paramedics, and technicians as the "healthcare workers group" and auxiliary health staff and clerks as the "other group," it was found that neither group had sufficient knowledge that COPD is a disease affecting individuals over 40 years. Regarding whether COPD is a treatable disease, 46.2% (98) of healthcare workers responded "yes," while 43.9% (93) answered "no". In general, the level of knowledge about COPD and asthma was higher in the healthcare workers group.

CONCLUSION: Although the study population is quite heterogeneous and has a low participation rate from doctors, it is thought to represent hospital workers well. Awareness about asthma and COPD is low. In particular, the group with a longer duration of work was less aware of these two diseases than other groups. We believe that hospital staff should receive in-service training on these diseases at regular intervals.

Keywords: COPD, asthma, awareness, healthcare workers

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INTRODUCTION

Chronic respiratory diseases are a significant burden on health systems worldwide. These conditions, specifically asthma and chronic obstructive pulmonary disease (COPD), account for the vast majority (65%) of chronic respiratory illnesses. Nearly half a billion people live with asthma and COPD, and these two diseases cause approximately 4 million deaths each year.[1] The prevalence of chronic respiratory diseases is expected to increase in the coming years due to changes in the age structure of populations and rising smoking rates, especially in developing countries. Therefore, the likelihood of healthcare workers encountering these patients is also increasing.

COPD is a preventable and treatable disease characterized by airflow limitation that is not fully reversible.[2] This airflow limitation is usually progressive and is associated with an abnormal inflammatory response in the lungs to harmful particles and gases.[2] Today, COPD is defined as a preventable and partially treatable disease, particularly affecting adults aged 40 and older.[2] COPD is a significant and increasingly prevalent cause of morbidity and mortality worldwide. Currently, COPD ranks third among the leading causes of death from chronic diseases.[1] However, the disease is not sufficiently recognized, often underdiagnosed, misdiagnosed, and undertreated. The lack of awareness and diagnosis of COPD has led to inadequate reporting of the disease. Consequently, there have been significant differences in data related to the disease burden across countries, depending on awareness among healthcare personnel, the organization of healthcare services for chronic diseases, and the availability of medications for COPD.[3]

Asthma, another chronic airway disease like COPD is characterized by chronic airway inflammation and airflow limitation. The chronic inflammation in asthma is associated with airway hyperresponsiveness, which leads to recurrent episodes of wheezing, shortness of breath, chest tightness, and coughing, particularly at night or in the early morning.[4] It can occur in individuals of all ages and in all geographical regions. According to the World Health Organization (WHO), it is estimated that 350 million people worldwide have asthma, and more than 400,000 asthma-related deaths occur globally each year.[1] It has been stated that the causes of death are largely preventable, often due to a lack of access to healthcare during acute episodes and inadequate long-term medical treatment.[5] Asthma is a disease with a high economic burden, but in developed countries, diagnostic and treatment programs have reduced costs.

Due to the mortality, morbidity, and economic burden caused by chronic diseases worldwide, the WHO has made an urgent call to action for the prevention and control of chronic diseases. As part of this effort, the "Global Alliance Against Chronic Respiratory Diseases (GARD)" was established.[1,6,7] A study on chronic airway diseases conducted within the framework of the Turkish National GARD Program revealed that asthma and COPD are not well known in Türkiye.[8] In our country, there are no scientific data regarding asthma and COPD awareness, either among the general population or healthcare workers. The aim of this study is to investigate asthma and COPD awareness among hospital staff.

MATERIALS AND METHODS

This is a questionnaire study. This study was approved by the Ethics Committee of Dr. Burhan Nalbantoğlu State Hospital (approval number: YT.1.01, date: 25.05.2020), with personnel working at one university hospital and three state hospitals. The questionnaire, in addition to collecting demographic data, consisted of 22 questions related to COPD and Asthma, determined by the Turkish Ministry of Health in 2013 as part of the GARD-Türkiye Project.

A total of 500 personnel were approached, and 316 agreed to participate in the survey.To ensure representation of both healthcare workers and the general population, personnel from each department were included. Doctors, nurses, paramedics, technicians, other auxiliary healthcare staff, and administrative personnel were involved in the study. The personnel who agreed to participate were divided into two groups based on the unit they worked in: the health field workers group (HFG) and the other field workers group (OFG). The HFG group consisted of personnel who directly interacted with patients, such as doctors, nurses, and paramedics. The OFG group consisted of personnel who did not directly interact with patients, such as technicians, other auxiliary healthcare staff, and administrative personnel.

Additionally, data analysis was performed based on the length of service at the institution. Personnel were categorized into three groups: those with 0-5 years of service, those with 6-10 years of service, and those with more than 10 years of service.

Inclusion criteria are being employed at a hospital, being over 18 years old, and agreeing to complete the survey. Exclusion criteria include being under 18 years old and refusing to participate in the study.

Statistical Analysis

The analysis was performed using SPSS 27. The Kolmogorov-Smirnov test was applied to assess normality. Descriptive statistics were used to calculate the frequency and percentage for categorical data or the mean and standard deviation for continuous data. The chi-square test was used to compare categorical variables between two independent groups, whereas the Kruskal-Wallis test was used to compare non-parametric data among more than two independent groups. A statistical significance level of $p<0.05$ was accepted.

RESULTS

The questionnaire participation rate is 63.2%. Three hundred sixteen staff from four hospitals participated in the study. Of the participants, 71.2% (n=225) were female and 28.2% (n=89) were male. Of these, 64 (20.3%) were physicians, 107 (33.9%) were nurses, 19 (6%) were paramedics, 23 (7.3%) were technicians, 61 (19.3%) were other auxiliary healthcare staff, and 41 (13%) were civil servants. The range of age is 18-59 (36±9.82) years, average service period is 11.35±9.53 years. The majority of the study population consisted of those with less than 5 years of work experience (40.6%) and those with more than 10 years of experience (41.8%). All demographic data are shown in Table 1.

In total, 16 questions were asked to evaluate the level of knowledge about COPD (8 questions) and asthma (8 questions). The answers were examined separately according to both staff categorization (HFG and other group) and working period (0-5 years, 6-10 years, and 11 years and over).

Evaluation of Knowledge About Chronic Obstructive Pulmonary Disease

Answers to questions regarding knowledge of COPD are shown in Table 2. When the groups were compared according to the field of work, the following results were obtained: the vast majority of both groups knew that COPD is a lung-related disease and that smoking is the biggest risk

Table 1. Demographic features of participants		
		n (%)
Age (year) (mean ± SD)	36±9.82	
Sex	Male	225 (71.2)
	Female	89 (28.2)
Smoking status	Yes	114 (36.1)
Comorbitiy	Yes	59 (18.7)
Type of service to the institution	Physician	64 (20.3)
	Nurse	107 (33.9)
	Paramedic	19 (6)
	Technician	23 (7.3)
	Other auxiliary health personnel	61 (19.3)
	Officer	41 (13)
Duration of service to the institution	Mean 11.35±9.53	
	0-5 years	125 (40.6)
	6-10 years	51 (16.6)
	>11 years	132 (41.8)
Type of isnstitution	State hospital	230 (72.8)
	University hospital	86 (27.2)

SD: Standard deviation.

factor (p=0.230, p=0.364, respectively). In both groups, the majority mistakenly believed that COPD is a disease of young adults (HFG 84.9%, OFG 65.7%). The proportion of those who believed that COPD can occur at any age was higher in the OFG (29.3%). The proportion of those who thought that COPD is a disease seen after the age of 40 was higher in the OFG group (5.1% vs. 1.4%). The age at which COPD is observed was statistically significant between the two groups (p<0.001). 84% of the HFG group and 68.9% of the OFG group believed that cough, sputum, and shortness of breath symptoms occur together in COPD (p=0.019). 43.9% of the HFG group and 29.4% of the OFG group believed that COPD is an incurable disease (p=0.001). The proportion of those who thought COPD is treatable was similar in both groups (HFG: 46.2%, OFG: 46.1%). Most individuals in both groups knew that the first step in preventing and treating COPD is quitting smoking (p=0.298). The proportion of those who knew that spirometry is required to diagnose COPD was higher in the HFG (75% vs. 53.5%, p<0.001).

When the responses to the questions were analyzed according to the length of service, the awareness that COPD is a lung-related disease and that smoking is the most important cause was similar in all three groups (p=0.341, p=0.265, respectively). Those with more than 10 years of service tended to believe that COPD is frequently seen in young adults (84.1%). The proportion of those who believed that COPD can occur at any age was higher in the groups with 0-5 and 6-10 years of service (20.8%, 21.5%, respectively). The percentage of individuals who believe that COPD is a disease seen after the age of 40 was zero in the group with more than 10 years of service, while it was around 4% in the other groups (p=0.008).

In all three groups, the majority believed that all symptoms would be present in COPD (p=0.757). The responses to the question of whether COPD is a treatable disease were similar, with no statistical significance (p=0.428). The most frequently given answer in all groups for preventing and treating COPD was quitting smoking (94.4%, 96%, 95.5%, respectively, p=0.998). The proportion of those who knew that spirometry is required to diagnose COPD was lowest in the group with 0-5 years of service (58.4%) and highest in the group with more than 10 years of service (80%), with statistically significant differences between the responses of the three groups (p=0.001).

Evaluation of Knowledge About Asthma

Answers to questions regarding knowledge of asthma are shown in Table 3. When groups were compared according to the field of work, the following results were obtained: 95.2% of the HFG group and 87.3% of the OFG group believed that asthma is not a contagious disease, but 11.8% of the OFG had no opinion on this (p=0.002). 70.4% of the HFG and 58.8% of the OFG knew that asthma could be hereditary, although 21.4% in the HFG thought asthma could not be hereditary, and 23.5% of the OFG had no opinion on the matter (p=0.001). 80.4% of the HFG believed that all symptoms could be present in asthma, while this rate was 57.8% in the OFG (p<0.001). The response indicating that asthma can occur at any age was similar in both groups (HFG: 90.9%, OFG: 95.1%, p=0.258). The proportion of those who knew that asthma treatment is administered via inhalation was similar in both groups (HFG: 98.1%, OFG: 93.1%, p=0.061). The belief that asthma medications do not cause addiction was higher in the HFG (58.1%), while 54.9% of the OFG had no opinion (p<0.001). 69.9% of the HFG believed that asthma cannot be completely cured, while 33.3% of the OFG had no opinion (p<0.001).

When the groups were compared according to the length of service, the rates of knowing that asthma is not contagious, that it can be hereditary, that it can occur at any age, and that treatment is administered via inhalation were similar in all three groups (p=0.293, p=0.331, p=0.246, p=0.131, respectively). 64.8% of those with 0-5 years of service; 78.4% of those with 6-10 years of service; and 75.6% of those with more than 10 years of service believed that all symptoms of asthma could be present.

Table 2. Comparison of knowledge about COPD according to groups

Questions	Health field workers group (n=213)	Other field workers group (n=103)	p	0-5 years (n=125)	6-10 years (n=51)	>11 years (n=132)	p
COPD is a lung-related disease			0.230				0.341
Yes	210 (98.6%)	99 (96.1%)		121 (96.8%)	51 (100%)	130 (98.5%)	
No	0 (0)	1 (1%)		1 (0.8%)	0 (0)	0 (0)	
No idea	3 (1.4%)	3 (2.9%)		3 (2.4%)	0 (0)	2 (1.5%)	
The most important etiological factor of COPD is smoking			0.364				0.265
Yes	206 (96.7%)	96 (93.2%)		117 (93.6%)	50 (98%)	128 (97%)	
No	3 (1.4%)	3 (2.9%)		2 (1.6%)	1 (2%)	2 (1.5%)	
No idea	4 (1.9%)	4 (3.9%)		6 (4.8%)	0 (0)	2 (1.5%)	
In which age group is COPD more common?			<0.001				0.008
Childhood period	3 (1.4%)	0 (0)		0 (0)	0 (0)	3 (2.3%)	
Young adults	180 (84.9%)	65 (65.7%)		90 (72)	38 (74.5%)	111 (84.1%)	
Over 40 years old	3 (1.4%)	5 (5.1%)		6 (4.8%)	2 (4%)	0 (0)	
At any age	26 (12.3%)	29 (29.3%)		26 (20.8%)	11 (21.5%)	16 (12.1%)	
What are the complaints of a COPD patient?			0.019				0.757
Cough	2 (0.9%)	1 (1%)		1 (0.8%)	0 (0)	2 (1.5%)	
Phlegm	2 (0.9%)	2 (1.9%)		1 (0.8%)	0 (0)	3 (2.3%)	
Dyspnea	30 (14.1%)	29 (28.2%)		24 (19.2%)	9 (17.6%)	24 (18.2%)	
All	179 (84%)	71 (68.9%)		99 (79.2%)	42 (82.4%)	103 (78%)	
Is COPD a treatable disease?			0.001				0.428
Yes	98 (46.2%)	47 (46.1%)		64 (51.2%)	20 (39.2%)	58 (44%)	
No	93 (43.9%)	30 (29.4%)		42 (33.6%)	23 (45.1%)	57 (43.2%)	
No idea	21 (9.9%)	25 (24.5%)		19 (15.2%)	8 (15.7%)	14 (10.6%)	
The first step in preventing and treating COPD is to quit smoking or stay away from smoking environments			0.298				0.998
True	205 (96.7%)	94 (93.1%)		118 (94.4%)	49 (96%)	126 (95.5%)	
False	3 (1.4%)	2 (2%)		3 (2.4%)	0 (0)	2 (1.5%)	
No idea	4 (1.9%)	5 (5%)		4 (3.2%)	2 (4%)	4 (3%)	
Which test is required to diagnose COPD?			<0.001				0.001
Blood tests	2 (0.9%)	2 (2%)		2 (1.6%)	0 (0)	2 (1.5%)	
Spirometry	159 (75%)	54 (53.5%)		73 (58.4%)	32 (62.7%)	105 (80%)	
Chest X-ray	51 (24.1%)	41 (40.6%)		47 (37.6%)	17 (33.3%)	23 (17.4%)	
Sputum culture	0 (0)	4 (4%)		1 (0.8%)	2 (4%)	1 (0.8%)	
Have you been diagnosed with COPD by a physician?			0.076				0.760
Yes	3 (1.4%)	6 (5.9%)		3 (2.4%)	0 (0)	6 (4.5%)	
No	207 (97.2%)	94 (92.2%)		120 (96%)	51 (100%)	123 (93.2%)	
No idea	3 (1.4%)	2 (2%)		2 (1.6%)	0 (0)	3 (2.3%)	

COPD: Chronic obstructive pulmonary disease.

DISCUSSION

This study identified that asthma and COPD are not sufficiently understood among hospital staff in Turkish Republic of North Cyprus.

In a study conducted by Omotola[9] using the Bristol COPD Knowledge Questionnaire (BCKQ), COPD awareness among healthcare workers was found to be higher than in many other studies[10-12] but lower than in the study by White et al.[13] However, the BCKQ[13] is a questionnaire designed to assess the effectiveness of education, which means that participants are first educated about COPD, and then their knowledge is measured. The original sentence lacks sufficient context, making it difficult to refine while maintaining its intended meaning. Please provide additional information or context for accurate editing. Our study was designed to measure spontaneous knowledge and to develop an action plan based on the results.

In our study, the GARD questions, which are used to assess knowledge in the general population, were employed. Accordingly, both HFG and OFG participants were largely aware that COPD is a lung disease and that smoking is the biggest risk factor. In al.'s[8] study in the general population in Türkiye, using GARD questions, 50% of the population correctly identified COPD as a lung disease, and 51% identified smoking as the most important etiological factor.

The rate of awareness that spirometry is used to diagnose COPD was higher in the HFG group, which was expected. This is because individuals in the OFG group had not received any education about COPD during their lives, whereas those in the HFG group had received COPD education during their professional training. Both groups generally knew that smoking cessation is the first approach in the treatment. This may be due to the heavy emphasis on smoking and COPD in general media materials to date. Another reason might be that as the prevalence of COPD increases in society, hospital staff may encounter it more frequently within their own families.

Our study showed that as service duration increases, knowledge about COPD decreases. Particularly, the rate of knowing that COPD is a disease seen after the age of 40 was close to zero. This may have several reasons. First, they may have attributed COPD to all age groups, thinking of it as a general respiratory disease, like asthma. Second, their knowledge may not have been updated due to the lack of in-service training on COPD. Another possibility is that media materials intended for the public

Table 3. Comparison of knowledge about asthma according to groups

Sorular	Health field workers group (n=213)	Other field workers group (n=103)	p	0-5 years (n=125)	6-10 years (n=51)	>11 years (n=132)	p
Is asthma contagious?			0.002				0.293
Yes	5 (2.4%)	6 (1.9%)		2 (1.6%)	0 (0)	4 (3%)	
No	199 (95.2%)	89 (87.3%)		113 (90.4%)	47 (92.2%)	121 (91.7%)	
No idea	5 (2.4%)	12 (11.8%)		9 (7.2%)	3 (5.9%)	5 (3.8+)	
Can asthma be hereditary?			0.001				0.331
Yes	148 (70.4%)	60 (58.8%)		78 (62.4%)	37 (72.5%)	90 (68.2%)	
No	45 (21.4%)	18 (17.6%)		27 (21.6%)	8 (15.7%)	26 (19.7%)	
No idea	17 (8.1%)	24 (23.5%)		19 (15.2%)	5 (9.8%)	38 (28.8%)	
What are the complaints of an asthma patient?			<0.001				0.026
Cough	2 (1%)	3 (2.9%)		2 (1.6%)	0 (0)	3 (2.3%)	
Dyspnea	28 (13.4%)	32 (31.4%)		36 (28.8%)	7 (13.7%)	17 (12.9%)	
Wheezing	11 (5.3%)	8 (7.8%)		5 (4%)	3 (5.9%)	10 (7.6%)	
All	168 (80.4%)	59 (57.8%)		81 (64.8%)	40 (78.4%)	100 (75.6%)	
In which age group is asthma seen?			0.258				0.246
Childhood period	6 (2.9%)	3 (2.9%)		4 (3.2%)	2 (3.9%)	4 (3%)	
Adults	13 (6.2%)	2 (2%)		2 (1.6%)	2 (3.9%)	10 (7.6%)	
At all age	190 (90.9%)	97 (95.1%)		118 (94.4%)	46 (90.2%)	115 (87.1%)	
How are asthma medications usually used?			0.061				0.121
Injection	2 (1%)	2 (2%)		1 (0.8%)	2 (3.9%)	1 (0.8%)	
Pill	2 (1%)	5 (4.9%)		1 (0.8%)	2 (3.9%)	4 (3%)	
Inhalation	206 (98.1%)	94 (93.1%)		122 (97.6%)	46 (90.2%)	125 (94.7%)	
Are asthma medications addictive?			<0.001				0.035
Yes	33 (15.7%)	18 (17.6%)		23 (18.5%)	6 (11.8%)	22 (16.7%)	
No	122 (58.1%)	28 (27.5%)		46 (37.1%)	26 (51%)	77 (58.3%)	
No idea	55 (26.2%)	56 (54.9%)		55 (44.3%)	18 (35.2%)	32 (24.2%)	
Can asthma be cured completely?			<0.001				0.070
Yes	37 (17.7%)	19 (18.6%)		16 (12.8%)	11 (21.6%)	29 (22%)	
No	146 (69.9%)	49 (48%)		79 (63.2%)	31 (60.8%)	82 (62.1%)	
No idea	26 (12.4%)	34 (33.3%)		28 (22.4%)	8 (15.7%)	20 (15.2%)	
Have you been diagnosed asthma by a physician?			0.931				0.723
Yes	19 (9.3%)	9 (8.8%)		13 (10.4%)	4 (7.8%)	11 (8.3%)	
No	183 (89.3%)	92 (90.2%)		109 (87.2%)	44 (86.3%)	115 (87.1%)	
No idea	3 (1.5%)	1 (1%)		1 (0.8%)	1 (2%)	2 (1.5%)	

might not have sufficiently emphasized this issue. However, knowledge levels were also very low in the group with shorter service duration. Therefore, even if they had received COPD training, it suggests that this topic may not have been conveyed effectively. We did not come across any study comparing this data among hospital workers. However, looking at general population studies, al.'s[8] found that approximately half of the general population was unaware of which age group COPD occurs in.

When looking at the levels of knowledge about asthma, the level of awareness that asthma is not contagious, that it may be hereditary, that various symptoms can occur, and that asthma medications do not cause addiction was higher in the HFG group. In a study conducted in Jordan with 300 healthcare workers, including pharmacists (103), nurses (87), clinical pharmacists (28), and doctors (82), 84% knew that asthma could be hereditary, and more than 90% knew the symptoms of asthma.[14] In the study by Reza and Saha[15] colleagues on nurses, it was concluded that all participants knew about asthma and its management. In our study, the rate of knowing that asthma is not contagious was 95.2% in the HFG group and 87.3% in the OFG group, much higher than the 58% in Yıldız et al.'s[8] study of the general population.

The awareness that medications used in the treatment of asthma do not cause addiction was 58.1% in the HFG group, and higher than in the OFG group. In our study, the belief that asthma medications might cause addiction was most prevalent among those with 0-5 years of service and lowest among those with more than 10 years of service. In a study conducted in Brazil, 30% of the general population thought that asthma medications do not cause addiction[16]; and in Yıldız et al.[8] study, this rate was 27%. In our study, 69.9% of the HFG group believed that asthma cannot be cured, while 33.3% of the OFG group had no opinion on the matter. In Yıldız et al.[8] study, 35.2% of participants thought that asthma could not be completely cured. Just as with COPD, inadequate in-service training and insufficient coverage of the issue in the media may be among the explanations for the current results concerning asthma.

The strengths of our study can be listed as follows. This is the first study conducted in North Cyprus on awareness of chronic airway diseases. Although the study was conducted only among hospital workers, including non-patient-facing staff (clerks) provides an aspect of representing the general population. The fact that we treated the study population as separate groups of healthcare staff directly dealing with patients (HFG) and auxiliary healthcare staff (OFG), and examined based on service duration is an important advantage. The weaknesses are a limited number of questions and an inability to explore the reasons behind the given responses. However, had the number of questions been higher, participation in the survey might have been lower. Therefore, in its current form, this study should be considered a situational analysis.

Study Limitations

Our study has some limitations. The first is the numerical difference between the groups. The second is the low participation rate in the survey. However, given that this is the first awareness study about airway diseases in our country, the current participation rate is significant.

CONCLUSION

Although the population in this study was quite heterogeneous, with low participation from doctors, we believe it adequately represents healthcare workers. Awareness of asthma and COPD is low in this group. Notably, the level of knowledge about these two diseases is lower in the group with longer service duration compared to other groups. We believe that periodic in-service training is necessary to educate hospital staff about these diseases and that increasing the visibility of COPD and asthma in the general population through media could contribute to improving knowledge levels.

MAIN POINTS

- The prevalence of chronic respiratory diseases [(COPD)and asthma] is increasing globally, leading to significant morbidity and healthcare costs. The level of knowledge among healthcare workers about these diseases is the most important factor facilitating the recognition and management of COPD and asthma.
- The level of knowledge about COPD and Asthma among hospital staff in the Turkish Republic of North Cyprus is low.
- All healthcare sector employees should receive in-service training and similar methods to provide information on chronic respiratory diseases.

ETHICS

Ethics Committee Approval: This study was approved by the Ethics Committee of Dr. Burhan Nalbantoğlu State Hospital (approval number: YT.1.01, date: 25.05.2020).

Informed Consent: This is a questionnaire study. The questionnaire form contains information about the study at the beginning, and those who accepted this information filled out the survey.

Footnotes

Authorship Contributions

Concept: A.B., F.Y., Design: A.B., F.Y., Data Collection and/or Processing: A.B., E.Ü.E., H.Y., F.C., D.Ö.R., Analysis and/or Interpretation: A.B., E.Ü.E., H.Y., F.C., D.Ö.R., Literature Search: A.B., F.Y., E.Ü.E., H.Y., F.C., D.Ö.R., Writing: A.B.

DISCLOSURES

Conflict of Interest: One author of this article, Ayşe Baha, is a member of the editorial board of the Cyprus Journal of Medical Sciences. However, he did not take part in any stage of the editorial decision of the manuscript. The editors who evaluated this manuscript are from different institutions. The other authors declared no conflict of interest.

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RESEARCH ARTICLE

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Retrospective Evaluation in Child and Adolescent Victims of Sexual Abuse: Analysis of Gender and Age Differences

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Abstract

BACKGROUND/AIMS: This study aimed to investigate the socio-demographic characteristics of children and adolescents who were victims of sexual abuse (SA) admitted to the child psychiatry clinic by the judicial authorities, to examine the characteristics of the abuse and the perpetrator, and to compare these characteristics in terms of age and gender.

MATERIALS AND METHODS: Our study included 388 cases of SA referred for a forensic report. Data were obtained retrospectively from the forensic files and outpatient clinic registration files of the cases.

RESULTS: Of 388 sexually abused cases, 357 (92%) were girls. The mean age of the cases was 13.41±2.99 years, and the mean age of the boys was lower than that of the girls. It was found that the rate of abuse was higher among adolescent girls. It was found that 99.2% of the perpetrators were male. One person was responsible for 93.5% of all instances of abuse. 50.4% of the victims experienced abuse more than once, and the victim's statement was responsible for revealed 44.8% of the abuse cases. It was found that in 44.4% of cases, the perpetrator was the victim's boyfriend, 14.9% of cases were married at an early age, 20.6% had a pregnancy after abuse, and 65.4% of cases had no psychiatric diagnosis.

CONCLUSION: Our findings showed that the majority of SA victims were girls, the frequency of abuse increased with age, the majority of perpetrators were the victims' boyfriends, and the reporting rate of abuse incidents by victims was low. Starting education about sexual health and SA at a very young age will be beneficial in protecting individuals from becoming victims of abuse, reporting abuse, and seeking help.

Keywords: Adolescent, child, psychopathology, sexual abuse

INTRODUCTION

Child abuse and neglect, known to be as old as human history and one of humanity's most significant social wounds, is a health problem whose extent is not well known in societies, tends to be hidden, and has victims who are afraid to speak out.[1,2] Sexual abuse (SA), which is a subset of child maltreatment, is defined in two ways: (1) any act that occurs as a result of coercion, threat, deception, or fraud without the consent of the child or adolescent; (2) the involvement of a child under the age of consent in an act that results in the sexual gratification of a sexually mature adult or the condoning of such a situation.[3,4] Sexual behavior can take the form of sexual intercourse, attempted sexual intercourse, oral-genital contact, and fondling of the genitals directly or through clothing. Non-contact behaviors, such as sexually explicit language, exhibitionism, and voyeurism, are also included in the concept of SA.[5] In recent years, the view has prevailed that all behavior with sexual content should be considered within the scope of sexual activity in a broad sense.[6] Many factors, such as the variable nature of SA, the time lag between abuse and examination, the experience of the examiner, and the lack of standardization of examinations, make detecting physical signs of abuse difficult. While it has been reported that in most cases of SA, there are no physical findings[7], Green found that SA had more psychiatric effects.[8]

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In many societies, SA is concealed by the victim of abuse, and therefore, a large proportion of SA cases are not reported to the judicial authorities.[9] It is difficult to obtain accurate statistical data about the prevalence of SA because only 15% of SA victims report.[10] It has been reported that the prevalence of SA is between 10-40% in children, 3-17% in boys and 8-31% in girls. Females are at two to three times the risk of experiencing SA during childhood compared to males.[11] In a meta-analysis by Pereda et al.[12] in which 38 articles from 21 countries were evaluated, it was reported that girls were sexually abused 1.5-5.5 times more than boys in all age groups except 2 studies. It is known that the abuser may be a stranger to the child or an acquaintance, relative, or family member.[13-15]

It has been reported, that 47% of people who have been sexually abused in childhood have psychiatric disorders that begin in childhood. In comparison, 26-32% have psychiatric disorders that begin in adulthood.[16,17] In a retrospective study conducted among adults in Türkiye, the rate of childhood SA was found to be 2.5%.[18] It has been highlighted suicide attempts following childhood SA are more common in girls.[19]

Although the number of studies on childhood SA is gradually increasing in Türkiye[4,6,9,13-15,20-30], data from different years and different regions are important to increase knowledge about the incidence, pattern, and impact of SA. This study aimed to determine the socio-demographic characteristics, psychiatric diagnoses, and characteristics related to abuse and perpetrator of SA victims referred to Trakya University Faculty of Medicine, Child Psychiatry Outpatient Clinic for forensic evaluation.

MATERIALS AND METHODS

The sample of our study consisted of victims of SA abuse who were referred for forensic evaluation to Trakya University Faculty of Medicine, Child and Adolescent Mental Health Outpatient Clinic between June 2008 and June 2013. In this retrospective descriptive study, the principles of confidentiality were respected, and no details could reveal the children, their families, or the judicial process.

Clinical interviews were conducted with all cases of SA, and an anamnesis form containing socio-demographic data was completed by the research assistants who conducted the interviews. The information form used for each case admitted to the outpatient clinic asked about the socio-demographic characteristics of the child and parents, including the age and educational status of the cases and parents, psychiatric diagnoses of the cases and drug treatments, if any, and family structure, as well as the characteristics of the abuse and the perpetrator. A psychometric test (Stanford Binet, Cattell 2A) was administered to the cases whose language development was complete and whose cooperation could be established. The data related to the abuse incident in the cases were obtained by analysing the diagnoses received in the outpatient clinic follow-up and in the forensic committee according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) diagnostic criteria, the number of outpatient clinics related to the follow-up, the data associated with the use of drug treatment, the outpatient clinic files and the forensic committee reports. As the DSM-IV-TR was the version in effect during the years the study data were collected, this version was used. This study was approved by the Non-Interventional Clinical Research Ethics Committee of Trakya University Faculty of Medicine (approval number: 17/14, date: 31.07.2013).

Statistical Analysis

Statistical data analysis was performed using SPSS 15.0 for Windows, at a 95% confidence level. Mean, standard deviation, median, minimum, maximum, frequencies, and ratios were used in the descriptive statistics of the data. A one-sample Kolmogorov-Smirnov test was used to measure the conformity of variables to the normal distribution. Pearson chi-square was used to compare categorical data between groups, and Mann-Whitney U statistical analyses were used to compare continuous data that did not have a normal distribution between groups. $p<0.05$ was considered statistically significant.

RESULTS

The cases evaluated in the study consisted of girls and boys aged 3-18 years, of whom 357 (92.0%) were girls. Most cases (43.6%) were aged between 15 and 18 years, and the mean age was 13.41±2.99 years. The sociodemographic data of the cases are shown in Table 1. The majority of female subjects (45.7%) were aged 15-18 years, while the majority of male subjects (41.9%) were aged 7-11 years. It was found that the rate of abuse increased with increasing age in girls and in the total group, whereas it decreased with increasing age in boys. The mean age of the cases by sex was compared and showed that the male cases had a lower female cases ($p=0.001$). Similarly, the mean maternal age of the male cases was lower than that of the female cases ($p=0.012$) (Table 2).

The average age of the parents of the victims of SA was 37.42 and 42.22 years for mothers and fathers, respectively; the ratio of working mothers and fathers was 27.7% and 88.3%, respectively; 60.6% of the mothers and 67.4% of the fathers had completed primary school, and 66.8% of the cases lived in a nuclear family.

The characteristics of the abuse and the perpetrators were analyzed. In terms of the type of abuse, only 44.8% of the victims reported the incident; vaginal penetration was the most common type of abuse; 53.9% of the abuse involved coercion; and 50.4% of the victims were victimized more than once (Table 3).

The analyzed cases included those that were “married” by their definition. These cases were young people younger than 18 who were married with the consent of their families but they were not officially married. When the cases were analyzed in terms of early marriage, pregnancy after abuse, and suicide, it was found that 14.9% had an early marriage, 20.6% had a pregnancy after abuse, and 6.7% had attempted suicide following abuse.

The analysis of age groups among children (3-11 years) and adolescents (12-18 years) revealed that in both groups, the perpetrator was someone outside the family ($p<0.001$).

Gender and age were compared regarding the number and type of abuse, perpetrator information, penetration during abuse, and psychiatric diagnosis. These comparisons are presented in Tables 2, 4.

Table 1. Demographic characteristics of cases

		n	%
Gender	Girls	357	92.0
	Boys	31	8.0
Age of abuse	3-6 years old	15	3.9
	7-11 years old	70	18.0
	12-14 years old	134	34.5
	15-18 years old	169	43.6
	Mean ± SD 13.41±2.99		
Education	Not of school age	10	2.7
	Illiterate	25	6.8
	Dropped out of primary education	49	13.3
	Currently attending primary education	141	38.2
	Primary school graduate	46	12.5
	High school dropout	26	7.0
	Currently attending high school	71	19.2
	High school graduated	1	0.3
IQ	Normal	308	81.3
	Borderline intellectual functioning	34	9.0
	Mild intellectual disability	18	4.7
	Moderate intellectual disability	5	1.3
	Severe intellectual disability	2	0.5
	High intelligence	12	3.2
Family characteristics	Nuclear family	169	66.8
	Extended family	34	13.4
	Parents divorced	38	15.0
	Mother/father deceased	5	2.0
	Under protection of social services	7	2.8
Psychiatric diagnosis	No diagnosis	253	65.4
	PTSD	60	15.5
	Depression	7	1.8
	Anxiety disorder	2	0.5
	ASD	47	12.1
	Adjustment disorder	7	1.8
	Selective mutism	1	0.3
	PTSD + depression	6	1.6
	Depression + ASD	2	0.5
	Depression + adjustment disorder	1	0.3
	Diagnosis unknown	1	0.3
Medical treatment	Used	72	18.6
	Not used	315	81.4
Clinical follow-up	Yes	68	17.5
	No	278	71.7
	Didn't attend appointments	42	10.8

PTSD: Post-traumatic stress disorder, ASD: Acute stress disorder, SD: Standard deviation.

DISCUSSION

This study investigated the sociodemographic and clinical characteristics of SA cases referred to the Child and Adolescent Psychiatry Clinic of a University Hospital in Edirne province as forensic cases with a report request within 5 years. Comparisons were made according to gender and age factors. In our study, the mean age of the 388 cases evaluated for SA was 13.41±2.99 years. The mean age of female patients was higher than that of male patients. Our findings were similar to the results of studies in the literature.[4, 20-24] In previous studies, girls were found to undergo SA more frequently than boys.[6,12,25-27]

Studies on gender differences in the reporting of SA have found that girls report more cases of abuse, while boys tend to under-report. Factors contributing to this under-reporting include the fear of being perceived as homosexual in the presence of a male perpetrator. In the presence of a female perpetrator, boys perceive the experience as a sexual relationship, do not feel victimized, and do not report the abuse. It is also emphasized that male victims are usually threatened with more violence and power and are, therefore, reluctant to report. The effect of these factors leads to the conclusion that boys are more hesitant to report abuse than girls.[31]

When we analyzed the number of cases by age group, we found that most of our cases (43.6%) were in the 15-18 age group. When analyzed by gender, the majority of male cases (41.9%) were in the 7-11 age group, and the majority of female cases (45.7%) were in the 15-18 age group. In our study, the 3-6 age group accounted for only 3.9% of cases. It was found that the rate of abuse was higher in boys in the 3-6 and 7-11 age groups, whereas the rate of abuse was higher in girls in the 12-14 and 15-18 age groups ($p<0.001$). Similar to the results of our study, Cengel-Kültür et al.[23] found that boys were most often sexually abused during the school years (7-11 years) and girls during adolescence (12 years and older). The literature suggests that the risk of SA increases with age.[4,32] In another study, the frequency of abuse was found to have a bimodal age distribution, with abuse concentrated in children aged 5 and 14 years, and rates of abuse increasing with age beyond 14 years.[33] A study by Bassani et al.[34] in a community-based sample reported that prevalence decreased with age in boys and increased in girls. Abuse is often observed in prepubertal boys because male cases may become more suitable for self-protection with increasing age. In contrast, adolescent girls are seen as more vulnerable sexual objects due to the development of secondary sexual characteristics.[35]

Our results showed that the number of cases was low in the age group of 3-6 years. This finding is consistent with studies in the literature. It is thought that the low number of cases in the 3-6 year age group may be due to the inability of this age group to understand or express the occurrence of SA.[35] Another reason may be that families are skeptical about the narratives of cases at this age, or want to protect the child from possible trauma that may develop in the forensic process. It may not, therefore, be responsive to the forensic process or the physician.

Studies investigating the prevalence of intellectual disability in victims of SA have reported rates ranging from 13.2% to 35.4% in different sources.[20,21,24,25,28] It has been reported that children with intellectual disabilities are vulnerable to deception, and this is considered a risk factor for abuse.[20] It has been reported that the risk of abuse is higher in children with intellectual disability and borderline intelligence because their perception and reasoning skills are limited, and children with

Table 2. Relationship between sociodemographic and clinical characteristics related to abuse and gender

		Gender				Total		p
		Girls		Boys				
		n	%	n	%	n	%	
	3-6 years old	12	3.4	3	9.7	15	3.9	0.001
	7-11 years old	57	16.0	13	41.9	70	18.0	
	12-14 years old	125	35.0	9	29.0	134	34.5	
	15-18 years old	163	45.7	6	19.4	169	43.6	
	Total	357	92.0	31	8.0	388	Total	
Working mother		67	28.2	5	22.7	72	27.7	0.586
Working father		215	87.8	19	95.0	234	88.3	0.332
Perpetrator's proximity								
Within the family		54	15.2	8	25.8	62	16.0	0.128
Outside the family		302	84.8	23	74.2	325	84.0	
Total		356	92.0	31	8.0	387	100.0	
Frequency of abuse								
Once		172	48.5	19	63.3	191	49.6	0.117
Several		183	51.5	11	36.7	194	50.4	
Total		355	92.2	30	7.8	385	100.0	
Number of perpetrators								
One		334	94.1	27	87.1	361	93.5	0.130
>1		21	5.9	4	12.9	25	6.5	
Total		355	92.0	31	8.0	386	100.0	
Psychiatric diagnosis								
Yes		117	33.0	16	51.6	133	34.5	0.036
No		238	67.0	15	48.4	253	65.5	
Total		355	92.0	31	8.0	386	100.0	
The presence of penetration in abuse								
Yes		202	56.6	10	33.3	212	54.8	0.014
No		155	43.4	20	66.7	175	45.2	
Total		357	92.2	30	7.8	387	100.0	
Type of penetration								
Anal penetration		13	6.4	9	81.8	22	10.3	0.001
Vaginal penetration		175	86.6	-	-	175	82.2	N/A
Oral penetration		3	1.5	2	18.2	5	2.3	0.053
Anal-vaginal penetration		11	5.4	-	-	11	5.2	N/A
Total		202	94.8	11	5.2	213	100.0	
Mean Age						**p**		
Child's age		13.59±2.85		11.32±3.71		0.001		
Mother's age		37.73±6.44		34.09±5.04		0.012		
Father's age		42.34±7.5		40.8±6.18		0.424		

*p<0.05, N/A: Not applicable.

intellectual disability may have difficulty assessing the incident and reporting it to authorized persons.[36] It is noted that the rate of cases with intellectual disability was low in our study. The rates in our study may have been low because individuals with borderline intelligence or mental retardation had difficulty reporting their victimization and were exposed to abuse that did not cause physical findings. When they shared this situation with their families, the families viewed the incident with suspicion and did not report it. On the other hand, the proportion of cases with mental retardation may have been lower, as 14.9% of the cases were due to early marriage.

The maternal and paternal ages of the subjects maternal and paternal ages were analyzed according to gender. The mean maternal age of male subjects was lower than that of female subjects, and this difference was statistically significant. No comparison can be made because there aren't enough studies evaluating parental age. However, our results should be interpreted with caution. The mean age of male subjects may be younger because our sample was predominantly female and mainly in the 15-18 age range, whereas the male cases were mostly in the 7-11 age range.

Table 3. Findings related to abuse and abuser

		n	%
Disclosure type	Victim's statement	172	44.8
	Witnessed by someone else	43	11.2
	Discovered due to pregnancy	72	18.7
	Other	98	25.3
Type of abuse	Anal penetration	32	8.2
	Vaginal penetration	188	48.5
	Touching-fondling	97	25.0
	Kissing	27	7.0
	Interfemoral intercourse	26	6.7
	Oral penetration	5	1.3
	Exposing-touching genitalia	6	1.5
	Verbal and other	35	9.0
	Attempted rape	9	2.3
Frequency of abuse	Once	191	49.6
	More than once	194	50.4
Method of abuse	Physical force	207	53.9
	Deception	24	6.3
	Voluntarily	137	35.7
	Through coercion and deception	16	4.1
Number of perpetrators	1	361	93.5
	>1	25	6.5
Gender of perpetrator	Man	384	99.2
	Woman	3	0.8
The perpetrator's relationship/ proximity	Boyfriend	172	44.4
	Family member	19	4.9
	Relative	25	6.5
	Neighbor-acquaintance	97	25.1
	Stranger	56	14.5
	Stepfather/stepmother	4	1.0
	Other	14	3.6
Perpetrator's age	Mean ± SD 28.5±14.65		

Another issue analyzed in studies of SA is the relationship between age and the number of incidents of abuse. When we examined the relationship between age and repeated abuse, we found that abuse was mainly repeated once in the 3-11 age group, whereas it was mostly repeated in the 12-18 age group ($p<0.001$). It has been reported in the literature that the risk of being a victim of repeat abuse is higher in adolescence than in childhood.[37,38] It was observed that the rates of SA reoccurrence, reported in the studies, varied from 25% to 89.6%. Consistent with our findings, the rates of abuse reoccurrence increased with advancing age.[13,22,23,25,29,39-43]

In studies where the forms of abuse were assessed, the most common were vaginal penetration, anal penetration, fondling, and interfemoral intercourse.[35,41,44] When analyzed by gender, vaginal penetration and fondling were reported to be the most common forms of abuse in girls. Anal penetration and frictional abuse were the most common forms of abuse in boys.[4,21,35] In studies of non-clinical samples, touching and rubbing were found to be the most common forms of abuse.[45,46] Two studies from Sweden and Australia reported that non-contact abuse was more common than contact abuse.[47,48] It has been noted in the literature that the penetration rate found in the non-clinical sample is lower than that in the clinical sample. It is thought that non-contact forms of abuse, such as touching, are more common in some studies in the literature, whereas genital penetration is more common in studies in Türkiye, because the low level of reporting of touching forms of abuse may explain this discrepancy.[35] Similar to the literature, the results of our study found that abuse involving penetration was most prevalent in the adolescent age group and among girls, and the rate of vaginal penetration was 49.0%. In addition, the fact that 14.9% of our sample were assessed for "early marriage" impacted the higher rate of these findings.

One of the important issues in the assessment of sexual activity is voluntary sexual intercourse before the age of 18. This issue has been analyzed in different countries, and a study conducted in Australia reported that about 50% of Australian adolescents had voluntary sexual intercourse before the age of 17 or 18. A study conducted in a non-clinical sample in Sweden found that most cases involved voluntary sexual intercourse.[39,49] In our study, 35.7% of the cases were found to have had sexual intercourse voluntarily. In a study conducted in Mersin, this rate was found to be 24.8%.[35] In another study, the rate of SA without the use of coercion and physical violence was reported to be 45.7%.[50]. As sexual intercourse before the age of 18, even before marriage, is generally not approved in our country, it is not surprising that the majority of the group who said they did not consent actually did not consent. According to the Convention on the Rights of the Child, everyone under the age of 18 is considered a child, so it seems problematic to talk about the consent of a child. It is assumed that all kinds of interactions in which the child is used to satisfy the sexual desires of the adult should be accepted as SA, whether they involve consent or not.[35]

Another significant finding of our study was that the perpetrator in the "child" and "adolescent" age groups was someone outside the family ($p<0.001$). the study by Alikasifoglu et al.[46] reported that when analyzing the relationship between age and whether the perpetrator was inside or

Table 4. Relationship between characteristics of abuse and children's age

	Years				Total		p
	Child (3-11 years)		Adolescent (12-18 years)				
	n	%	n	%	n	%	
Perpetrator's proximity							
Within the family	27	32.1	35	11.6	62	16.0	<0.001
Outside the family	57	67.9	268	88.4	325	84.0	
Total	84	21.7	30,3	78.3	387	100.0	
Frequency of abuse							
Once	65	78.3	126	41.7	191	49.6	<0.001
Several	18	21.7	176	58.3	194	50.4	
Total	83	21.6	302	78.4	385	100.0	
The presence of penetration in abuse							
Yes	6	7.1	206	68.0	212	54.8	<0.001
No	78	92.9	97	32.0	175	45.2	
Total	84	21.7	303	78.3	387	100.0	
Number of perpetrators							
1	232	92.1	129	96.3	361	93.5	0.110
>1	20	7.9	5	3.7	25	6.5	
Total	252	65.3	134	34.7	386	100.0	
Psychiatric diagnosis							
Yes	35	42.2	98	32.3	133	34.5	0.095
No	48	57.8	205	67.7	253	65.5	
Total	83	21.5	303	78.5	386	100.0	

*p<0.05.

outside the family, cases of abuse under the age of 12 were mostly by someone outside the family. One study suggested that reasons for the high incidence of out-of-family abuse include cultural factors that allow abuse to remain a secret within the family.[35] Although the results of our study are similar to those of previous studies, there is not sufficient research in the literature.

In our study, penetration was assessed according to four age groups. In most of the cases in the 3-6 age/7-11 age group, a form of abuse without penetration was found. In contrast, forms of abuse with penetration were found in the 12-14 age/15-18 age group. This difference between the rates was statistically significant. A study conducted by Metin et al.[35] in Mersin reported findings consistent with those of our study. A survey by Akbaş et al.[22] in Samsun found that older children were often exposed to multiple forms of abuse, and the rate of abuse involving vaginal penetration increased with age in girls. It has been reported in the literature, that cases exposed to penetrative SA were in the older age group compared to those exposed to non-penetrative SA.[51]

Our study found that the pregnancy rate after confidence interval was 20.6%. In a study conducted in Mersin, the rate of pregnancy history after SA was found to be 8.6%, while in a study conducted in Samsun, this rate was 4.2%.[22,35] In their meta-analyses, Noll et al.[52] found that the presence of SA increased the risk of adolescent pregnancy by a factor of 2.21 and that approximately 5 out of 10 pregnant adolescents may have a history of SA. In our study, the rates of pregnancies were higher than those reported in the literature. We believe that the high rate (14.9%), of cases, referred to our outpatient clinic by forensic units as victims of SA due to unofficial marriages performed with the consent of the families, influenced the results of our study.

Our study found no psychopathology in 65.4% of cases assessed according to the DSM-IV-TR diagnostic and classification system. In 4 studies that evaluated the status of receiving a psychiatric diagnosis in victims of sexual assault in our country, the rates ranged from 76.4% to 91.7%, and it was reported that most cases were diagnosed with post-traumatic stress disorder (PTSD), acute stress disorder, and depression.[4,21,25,30,35] In studies of children and adolescents exposed to SA, PTSD has been reported in 44-71%. Although some children do not meet all the diagnostic criteria for PTSD, they may show symptoms of re-experiencing, fear, anxiety, and difficulty concentrating.[53] There are studies in the literature, reporting that 21-36% of child victims of SA have no symptoms in the short term and 64-79% have a variable spectrum of symptoms. Additionally, there are studies reporting that approximately 40% of children exposed to SA have very few or no symptoms.[5,53] It has been reported that 10-20% of asymptomatic cases may show symptoms within 12-18 months. It is thought that the reason why undiagnosed cases do not show symptoms may be that they have been exposed to milder abuse, are more resilient children, or have a coping style that masks their distress.[5] A review of the literature related to the outcomes of SA suggests that SA does not have a single and universal effect. Therefore, not every child who has been exposed to SA may show a post-traumatic response to abuse.[35] For these reasons, we believe the diagnosis rate was lower in our study.

Study Limitations

The limitations of our study include the inability to use a scale because it was conducted using the retrospective file review method, the lack of a control group, and the fact that the psychological evaluation was conducted during the forensic process. However, as it represents a single region and a high number of cases, our results make an essential contribution to the literature.

CONCLUSION

Our study found that the majority of victims of SA were girls, males were abused in childhood and girls in adolescence, the frequency of abuse generally increased with age, the victim was exposed to more than one abuse with increasing age, the number of abuses involving penetration also increased with increasing age, the number of "early marriages" was 14.9% and the rate of pregnancy was 20.6%. On the other hand, the fact that incidents were reported where the victim consented at a rate of 35.7% and that 44.4% of perpetrators were the victim's boyfriend suggests that it is important to assess the need for increased sexual health education in adolescence. Starting education about SA which is an important public health problem at a very young age may encourage victims to report abuse. Although the number of studies addressing SA and evaluating victims of SA is increasing, there is still a need for studies on prevention, treatment, and aftercare in this area.

MAIN POINTS

- Our study contributes to the literature on sexual abuse in children and adolescents, and a significant majority of the abuse victims (92%) are girls in the adolescent age group.
- Girls are more often subjected to penetration-related abuse, while anal penetration is more commonly seen among male children.
- Less than half of the victims report the abuse themselves.
- In reported cases, more than half involved multiple instances of abuse, with repeated abuse being more prevalent among adolescents.
- Most perpetrators (99.2%) are male, and often individuals outside the family.

ETHICS

Ethics Committee Approval: This study was approved by the Non-Interventional Clinical Research Ethics Committee of Trakya University Faculty of Medicine (approval number: 17/14, date: 31.07.2013).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: L.B., I.G., Design: L.B., I.G., Data Collection and/or Processing: L.B., Analysis and/or Interpretation: L.B., Literature Search: L.B., I.G., Writing L.B., I.G.

DISCLOSURES

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RESEARCH ARTICLE

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Serum Lactate Dehydrogenase: A Diagnostic Test for Acute Leukemia Subtypes

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Abstract

BACKGROUND/AIMS: Acute leukemia can be categorized into two primary subtypes, acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), each of which necessitates distinct therapeutic strategies. This research investigated the diagnostic utility of serum lactate dehydrogenase levels (LDH) for differentiating between ALL and AML, and monitoring disease progression.

MATERIALS AND METHODS: The study cohort comprised 82 individuals diagnosed with acute leukemia between January 2015 and December 2020. Serum lactate dehydrogenase concentrations were evaluated at three clinical stages: initial diagnosis, remission, and relapse. Analytical approaches include descriptive statistics, nonparametric Mann-Whitney U tests for intergroup comparisons, and receiver operating characteristic (ROC) curve analysis to determine the diagnostic utility of lactate dehydrogenase.

RESULTS: Serum lactate LDH were markedly higher in ALL patients than in AML patients (1.669±1.038 vs. 413±146 IU/L; $p<0.001$). Lactate dehydrogenase was strongly correlated with blast counts ($r=0.62$, $p<0.001$) and moderately correlated with white blood cells ($r=0.45$, $p=0.02$). ROC analysis revealed 400 IU/L as the optimal cutoff, yielding 70% sensitivity and 68% specificity (area under the curve =0.75).

CONCLUSION: Elevated serum LDH are strongly linked to ALL and could function as a diagnostic marker for distinguishing acute leukemia subtypes and assessing disease progression. Subsequent investigations with expanded patient cohorts are essential to establish its prognostic significance and clinical applicability.

Keywords: Lactate dehydrogenase, acute leukemia, acute myeloid leukemia, acute lymphoblastic leukemia, hematologic malignancies

INTRODUCTION

Acute leukemia is an aggressive hematologic malignancy characterized by the rapid, dysregulated proliferation of abnormal white blood cells in the bone marrow and bloodstream.[1] Leukemia is broadly categorized into two primary types-acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL)-which differ in the hematopoietic lineage involved (myeloid vs. lymphoid) and their distinct clinical and pathological features.[2] However, distinguishing between ALL and AML remains clinically challenging because of overlapping clinical presentations, such as fever, fatigue, bleeding, laboratory findings like elevated white blood cell counts, which can be observed in both subtypes.[3] Additionally, bone marrow morphology can be ambiguous, and immunophenotypic markers, although useful, may overlap between the two conditions, complicating diagnosis.[4] Misdiagnosis or delayed differentiation of these leukemia subtypes can lead to inappropriate treatment, potentially resulting in poor prognosis, unnecessary toxicity, and delayed disease monitoring, which may negatively affect patient outcomes.[5] The application of advanced molecular techniques, such as fluorescence *in situ* hybridization, polymerase chain reaction, and next-generation sequencing, is essential to accurately differentiate between these subtypes and guide effective treatment strategies.[6] Early and accurate diagnosis is crucial for selecting the appropriate therapy and improving survival rates in these patients.[7]

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Lactate dehydrogenase (LDH) is an essential enzyme involved in the conversion of pyruvate to lactate during anaerobic metabolism and plays a critical role in cellular energy production under low-oxygen conditions.[8] It consists of five isoenzymes, with LDH-1 primarily found in cardiac muscle, red blood cells, and renal tissue, while LDH-5 is abundant in skeletal muscle, hepatic tissue, and white blood cells.[9] Elevated serum LDH levels are frequently observed in pathological states with increased cellular turnover and metabolic stress, both of which are characteristic features of hematologic malignancies, including leukemia. In leukemia, the rapid proliferation of leukemic cells and their high metabolic demands, along with associated tissue damage, result in elevated LDH levels, making LDH a useful biomarker for the diagnosis and monitoring of disease progression.[10]

Apart from its metabolic function, LDH has been recognized as a prognostic marker in leukemia, with correlations with disease progression, treatment response, and overall survival (OS).[11,12] Elevated LDH levels are strongly linked to high-risk leukemia variants and adverse clinical outcomes.[11,13,14] Although its role in leukemia prognosis is well established, its effectiveness in differentiating between ALL and AML has not been thoroughly explored in clinical practice.

LDH has also been proposed as a diagnostic marker in oncology, given its association with tumor burden and disease activity.[13,15] Elevated serum LDH concentrations in individuals with hematologic malignancies correlate with decreased OS rates and a heightened risk of disease recurrence.[13,16] In pediatric patients with ALL, LDH levels at diagnosis have been shown to predict treatment outcomes and disease progression.[17] Multiple studies have explored the potential of LDH levels in distinguishing between acute leukemia subtypes. Kornberg and Polliack [18] reported significantly elevated LDH levels in patients with ALL compared with those with AML, suggesting its potential as a tool for differentiating between these leukemia subtypes. However, further research is needed to establish the clinical reliability of a diagnostic tool.

Despite advancements in diagnostic techniques, differentiating between ALL and AML remains a significant challenge because of overlapping clinical features and laboratory findings. Previous research has focused largely on conventional diagnostic methods, yet a gap in understanding the role of metabolic biomarkers, such as LDH, in distinguishing these two subtypes remains. This study aims to address this gap by evaluating the diagnostic utility of serum LDH levels in differentiating ALL from AML and exploring its relationship with disease progression. By analyzing LDH levels in relation to blast counts during remission and relapse, this research seeks to provide novel insights into the potential of LDH as a biomarker in hematologic oncology, ultimately contributing to more accurate diagnostic and prognostic approaches in leukemia management.

MATERIALS AND METHODS

Study Design and Participants

This descriptive cross-sectional study was conducted in the hematology department from January 2015-December 2020 and included 82 patients newly diagnosed with acute leukemia-36 with ALL and 46 with AML. A descriptive design was intentionally chosen to offer an observational overview of serum LDH levels across different disease stages without introducing interventions. This approach is well suited for identifying patterns and generating hypotheses in a real-world clinical setting, particularly in a heterogeneous patient population. It also facilitates the collection of baseline data that can inform future analytical or interventional studies.

Eligible participants had a confirmed diagnosis of ALL or AML on the basis of the World Health Organization classification. Only patients whose serum LDH values were documented at the time of diagnosis and who provided informed consent were included. To ensure the accuracy of LDH levels at baseline, the exclusion criteria were the presence of other malignancies, comorbidities known to affect LDH levels (e.g., liver disease, hemolysis), and any prior chemotherapy or cancer therapy. This study was approved by the Ethics Committee of Dali Referral Hospital (approval number: 57/14, date: 24.11.2014).

Data Collection

Patient data were collected at three clinically relevant stages: diagnosis, remission, and relapse. Demographic information, hematologic parameters (including complete blood counts), and diagnostic assessments (bone marrow examination, immunophenotyping, and cytogenetic results) were retrieved from medical records.

Lactate Dehydrogenase Measurement

Serum LDH concentrations were measured via an enzymatic colorimetric method based on the oxidation of lactate to pyruvate, which is catalyzed by LDH in the presence of NAD+ and results in NADH formation. The rate of NADH production was monitored spectrophotometrically at 340 nm. The assay was performed via an automated chemistry analyzer, with internal quality controls and interlaboratory comparison protocols in place to ensure accuracy and reproducibility. LDH values were interpreted via established laboratory reference ranges, and elevated levels were considered indicative of disease activity.

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics. Categorical data are presented as frequencies and percentages, whereas continuous variables are expressed as the means ± standard deviations. The Shapiro-Wilk test was used to assess data normality. Given the nonparametric distribution of LDH levels, the Mann-Whitney U test was used to compare LDH values between the two leukemia subtypes. Receiver operating characteristic (ROC) curve analysis was used to evaluate the sensitivity and specificity of LDH for differentiating between subtypes. A p value <0.05 was considered statistically significant. Analyses were performed using SPSS.

RESULTS

Patient Characteristics

The study included 82 patients with acute leukemia, comprising 36 patients with ALL and 46 patients with AML. The mean age of the cohort was 45.6±12.7 years, with a male-to-female ratio of approximately 1.4:1.

Symptom incidence was analyzed separately for each subtype. Among patients with ALL, the most common presenting symptoms were fatigue (92%), fever (89%), and bleeding (85%). In AML patients, fatigue was reported in 95%, fever in 91%, and bleeding in 88% of patients. These findings reflect the non-specific yet common clinical presentation of acute leukemia. Diagnosis and classification were confirmed by bone marrow aspiration, biopsy, immunophenotyping, and cytogenetic

analysis. A detailed summary of the demographic and clinical features is presented in Table 1.

Lactate Dehydrogenase Levels in Acute Leukemia Subtypes

At diagnosis, patients with ALL presented significantly higher serum LDH levels than did those with AML. The mean LDH level was 1.669±1.038 IU/L for ALL patients and 413±146 IU/L for AML patients ($p<0.001$).

Among the ALL patients, 78.9% had LDH levels exceeding 900 IU/L, whereas 66% of the AML patients presented elevated LDH levels. These results suggest that LDH may serve as a biomarker for distinguishing between ALL and AML. The distributions of the serum LDH levels at diagnosis, remission, and relapse are presented in Table 2.

Diagnostic Performance of Lactate Dehydrogenase

The diagnostic ability of LDH levels for distinguishing between ALL patients and AML patients was evaluated via ROC curve analysis. The area under the curve was 0.75, indicating moderate discriminative ability.

An LDH cutoff value of 400 U/L was identified as optimal, providing 70% sensitivity and 68% specificity (Table 3). The ROC curve (Figure 1) visually represents the diagnostic performance of LDH in differentiating between the two leukemia subtypes.

Correlation with Clinical Parameters

Serum LDH levels demonstrated a strong positive correlation with blast count at diagnosis ($r=0.62$, $p<0.001$), supporting its potential role in assessing disease activity. Additionally, a moderate positive correlation was observed with white blood cell count ($r=0.45$, $p=0.02$), whereas a negative correlation was found with platelet count ($r=-0.38$, $p=0.04$).

However, no significant correlation was found between LDH levels and blast counts during remission or relapse, suggesting that LDH is primarily useful as a diagnostic marker rather than a prognostic indicator in later disease stages. These findings are summarized in Table 4.

DISCUSSION

This study contributes to the expanding evidence supporting the diagnostic utility of serum LDH in acute leukemia, emphasizing its role in distinguishing between ALL and AML. These findings revealed significantly elevated LDH levels in ALL patients compared with those in patients with AML, suggesting the potential of LDH levels as a supplementary biomarker for early subtype differentiation. Since ALL and AML have distinct treatment regimens-requiring intensive multiagent chemotherapy and central nervous system prophylaxis and AML often involves cytarabine-based induction therapy followed by consolidation with stem cell transplantation in high-risk patients-accurate early differentiation is crucial for optimizing therapeutic decisions and improving patient prognosis.[19,20] Elevated LDH levels may also reflect the aggressive nature of leukemic cell proliferation and metabolic dysregulation, which can aid in risk stratification and monitoring treatment response.[21] Future studies integrating LDH with genetic and immunophenotypic markers may further refine its clinical applicability in hematologic oncology.

Our results revealed that the mean LDH level in ALL patients was 1.669±1.038 IU/L, which was significantly greater than the 413±146 IU/L observed in AML patients ($p<0.001$). These findings align with previous studies suggesting that the increased LDH levels in ALL are a consequence of the high proliferative activity, rapid cell turnover, and glycolytic metabolic reprogramming characteristic of lymphoblasts.[22-24] Unlike myeloid leukemic cells, which rely more on oxidative phosphorylation,

Table 1. Demographic and clinical characteristics of the patients

Characteristic	Acute lymphoblastic leukemia (n=36)	Acute myeloid leukemia (n=46)	Total (n=82)
Median age (years)	45	45	45
Gender			
Male	20 (55.6%)	25 (54.3%)	45 (54.9%)
Female	16 (44.4%)	21 (45.7%)	37 (45.1%)
Symptoms at presentation			
Fatigue	28 (77.8%)	35 (76.1%)	63 (76.8%)
Fever	26 (72.2%)	33 (71.7%)	59 (71.9%)
Bleeding	22 (61.1%)	27 (58.7%)	49 (59.8%)

Table 2. Lactate dehydrogenase levels at diagnosis, remission, and relapse

Condition	Acute lymphoblastic leukemia (U/L)	Acute myeloid leukemia (U/L)
Diagnosis	450 (300-700)	350 (200-500)
Remission	190 (150-230)	180 (140-220)
Relapse	500 (400-800)	400 (300-600)

Table 3. Receiver operating characteristic curve analysis for lactate dehydrogenase

Statistic	Value
Area under curve (AUC)	0.75
Optimal cut-off (U/L)	400
Sensitivity (%)	70
Specificity (%)	68

lymphoblastic leukemia cells exhibit an increased dependence on anaerobic glycolysis (the Warburg effect), leading to excessive lactate production and subsequent LDH elevation.[25,26] Additionally, leukemic cells undergoing apoptosis or necrosis release intracellular LDH into the circulation, further contributing to the observed elevation, particularly in high-burden disease states.[27]

This study uniquely contributes to the literature by not only confirming the diagnostic value of LDH in differentiating ALL from AML, but also providing a quantitative analysis of LDH levels at diagnosis. The significantly higher LDH levels in ALL patients reinforce its potential as an adjunctive biomarker for early leukemia classification, which can facilitate prompt initiation of subtype-specific treatment. Moreover, our findings suggest that LDH could serve as a surrogate marker for leukemic burden, aiding in risk stratification and potentially guiding treatment response monitoring. Future research integrating LDH with other metabolic and molecular markers may further refine its prognostic significance in acute leukemia.

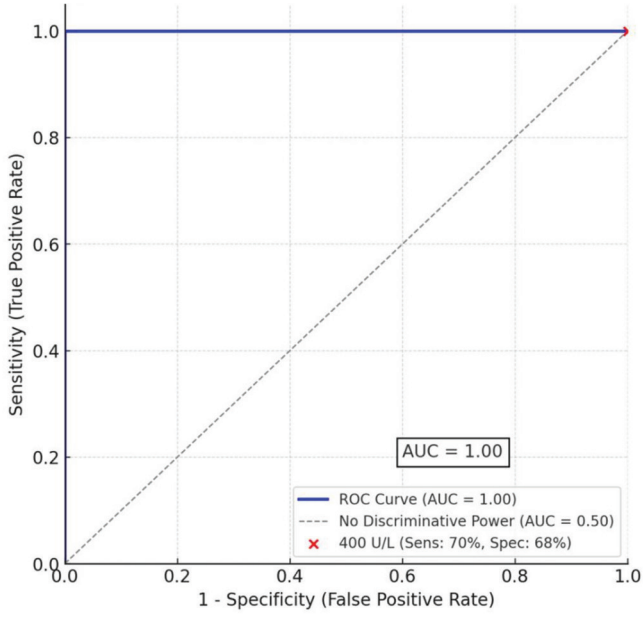

Figure 1. ROC curve for LDH in differentiating ALL from AML.

The receiver operating characteristic (ROC) curve illustrates the diagnostic performance of lactate dehydrogenase (LDH) in distinguishing acute lymphoblastic leukemia (ALL) from acute myeloid leukemia (AML). The area under the curve (AUC) was 0.75, indicating moderate discriminative ability.

The optimal cut-off value of 400 U/L is highlighted in red, corresponding to 70% sensitivity and 68% specificity (as shown in Table 3). The dashed diagonal line represents a random classifier (AUC =0.50), serving as a reference for no discrimination. The closer the curve is to the upper left corner, the better the test's performance in distinguishing between the two leukemia subtypes.

Table 4. Correlations of lactate dehydrogenase levels with clinical parameters

Parameter	Correlation coefficient (r)	p
Number of blasts at diagnosis	0.62	<0.001
Blast count during remission	Not significant	-
Blast count during relapse	Not significant	-

In addition to its diagnostic potential, our study explored the correlation between LDH levels and disease activity. We found a strong positive correlation between LDH levels and blast count at diagnosis ($r=0.62$, $p<0.001$), which further supports its role as an indicator of leukemic cell proliferation and disease activity. This finding is in line with findings from other studies showing LDH is a marker for disease burden and treatment response in leukemia patients.[10,11,28,29] Additionally, a moderate positive association was identified between LDH levels and white blood cell count ($r=0.45$, $p=0.02$), suggesting that this relationship could be attributed to the continued proliferation of leukemia cells. These results reinforce the utility of LDH in monitoring disease progression and assessing the effectiveness of treatment strategies.

While elevated LDH levels are commonly observed in ALL, elevated LDH is also observed in other hematologic conditions, such as chronic myeloid leukemia (CML), during a blastic crisis. This may complicate the differentiation between ALL and CML. However, additional clinical parameters, such as the presence of the Philadelphia chromosome and disease progression patterns, can help distinguish these conditions. Patients in the chronic phase of CML typically exhibit LDH levels close to normal, which supports the test's utility in differentiating between these two leukemias.[19]

In addition to its diagnostic utility, LDH has been widely recognized as a prognostic marker in acute leukemia, with elevated levels correlating with adverse clinical outcomes. High serum LDH is associated with advanced disease stages, high leukemic burden, increased genetic risk, and treatment resistance.[21,30] In ALL, elevated LDH levels have been linked to a greater likelihood of minimal residual disease persistence, higher relapse rates, and significantly reduced OS.[31,32] Studies have demonstrated that patients with markedly increased LDH levels at diagnosis often exhibit a poor response to induction chemotherapy and require intensified treatment regimens.[33] Furthermore, LDH has been integrated into prognostic models, such as the LDH-based risk stratification score in ALL, which aids in predicting treatment response and guiding therapeutic decisions.[34] In AML, high LDH levels are associated with complex karyotypes, increased FLT3-ITD mutation frequency, and worse progression-free survival and OS.[35] These findings emphasize the dual role of LDH, not only as a diagnostic biomarker but also as a key prognostic indicator that can help refine risk stratification and guide personalized treatment approaches in acute leukemia patients.

Study Limitations

While this research advances the understanding of the role of LDH in acute leukemia diagnosis and prognosis, its findings are tempered by certain limitations. The retrospective study design hinders establishing causal links between LDH levels and leukemia progression, whereas the restricted sample size from a single institution reduces the external validity of the findings. Subsequent research should prioritize expanded, multi-institutional cohorts to verify these findings and assess the applicability of LDH in various demographic groups. Additionally, to increase the predictive value of LDH, future research should focus on prospective cohort studies that monitor longitudinal changes in LDH levels throughout treatment and follow-up. Combining LDH with molecular markers and advanced diagnostic techniques, such

as flow cytometry and genetic profiling, may improve leukemia risk stratification and diagnostic accuracy. Furthermore, understanding the biochemical role of LDH in leukemia pathogenesis through genomics and proteomics could open avenues for developing targeted therapies.

CONCLUSION

This study underscores the clinical relevance of serum LDH as a diagnostic biomarker in acute leukemia, emphasizing its potential to enhance patient care and management. The significantly higher LDH levels observed in ALL patients than in those with AML suggest that LDH could serve as a rapid and accessible tool for distinguishing between leukemia subtypes. Early and accurate differentiation is critical, as ALL and AML require distinct therapeutic strategies, and timely intervention can significantly impact treatment success and patient outcomes. Additionally, LDH measurement is a cost-effective and widely available test, making it particularly useful in settings with limited access to advanced diagnostic modalities such as flow cytometry and molecular testing. The incorporation of LDH into initial diagnostic algorithms could streamline risk stratification, guide early therapeutic decisions, and improve prognostic assessments, ultimately contributing to more individualized and effective patient management. Moreover, the positive correlation between LDH levels and blast count at diagnosis reinforces its potential as a marker for disease activity and treatment monitoring.

Although further validation in larger, multicenter studies is needed, our findings suggest that LDH could play a crucial role in early leukemia diagnosis, prognostic assessment, and treatment decision-making. The incorporation of LDH into risk stratification models and precision oncology approaches could further improve leukemia patient care, facilitating the development of more personalized and effective treatment strategies.

MAIN POINTS

- Serum lactate dehydrogenase (LDH) is a diagnostic biomarker. Significantly higher serum LDH concentrations are observed in acute lymphoblastic leukemia (ALL) patients than in those with acute myeloid leukemia (AML), highlighting its potential role for differentiating these distinct leukemia subtypes.
- The correlation of LDH levels with disease activity strongly correlates with blast counts at diagnosis and white blood cell counts, reinforcing its role as an indicator of leukemic cell proliferation and disease severity.
- Moderate diagnostic accuracy-receiver operating characteristic curve analysis indicated that LDH has a moderate capacity to differentiate between ALL and AML, with a threshold of 400 U/L achieving 70% sensitivity and 68% specificity.
- Potential for disease monitoring-LDH levels fluctuate with leukemia progression, increasing at relapse and decreasing in remission, making LDH a useful marker for monitoring treatment response.

ETHICS

Ethics Committee Approval: This study was approved by the Ethics Committee of Dali Referral Hospital (approval number: 57/14, date: 24.11.2014).

Informed Consent: Informed consent has been obtained from the patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.A.A., A.F.B., H.T.C., Concept: A.A.A., A.F.B., H.T.C., Design: A.A.A., A.F.B., Data Collection and/or Processing: A.A.A., H.T.C., Analysis and/or Interpretation: A.A.A., A.F.B., Literature Search: A.A.A., H.T.C., Writing: A.A.A., A.F.B., H.T.C.,

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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RESEARCH ARTICLE

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Assesment of Cranial Traits for Gender Determination by Using 3D Models: A Retrospective CBCT Study

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Abstract

BACKGROUND/AIMS: Gender determination is the first stage in identification of human remains, as it is essential for accurately assessing other biological traits. The aim of the present study was to evaluate the cranial traits for gender determination in a Turkish subpopulation.

MATERIALS AND METHODS: For this study, 5 cranial traits including nuchal crest, mental eminence, supraorbital margin, mastoid process, and glabella were evaluated on three-dimensional (3D) reconstructions of cone beam computed tomography (CBCT) images of 239 individuals. The cranial traits were scored between 1 and 5 according to the diagram developed by Buikstra and Ubelaker. The data were analysed using descriptive statistics, Mann-Whitney U test, chi-squared test, and discrimination analysis.

RESULTS: The gender was estimated in two ways according to the mean score of cranial traits, and discriminant analysis. The accuracy rate was 94.1% according to the mean score of cranial traits and 95.8% according to the discrimination analysis. Among the cranial traits evaluated, the most distinctive structure was determined to be the glabella.

CONCLUSION: According to the results of the present study, 3D reconstructions of CBCT can be used to evaluate the cranial traits and are an effective way of determining gender with high accuracy.

Keywords: Cranium, forensic dentistry, forensic medicine, sex determination process, skull

INTRODUCTION

Forensic anthropology is often used to personally identify human remains at crime scenes or mass disasters.[1] Reliable determination of gender in the analysis of human skeletal remains represents an important goal of forensic medicine and forensic anthropology.[2,3]

Gender determination is the first stage of the identification process because the accurate definition of other biological characteristics used in determining identity (such as age, height, and weight) is closely related to gender.[4,5] Gender identification in forensic odontology and human anthropology predominantly relies on anatomical variations and various skeletal morphological features that serve to differentiate between males and females.[6,7] The skull is one of the most dimorphic parts of the human skeleton and shows significant dimensional and shape differences between genders, a feature useful for gender determination. The development of such dimorphic traits is inherently linked to fundamental developmental, biomechanical, and functional differences that are gender-specific. Although sexually dimorphic skull size and shape traits common among geographically and genetically distant populations exist, their size varies under the influence of local environmental and/or genetic factors.[8] In a study conducted on 750 skeletons, Krogman and İşcan[9] reported that the accuracy rate for gender determination was 100% if the skeleton was present as a whole, 92% when only the skull was present, and 98% when the pelvis and skull were evaluated together. Different growth and development patterns, including hormonal differences that occur during adolescence, cause

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dimensional and shape differences in the skulls of males and females. On average, male skulls are larger than female skulls. However, making morphological evaluations together with size instead of size alone contributes to the accuracy of gender determination.[10,11]

Morphological or morphometric methods are employed for gender estimation based on cranial bones. Anthropologists and forensic medical specialists traditionally conduct manual examinations of regions of sexual dimorphism, including general skull morphology, nuchal crest, orbits, glabella, mastoid process, and the mandible.[5] To make these evaluations easier, Buikstra[12] and Ubelaker and DeGaglia[2] developed a diagram based on a scoring system for the dimorphic features of these regions on the skull. Despite the simplicity and rapidity of morphological methods, visual evaluation of remains involves a certain level of subjectivity, which can lead to intra-observer and inter-observer errors. The use of morphometric methods provides a high level of confidence by reducing the subjectivity of morphological methods, but morphometric methods do not make a significant difference in the accuracy of gender estimation.[10]

Cone beam computed tomography (CBCT) is an imaging method that provides high-resolution images for the evaluation of bone structures and has some advantages compared to traditional computed tomography (CT). In addition to its advantages such as relatively small size, portability and low cost, has technical advantages such as good spatial resolution and reduction of metal artifacts.[13] Today, gender determination studies are conducted on the bones of individuals with known gender, using CT, magnetic resonance imaging, and CBCT. The findings obtained with these imaging methods are useful for examining social differences.[5,13-15]

Recently, it has been reported that volumetric images that allow three-dimensional (3D), reconstruction of bone structures are suitable data sources for sex determination.[14] Using 3D reconstructions for evaluation provides advantages such as not requiring a maceration process in decomposed corpses, shortening the examination time, preventing damage to bone tissue, reducing subjectivity, and intra-observer and inter-observer errors, and the availability of large data sets of recent samples from various populations.[5,10,14] It appears that the results of studies using CT images for gender estimation are similar to classical anthropological methods.[8,16] In a study conducted on 3D digital models of cranial CTs, the gender of the study population was determined correctly with a rate of over 90% (91.8% and 92.9%).[5] Franklin et al.[8] determined gender with 90% accuracy in their study using volumetric processed CT scans. The literature demonstrates the improved accuracy, reproducibility, and reliability of CBCT over traditional methods.[17] With CBCT technology, it is possible to obtain high-quality, distortion-free images that provide precise localization and identification of bone structures.[17,18]

It is known that the morphological features of the human skull vary significantly around the world. Both genetic and environmental differences within populations affect morphology, and morphological differences in the skull are observed between populations.[19] For this reason, it is thought that conducting studies on gender determination in different societies will increase reliability. The aim of this study is to investigate the feasibility of determining gender in a Turkish subpopulation using the diagram developed by Buikstra[12] and Ubelaker and DeGaglia[2] for conventional manual gender determination on 3D reconstruction images obtained with the CBCT technique, which is increasingly used in dental practice.

MATERIALS AND METHODS

This study was approved by the Non-Interventional Clinical Research Ethics Committee of Pamukkale University Faculty of Dentistry (approval number: 02, date: 23.01.2024).

CBCT images, which were taken between March 2019 and January 2024 and are in the archive of Pamukkale University Faculty of Dentistry, Department of Oral and Maxillofacial Radiology, were included in this study. In our institution, it is standard procedure to obtain informed consent from all patients prior to examination, including consent for the use of their radiographic data in scientific research. The inclusion criteria for the CBCT images included in the study were determined as having a field of view (FOV) (of 21x19, all anatomical structures to be evaluated in the study being viewable, having sufficient diagnostic quality, and having the age of the individuals 18 years or older. In addition, movement or metal artifact, evidence or history of trauma that would affect the anatomical structures to be evaluated, and the presence of a disease or syndrome affecting growth and development were used as exclusion criteria in the study. All CBCT images will be obtained with the Newtom 5G XL (Cefla, Imola, Italy) with the parameters 110 kVp, 3.00-8.73 mA, 3.6-5.4s scanning time, and voxel size 0.125-0.250 mm^3. All CBCT images were evaluated by a dentomaxillofacial radiologist (10 years of experience) twice, one month apart. Another dentomaxillofacial radiologist (8 years of experience) evaluated 20% of the images to assess the inter-observer agreement.

The study population included 133 (55.6%) females and 105 (44.4%) males. The individuals were grouped into age groups: 18-30 years (group 1), 31-50 years (group 2), and above 50 (group 3). After the CBCT images were selected from the archive according to the inclusion and exclusion criteria, a new data file was created without patient information. Both observers made evaluations blind to the actual gender of the participants. For the study, 5 cranial traits defined by Buikstra[12] and Ubelaker and DeGaglia[2] (Table 1), including nuchal crest, mental eminence, supraorbital margin, mastoid process, and glabella, were scored between 1-5 on the 3D reconstruction CBCT images. (Figure 1) Scoring according to the figure indicated 1= female, 2= probably female, 3= ambiguous gender, 4= probably male, 5= male. For each cranial trait, the scoring distribution and mean score were calculated according to gender. For supraorbital margin and mastoid process, the score was calculated as the mean of the right and left scores. Gender estimation was performed in two ways. The first method was by calculating the average score of five cranial traits manually; those with an average below 3 were classified as female; those with an average of 3 were considered ambiguous; and those with an average above 3 were classified as male. The second method involved determining gender using discrimination analysis.

Statistical Analysis

IBM SPSS v 22.0 (for Windows, SPSS Inc., Chicago, IL) was used for statistical analysis. For evaluation of intra-observer and inter-observer reliability, the Kappa value was calculated. For the frequencies, descriptive statistics were used. The Mann-Whitney U test was used to compare the ages of genders. The relationship between age groups and gender estimation and the relationship between actual gender and estimated gender were analyzed by a chi-squared test. Discriminant analysis was used to classify individuals into male and female groups based on cranial trait scores obtained from 3D CBCT reconstructions. This method was used to develop a statistical model that maximizes the

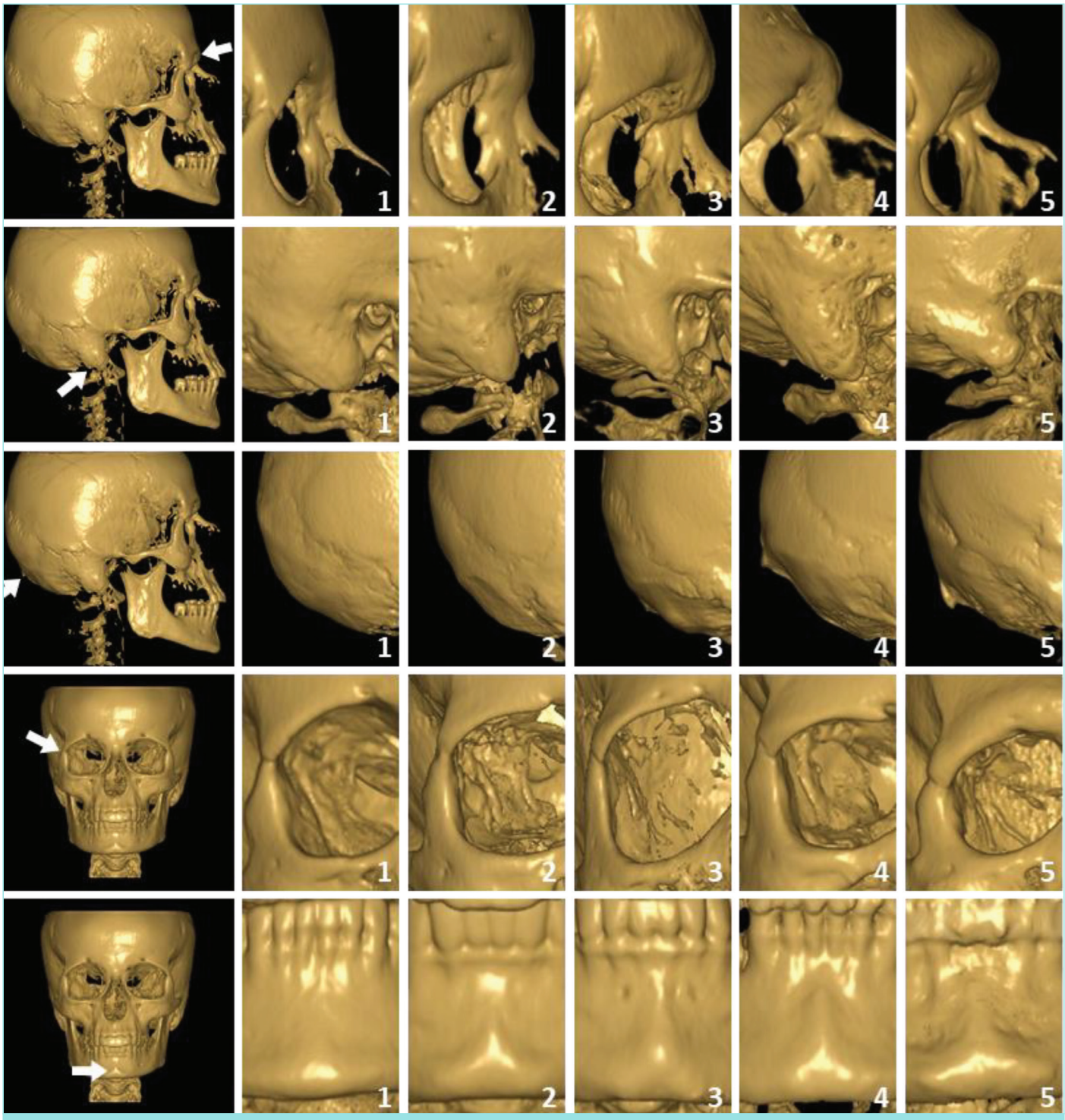

Figure 1. Scoring for cranial traits identified by Buikstra[12] and Ubelaker and DeGaglia.[2].

differentiation between the two groups by identifying the traits with the highest discriminatory power. The analysis involved calculating standardized discriminant function coefficients and structure matrix values to determine the relative contribution of each cranial trait. Model performance was evaluated using Wilks' Lambda and canonical correlation to ensure the effectiveness of the classification.

RESULTS

According to the results of kappa analysis performed to evaluate the agreement of cranial traits, intra-observer reliability Kappa values ranged from 0.805 to 0.876, and inter-observer reliability Kappa values ranged from 0.808 to 0.850. Kappa values were high and statistically significant for all cranial traits ($p<0.001$).

One hundred thirty-three females (55.6%,) and 106 males (44.4%,) aged between 18 and 89, with the mean age of 43.38±15.99 years, were included in the study. The mean age of females was 41.91±16.23, the mean age of males was 45.22±16.25, and there was no statistically significant difference in age between sexes (p=0.107). When the study population was grouped according to age, there were 60 (25.1%) individuals in group 1, 101 (42.3%) in group 2, and 78 (32.6%) in group 3.

The distribution of cranial trait scores according to gender is shown in Table 2. Mental eminence was the cranial trait scored most frequently as 3, indicating ambiguity, while glabella was the cranial trait most frequently scored at 1 and 5.

According to the mean cranial trait scores, the correct gender estimation rate was calculated as 95.5% for females and 92.5% for males. The accuracy rate for the entire study population was 94.1%.

Table 1. Examination of the cranial structures

Cranial trait	Scoring procedure
Nuchal crest	The skull is positioned so that the occipital region can be clearly seen, and the prominence and roughness of the nuchal crest are viewed from the side.
Mental eminence	The mandible can be assessed from frontal and lateral views, and the prominence of the chin is scored according to how far it projects from the mandible.
Supraorbital margin	It is scored by evaluating the sharpness of the supraorbital margin from lateral, anterior and inferior views.
Mastoid process	The skull is examined from the lateral aspect so that the mastoid process is clearly visible. The volume of the mastoid process relative to the temporal bone and the degree of outward protrusion are evaluated.
Glabella	The skull is positioned laterally and scored according to the level of glabellar prominence.

Table 2. Distribution of the genders according to the scores of cranial traits

	Gender	Score 1 n (%)	Score 2 n (%)	Score 3 n (%)	Score 4 n (%)	Score 5 n (%)
Nuchal crest	Female	30 (100%)	50 (94.3%)	38 (56.7%)	11 (19.6%)	4 (12.1%)
	Male	0 (0%)	3 (5.7%)	29 (43.3%)	45 (80.4%)	29 (87.9%)
	Total	**30 (12.6%)**	**53 (22.2%)**	**67 (28%)**	**56 (23.4%)**	**33 (13.8%)**
Mental eminence	Female	10 (100%)	59 (93.7%)	59 (61.5%)	5 (8.3%)	0 (0%)
	Male	0 (0%)	4 (6.3%)	37 (38.5%)	55 (91.7%)	10 (100%)
	Total	**10 (4.2%)**	**63 (26.4%)**	**96 (40.2%)**	**60 (25.1%)**	**10 (4.2%)**
Supraorbital margin (R-L)	Female	62 (75.6%)	111 (69.4%)	79 (50.6%)	12 (20.7%)	2 (9.1%)
	Male	20 (24.4%)	49 (30.6%)	77 (49.4%)	46 (79.3%)	20 (90.9%)
	Total	**82 (17.2%)**	**160 (33.5%)**	**156 (32.6%)**	**58 (12.1%)**	**22 (4.6%)**
Mastoid process (R-L)	Female	98 (90.7%)	101 (81.5%)	50 (40%)	17 (21.5%)	0 (0%)
	Male	10 (9.3%)	23 (18.5%)	75 (60%)	62 (78.5%)	42 (100%)
	Total	**108 (22.6%)**	**124 (25.9%)**	**125 (26.2%)**	**79 (16.5%)**	**42 (8.8%)**
Glabella	Female	60 (98.4%)	50 (90.9%)	21 (58.3%)	1 (2.6%)	1 (2%)
	Male	1 (1.6%)	5 (9.1%)	15 (41.7%)	37 (97.4%)	48 (98%)
	Total	**61 (25.5%)**	**55 (23%)**	**36 (15.1%)**	**38 (15.9%)**	**49 (20.5%)**

R: Right, L: Left.

The rate of gender indeterminacy was 2.3% in females, and 3.8% in males. Distribution of correctly estimated, incorrectly estimated, and ambiguous genders according to their actual gender is shown in Table 3. When the relationship between age groups and gender estimation was evaluated, it was found that age did not have a statistically significant effect (p=0.833) (Table 4).

According to the results of discriminant analysis shown in Table 5, the standardized coefficients indicated that glabella had the strongest effect on gender determination (0.672). The structure matrix further supported these findings, revealing the highest correlation between the discriminant function and glabella (0.809), followed by mental eminence (0.500) and nuchal crest (0.496). The analysis also produced a high canonical correlation of 0.870. The model showed a high accuracy of 96.2% for females and 95.3% for males (Table 6).

DISCUSSION

Gender determination is an important step in the identification process when developing a biological profile. Since gender-related differences are largely population-based and change over time, morphological and metric methods need to be continuously adapted to specific populations.[14] Although dimensional differences between the genders are still the most important aspect of gender determination, accuracy in predicting gender depends on various factors.[20]

Ethical concerns related to macroscopic procedures, advancements in imaging techniques, and increased accessibility have made imaging methods an alternative to traditional anthropological methods.[14] In addition, in a study comparing measurements made on both direct bone images and CT images, it was reported that 3D CT gave accurate results in morphological analysis.[21] In the present study, 3D

Table 3. Distribution of estimated gender according to actual gender

	Estimated gender				
Gender	Female n (%)	Male n (%)	Ambigious n (%)	Total	p
Female	127 (53.1%)	3 (1.3%)	3 (1.3%)	133 (55.6%)	<0.001*
Male	4 (1.7%)	98 (41%)	4 (1.7%)	106 (44.4%)	
Total	131 (54.8%)	101 (42.3%)	7 (2.9%)	239 (100%)	

*Statistically significant (p<0.05).

Table 4. Estimation of true and false/ambigious genders according to age groups

	Determination of gender			
Age	True	False/ambigous	Total	p
Group 1	57 (23.8%)	3 (1.3%)	60 (25.1%)	0.833
Group 2	94 (39.3%)	7 (2.9%)	101 (42.2%)	
Group 3	74 (31%)	4 (1.7%)	78 (32.7%)	
Total	225 (94.1%)	14 (5.9%)	239 (100%)	

Table 5. Estimation result values according to cranial traits using discrimination analysis

	Mean score		Correlation coefficient					
	Female	Male	Standardized	Non-standardized	Structure matrix	Wilks' Lambda	Canonical correlation	Accuracy
Nuchal crest	2.32	3.94	0.216	0.233	0.496	0.244	0.870	95.8%
Mental eminence	2.44	3.67	0.321	0.462	0.500			
Supraorbital margin (R-L)	2.2	2.98	0.111	0.115	0.231			
Mastoid process (R-L)	1.93	3.47	0.340	0.376	0.480			
Glabella	1.74	4.19	0.672	0.785	0.809			

R: Right, L: Left.

Table 6. Distribution of estimated gender using discriminant analysis

	Estimated gender			
Gender	Female n (%)	Male n (%)	Total	p
Female	128 (96.2%)	5 (3.8%)	133	<0.001*
Male	5 (4.7%)	101 (95.3%)	106	
Total	133	106	239	

*Statistically significant (p<0.05).

reconstruction of CBCT images was evaluated. CBCT provides non-distorted high-resolution radiological data. 3D modes present valuable morphologic information and are suitable for gender determination.[22] 3D imaging methods are very useful in the evaluation of fossil or modern skeletons. We can rotate the obtained 3D structures in space, and make original measurements. In addition, internal structures can be evaluated by making cross-sectional views. It is very important that these applications can be done without destroying the bone and without requiring maceration.[21,23] Compared to CT, CBCT has advantages such as lower cost, accessibility, short scanning time, and high resolution. Despite its widespread adoption in dentistry, CBCT is not without limitations related to cone-beam projection geometry, detector sensitivity, and contrast resolution. The clarity of CBCT images is compromised by artifacts, image noise, and poor soft tissue contrast. These artifacts may arise from beam hardening, patient motion, scanner imperfections, or the cone-beam geometry itself. Image noise results from the irradiation of large volumes, which increases scattered radiation and leads to non-linear attenuation detected with flat-panel detectors. Furthermore, CBCT systems offer noticeably lower soft tissue contrast compared to conventional CT, a limitation primarily due to increased noise, X-ray beam divergence, and inherent detector-based artifacts.[24]

Additionally, the forensic process of shipping bones or skulls to specialist laboratories presents numerous challenges: financial burden, the risk of sample loss, the requirement of special permits from judicial authorities, and diplomatic procedures involved in international transfers.[5] However, an important advantage is the ability to obtain 3D images from a nearby hospital and deliver them to the specialist, using any digital storage method.

In this study, satisfactory findings were obtained in gender determination. Based on the results of this study, glabella was identified as the cranial trait with the strongest effect on gender differentiation. Similarly, in another study conducted on the Turkish population, glabella, was also recognized as the cranial feature with the greatest influence on gender differentiation.[5] In a similar study by Walker[25], which evaluated the effectiveness of cranial traits for sex determination, the highest accuracy was found for glabella when assessed individually. However, when glabella was evaluated in combination with other traits, the accuracy rate increased. According to the results of our study, the least reliable cranial trait in sex determination was found to be the supraorbital margin. This result may be related to the fact that determining the sharpness level of the supraorbital margin is based on palpation.[12] In a study conducted by Garvin et al.[26], it was found that glabella and mastoid process were the strongest discriminators for gender determination, while nuchal crest was identified as the weakest cranial trait. According to our study, the nuchal crest was the cranial trait with the second-lowest correlation coefficient level after the supraorbital margin. In the same study, the accuracy of cranial traits for gender determination was compared between different populations, and it was found that there were statistically significant differences between the populations.[26] Accordingly, it is important to conduct forensic studies on different populations and races.

An easy and standardized diagram for determining sex was developed by Buikstra[12] and Ubelaker and DeGaglia[2], and this diagram was studied in various populations.[5,21,26-29] According to this diagram, different accuracy rates were obtained ranging from 75 to 96%.[5,26-29] In this study, the accuracy rate was determined in two different ways. The first method involved scoring five cranial traits for each individual, taking the average of these scores, and then classifying the individual as female, male, or ambiguous. To our knowledge, there is no study that uses the method of sex determination based on a single value by averaging all 5 cranial trait scores. However, the results are quite satisfactory. The second method of was determining the accuracy rate through discriminant analysis. The accuracy rate was determined to be slightly better than that of the first method. In our study, the accuracy rates were 94.1% according to mean scores and 95.8% based on discriminant analysis. To the best of our knowledge, only one study has been conducted on the Turkish population using this diagram on CT images. Based on the results of the study in question, which was conducted with scoring by three different observers, the accuracy in determining gender was found to range between 91.8 and 92.9%. 5 These studies were performed directly on the skull bones[26-29] or on 3D reconstructions of cranial CT images[5,21], and a high accuracy in sex determination was achieved. These studies, which were conducted in different populations and resulted in high accuracy, support the dimorphic feature of the skull as well as the validity of these cranial-traits-based diagram.

In a study evaluating both metric and shape features in the skull, it was determined that bizygomatic breadth, maximum cranial length, and cranial base length as well as mastoid height were dimorphic. Similar to this study, it was reported that among the shape features evaluated, the glabellar region was a strong cranial trait in gender differentiation.[16] In a study conducted by Franklin et al.[8], different measurements were made on the skull to determine sex, and[16] of the measurements showed a statistically significant difference between the sexes.[8] In the light of all these findings, it can be concluded that many of the skull's traits and dimensions are dimorphic. However, variations that affect dimorphism and exhibit ambiguous characteristics can be observed. It is known that factors such as reduced muscle activity, severe malnutrition, and extreme emaciation can affect the accuracy of the methods used. Since it is known that some intrinsic and extrinsic factors can influence cranial features, evaluation of multiple structures together is suggested to positively impact accuracy.[3]

Determining sex from human skeletons using non-metric methods has been criticized for not being objective. However, non-metric methods may be the only option for bones that have been damaged or exposed to taphonomic changes in skeletal remains. Additionally, non-metric methods are useful when there is no suitable reference for metric analysis.[28] Another disadvantage is that experts cannot feel the edges and crests of the bones by holding them in their hands when making morphological evaluations on 3D images.[5] This disadvantage can be overcome with additional morphological examinations[5] and the possibility of cross-sectional evaluation.

Study Limitations

This study has some limitations. Due to its retrospective design, individual factors such as height, weight and nutrition, which may influence cranial development, could not be considered. The inability to physically palpate bones in 3D images may affect the assessment of subtle traits like the supraorbital margin. Also, the use of non-metric visual methods introduces some subjectivity despite high observer agreement. Lastly, findings are based on a single Turkish subpopulation, which may limit generalizability to other groups.

CONCLUSION

This study has shown that CBCT offers high accuracy and quality in the morphological evaluation of bone. Among the 5 different cranial traits evaluated on the skull for the study, the glabella was determined to have the strongest, and the supraorbital margin the weakest, dimorphic feature. When cranial traits were evaluated together, the accuracy rate increased compared to those from individual evaluations. The accuracy rates in determining the sex of the study population were quite high at 94.1% and 95.8%.

MAIN POINTS

- The diagram developed by Buikstra and Ubelaker for conventional manual gender determination was applicable to three-dimensional reconstruction images for determining gender in a Turkish subpopulation.
- This study has shown that cone beam computed tomography offers high accuracy and high quality in the morphological evaluation of bone.
- When cranial traits were evaluated together, the accuracy rate increased compared to individual evaluations. The accuracy rates in determining the sex of the study population were determined to be quite high as 94.1% and 95.8%.

ETHICS

Ethics Committee Approval: This study was approved by the Non-Interventional Clinical Research Ethics Committee of Pamukkale University Faculty of Dentistry (approval number: 02, date: 23.01.2024).

Informed Consent: Informed consent has been obtained from the patients.

Footnotes

Authorship Contributions

Concept: B.K.A., D.İ., Design: B.K.A., D.İ., Data Collection and/or Processing: B.K.A., Analysis and/or Interpretation: B.K.A., Literature Search: D.İ., Writing B.K.A., D.İ.

DISCLOSURES

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RESEARCH ARTICLE

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Clinicopathological Profile and Outcomes of Appendiceal Neuroendocrine Tumors: A 10-Year Single-Center Study of 5,483 Appendectomy Specimens

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Abstract

BACKGROUND/AIMS: This study aims to assess the demographic, histopathological, and immunohistochemical (IHC) features of appendiceal neuroendocrine tumors (aNETs) and investigate their associations with tumor location, grade, size, and pathological stage. The follow-up data on survival and surgical outcomes is utilized to improve risk stratification and management strategies.

MATERIALS AND METHODS: A retrospective analysis was conducted on 5,483 appendectomy specimens evaluated between 2010 and 2020 in a single tertiary center. Among 115 neoplastic lesions, 45 cases were confirmed as aNETs. Demographic data, histopathological parameters, and IHC markers were reviewed. Survival data were collected from national records.

RESULTS: The median patient age was 35, with a female-to-male ratio of 1.37. Most tumors were located in the distal appendix (70.5%) and graded as G1 (82.2%). Mean tumor diameter was 0.91 cm, and the median Ki-67 proliferation index was 1%. Tumor grade and size were significantly associated with both tumor location and pathological tumor stage. Diffuse and proximal tumors were more likely to be G2, larger in size, and in advanced stages (pT4). Lymphovascular invasion, perineural invasion, and surgical margin positivity were more frequent in higher pT stages. Chromogranin A negativity was observed exclusively in pT1 cases.

CONCLUSION: aNETs are typically small, well-differentiated tumors with indolent behavior. However, tumor location, size, grade, and invasion features are associated with pathological stage and may serve as prognostic indicators. These parameters should be considered collectively to optimize clinical decision-making and surgical planning.

Keywords: Appendiceal neuroendocrine tumors, appendectomy, histopathological classification, immunohistochemistry

INTRODUCTION

Appendiceal neuroendocrine tumors (aNETs) are the most commonly encountered neoplasms of the appendix, often diagnosed incidentally during histopathological evaluation following appendectomy for suspected acute appendicitis (AA).[1-3] Despite their relative rarity, aNETs account for 30-80% of all appendiceal neoplasms and typically exhibit indolent biological behavior.[4-6] Most are well-differentiated, measure less than 2 cm, and are located at the distal tip of the appendix.[7-10] As such, simple appendectomy is considered curative in the majority of low-risk cases.[7,11]

Current clinical guidelines by the European Neuroendocrine Tumor Society (ENETS) and the North American ETS (NANETS) recommend right hemicolectomy (RH) for tumors larger than 2 cm or in the presence of high-risk histopathological features such as mesoappendiceal invasion (MAI), lymphovascular invasion (LVI), high Ki-67 index, or positive surgical margins.[11,12] However, the appropriateness of RH remains a

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subject of ongoing debate, particularly for intermediate-sized tumors (1-2 cm) without additional risk factors.[13,14]

Although tumor size (TS), grade, and invasion characteristics have been associated with recurrence risk and survival in prior studies, real-world data evaluating these variables regarding long-term outcomes remains limited, particularly in patients managed conservatively.[2,5] Furthermore, the prognostic relevance of tumor localization within the appendix (a parameter not consistently addressed in major series) warrants further investigation.

This study aims to evaluate the demographic, histopathological, and immunohistochemical (IHC) characteristics of aNETs diagnosed over ten years at a single tertiary care institution. In addition to characterizing tumor features, the study seeks to explore potential associations between tumor location, grade, size, and pathological tumor (pT) and to examine clinical follow-up data focusing on survival and the need for further surgical intervention. Through these objectives, the study intends to contribute meaningful data toward refining risk stratification and management strategies in patients with aNETs.

MATERIALS AND METHODS

This study is a single-center, observational cohort study based on the retrospective analysis of appendectomy specimens collected between 2010 and 2020. The study was approved by the University of Health Sciences Türkiye, Non-Interventional Clinical Research Ethics Committee of İstanbul Training and Research Hospital (approval number: 99, date: 02.05.2025) and all data were obtained in accordance with the principles of the Declaration of Helsinki.

Case Selection and Data Collection

We included 5,483 appendectomy specimens evaluated in our institution's pathology laboratory between April 1, 2010, and April 1, 2020. Pathology reports and the hospital information system were reviewed to identify 115 neoplastic lesions, of which 45 were confirmed as aNETs. Diagnoses were verified by reevaluating hematoxylin-eosin stained slides and IHC analyses.

Data were collected from the hospital's electronic archive system, including detailed reviews of pathology reports, radiological imaging results, surgical, and oncological treatment records.

Tumor characteristics, including tumor diameter, location, histological grade (HG), pT, resection margin status, presence of mesoappendiceal, lymphovascular, perineural invasion (PNI), and concurrent histopathological findings (CHF) such as AA and diverticulitis, were recorded. Tumor grading was based on mitotic count (per 10 HPF/2 mm^2) and Ki-67 proliferation index (PI). The evaluation criteria were guided by the current American Joint Committee on Cancer, Cancer Staging Manual.[15]

IHC staining results for synaptophysin (Syn), chromogranin A (CgA), and Ki-67 antibodies were recorded following re-evaluation. A staining threshold of >10% was considered positive for Syn and CgA. The Ki-67 PI was determined manually by counting at least 500-2,000 cells in hotspot areas.

Clinical Data and Follow-up

Demographic data and overall survival (OS) status were also recorded. OS was defined as the time from diagnosis to death from any cause or last follow-up. The presence of distant metastasis was evaluated at diagnosis and five-year follow-up. Additionally, whether patients underwent further surgical treatment after diagnosis (such as RH) was also recorded. Survival information was obtained through the Ministry of Health's Death Notification System.

Statistical Analysis

Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and Microsoft Office Excel 365 (Microsoft, Redmond, WA, USA). Continuous variables were tested for normality using the Shapiro-Wilk test. Normally distributed variables are expressed as mean and standard deviation (SD) and compared using the Independent Samples t-test, whereas non-normally distributed variables are presented as medians and analyzed using the Independent Samples Kruskal-Wallis test. Categorical variables are reported as frequencies and percentages and compared using the chi-square test, with Bonferroni correction applied for multiple comparisons. Survival analyses were conducted using the Kaplan-Meier method. Deaths that occurred between the date of diagnosis and April 2025 (the end date of the study) were recorded. Patients lost to follow-up or alive at the study endpoint were censored. The differences between survival curves were evaluated using the log-rank test, with a p-value of <0.05 considered statistically significant.

RESULTS

This study included 45 patients with aNETs. The mean age was 36 years (SD = 15), ranging from 14 to 70 years, with a median of 35 years. Of these, 26 patients (57.8%) were women, and 19 (42.2%) were men, resulting in a women-to-men ratio of 1.37:1 (Table 1).

Tumors were most frequently located in the distal appendix (70.5%), followed by diffuse (15.9%) and proximal (13.6%) locations. The mean TS was 0.91 cm (SD = 0.89), ranging from 0.1 to 5 cm. Histologically, 82.2% of tumors were classified as grade 1 and 17.8% as grade 2. No grade 3 tumors were observed.

Pathological staging revealed that 40% of tumors were pT1, 46.7% were pT3, and 13.3% were pT4. Surgical margins were negative in 90.5% of cases and positive in 9.5%. LVI was present in 17.8% of patients, PNI in 15.6%, and MAI in 6.7%. CHF included AA in 68.9%, mucinous neoplasia in 6.7%, and diverticulosis, and fibrous obliteration in 4.4% of cases (Table 1).

All tumors were positive for Syn. CgA was positive in 86.7% and negative in 13.3% of cases. The mean Ki-67 PI was 2.0% (SD = 2.9), with a median of 1%.

During follow-up, 93.3% of patients were alive, while 6.7% (n=3) had died. Two patients died due to cardiovascular comorbidities, and one patient died of sepsis. OS analysis was performed using the Kaplan-Meier method. Although only three deaths occurred during follow-up, a survival curve was generated for illustration (Figure 1). No statistical comparison was made due to the limited number of events.

At the time of diagnosis and during follow-up, no patients (0%) exhibited evidence of distant metastasis. Additionally, no patients underwent RH as a planned post-diagnostic treatment. However, four patients (8.9%) were diagnosed incidentally during RH procedures that had been performed for other clinical indications. Descriptive characteristics of the patients are summarized in Table 1.

Table 1. Patient characteristics

Characteristics		n (%)
Age (years)*		35 (14-70)
Sex		
	Women	26 (57.8)
	Men	19 (42.2)
Tumor localization		
	Proksimal half	6 (13.6)
	Distal half	31 (70.5)
	Body/diffuse	7 (15.9)
Tumor size (cm)*		0.7 (0.1-5)
pT		
	pT1	18 (40.0)
	pT2	0
	pT3	21 (46.7)
	pT4	6 (13.3)
HG		
	G1	37 (82.2)
	G2	8 (17.8)
	G3	0 (0.0)
Resection margin (positive)		4 (9.5)
MAI (present)		3 (6.7)
LVI (present)		8 (17.8)
PNI (present)		7 (15.6)
Synaptophysin (positive)		45 (100.0)
Chromogranin A (positive)		39 (86.7)
Ki-67 PI (%)*		1 (0-18)
CHF		
	Acute appendicitis	31 (68.9)
	Diverticulitis	2 (4.4)
	Mucinous neoplasia	3 (6.7)
	Fibrous obliteration	2 (4.4)
Post-diagnostic RH		0 (0.0)
Distant metastasis (present)		0 (0.0)

*Values are expressed as median (minimum-maximum)
pT: Pathological tumor stage, HG: Histological grade, MAI: Mesoappendiceal invasion, LVI: Lymphovascular invasion, PNI: Perineural invasion, PI: Proliferation index, CHF: Concurrent histopathological findings, RH: Right hemicolectomy

Correlation Between Tumor Location and Clinicopathological Features

Tumor location was significantly associated with HG (p=0.007), pT (p=0.045), and TS (p=0.042). Distal tumors were predominantly grade 1 (93.5%), while proximal (50.0%) and diffuse tumors (42.9%) demonstrated grade 2 differentiation. Similarly, pT1 tumors were mostly localized distally (51.6%), whereas diffuse tumors were more frequently staged as pT4 (42.9%, Table 2).

The median TS varied significantly by location, being largest in diffusely located tumors (1.00 cm), followed by distal (0.70 cm) and proximal (0.35 cm) locations (p=0.007).

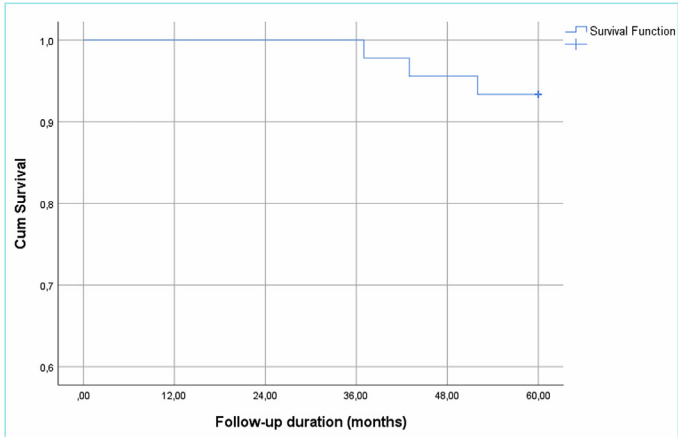

Figure 1. Kaplan-Meier curve illustrating overall survival of patients with appendiceal neuroendocrine tumors. A total of three deaths were observed during the follow-up period. No statistical comparisons were performed due to the limited number of events.

There was a borderline association between tumor location and positive surgical margins (p=0.060), with the highest rate observed in proximally located tumors (33.3%).

Other clinicopathological parameters, including sex, LVI, PNI, CHF, MAI, CgA expression and Ki-67 PI, were not significantly associated with tumor location (Table 2).

Correlation Between Pathological Tumor and Clinicopathological Parameters

pT was significantly associated with TS (p<0.001), Ki-67 PI (p=0.016), HG (p=0.003), LVI (p=0.038), and CgA expression (p=0.006) Table 3. TS and Ki-67 PI increased in higher pT stages, with median TSs of 0.30 cm, 0.80 cm, and 1.85 cm in pT1, pT3, and pT4 stages, respectively. Similarly, the median Ki-67 PI rose from 1.0% in pT1 and pT3 tumors to 5.5% in pT4 tumors. Grade 2 tumors were more frequently observed in advanced stages, accounting for 66.7% of pT4 tumors.

As shown in Table 3, LVI was absent in pT1 cases but present in 28.6% and 33.3% of pT3 and pT4 tumors, respectively. CgA negativity was exclusively observed in pT1 tumors (33.3%), whereas all pT3 and pT4 tumors were CgA positive.

There was a borderline association between pT and both PNI (p=0.054) and positive surgical margins (p=0.052), with rates of 33.3% in pT4 tumors for both parameters. No statistically significant associations were found between pT and age, sex, CHF, or MAI (Table 3).

DISCUSSION

This study evaluated the demographic, histopathological, and IHC characteristics of aNETs diagnosed over 10 years. Our main findings demonstrated that aNETs predominantly occur in middle-aged women, are most often localized at the distal tip of the appendix, and measure less than 1 cm. Most tumors were classified as WHO grade 1 with low Ki-67 PIs, and MAI was infrequent. Tumor location was significantly associated with HG, pT, and TS. OS outcomes were excellent, with a 93.3% survival rate during follow-up. These results are consistent

Table 2. Comparison of clinicopathological features according to tumor location

Clinicopathological features	Proximal (n=6)	Distal (n=31)	Diffuse (n=7)	p
Age (years)*	32 (20-70)	33 (14-64)	40 (24-65)	0.606
Sex				
Women	2 (33.3%)	17 (54.8%)	6 (85.7%)	0.151
Men	4 (66.6%)	14 (45.2%)	1 (14.3%)	
Tumor size (cm)*	0.35 (0.1-2.5)	0.7 (0.15-2.0)	1 (0.8-5.0)	0.007
Ki-67 PI (%)*	2.0 (1-6)	1.0 (0-5)	1.0 (1-18)	0.068
HG				
G1	3 (50.0%)	29 (93.5%)	4 (57.1%)	0.007
G2	3 (50.0%)	2 (6.5%)	3 (42.9%)	
pT				
pT1	2 (33.3%)	16 (51.6%)	0	0.045
pT3	3 (50%)	13 (41.9%)	4 (57.1%)	
pT4	1 (16.7%)	2 (6.5%)	3 (42.9%)	
LVI (present)	0	6 (19.4%)	2 (28.6%)	0.393
PNI (present)	1 (16.7%)	4 (12.9%)	1 (14.3%)	0.969
Resection margin (positive)	2 (33.3%)	1 (3.3%)	1 (16.7%)	0.060
MAI (present)	0	2 (6.5%)	0	0.644
Chromogranin A (positive)	5 (83.3%)	26 (83.9%)	7 (100%)	0.518
CHF (present)				
Acute appendicitis	5 (83.3%)	21 (67.7%)	5 (71.4%)	0.744
Diverticulitis	0	1 (3.2%)	1 (14.3%)	0.379
Mucinous neoplasia	0	2 (6.5%)	1 (14.3%)	0.589
Fibrous obliteration	1 (16.7%)	1 (3.2%)	0	0.288

*Values are expressed as median [minimum (min)-maximum (max)]. Continuous variables are presented as median (min-max), and categorical variables as counts (percentage). Statistical significance was assessed using the Kruskal-Wallis or Pearson chi-square tests, as appropriate.
PI: Proliferation index, HG: Histological grade, pT: Pathological tumor stage, LVI: Lymphovascular invasion, PNI: Perineural invasion, MAI: Mesoappendiceal invasion, CHF: Concurrent histopathological findings

with the existing literature and support current clinical management guidelines favoring simple appendectomy for small, well-differentiated tumors without adverse features.

In line with previous reports, the median age of our cohort was 35 years, with a slight female predominance (57.8%). These findings are consistent with several large series reporting median ages between 33 and 36.5 years and a female predominance ranging from approximately 54.5% to 64.5%.[2,3] These findings reinforce the understanding that aNETs typically affect young to middle-aged adults and exhibit a slight gender disparity. The demographic profile of our study thus mirrors the general epidemiological trends observed globally.

The predominant localization of tumors at the distal tip of the appendix (70.5%) and a mean TS of 0.91 cm were consistent with existing studies, which reported distal localization rates between 58.1% and 83.9% and TSs predominantly less than 1 cm in diameter.[2,10,16] This distribution is clinically relevant, as tumor location and TS significantly impact surgical decision-making and prognosis.

HG revealed that most tumors were grade 1 (82.2%), corroborating findings from prior studies where grade 1 tumors accounted for 60.7% to 90.9% of cases.[3,17] The observed low Ki-67 PI further reinforced the indolent nature of these neoplasms. Importantly, MAI was relatively infrequent (6.7%), supporting the generally favorable prognosis of small, well-differentiated aNETs.

Tumor location showed significant associations with HG, pT, and TS. Distally located tumors were more often grade 1 and staged as pT1, while diffuse tumors exhibited a tendency towards higher grades and stages. These results are in line with findings from Okut and Karahan[18] highlighting that proximally or diffusely located tumors warrant closer clinical scrutiny.

pT correlated strongly with TS, Ki-67 PI, HG, and invasion parameters, which echoesthe established understanding that deeper invasion, and larger TS are markers of more aggressive behavior.[9,19-21] LVI and PNIs, while relatively infrequent, were significantly associated with advanced pTs, aligning with international observations.[6,9]

All tumors showed positivity for Syn (100%), and 86.7%, were positive for CgA, comparable to prior reports where positivity rates for Syn and CgA exceeded 83%.10 The low Ki-67 PIs, with most cases under 3%, reflect the low proliferative activity that characterizes well-differentiated aNETs.

Notably, no patients in our cohort exhibited evidence of distant metastasis at the time of diagnosis or during the follow-up period.

Table 3. Comparison of clinicopathological features according to pathological tumor stage

Clinicopathological features	pT1 (n=18)	pT3 (n=21)	pT4 (n=6)	p
Age (years)*	36 (14-64)	35 (16-70)	34 (17-65)	0.896
Sex				
Women	10 (55.6%)	11 (52.4%)	5 (83.3%)	0.388
Men	8 (44.4%)	10 (47.6%)	1 (16.7%)	
Tumor size (cm)*	0.30 (0.1-1.0)	0.80 (0.1-2.5)	1.85 (0.8-5.0)	<0.001
Ki-67 PI (%)*	1.0 (0-3.8)	1.0 (0.4-5.0)	5.5 (1.0-18.0)	0.016
HG				
G1	16 (88.9%)	19 (90.5%)	2 (33.3%)	0.003
G2	2 (11.1%)	2 (9.5%)	4 (66.7%)	
LVI (present)	0	6 (28.6%)	2 (33.3%)	0.038
PNI (present)	0	5 (23.8%)	2 (33.3%)	0.054
Resection margin (positive)	0	2 (11.1%)	2 (33.3%)	0.052
MAI (present)	0	3 (14.3%)	0	0.159
Chromogranin A (positive)	12 (66.7%)	21 (100.0%)	6 (100.0%)	0.006
CHF (present)				
Acute appendicitis	12 (66.7%)	15 (71.4%)	4 (66.7%)	0.942
Diverticulitis	1 (5.6%)	1 (4.8%)	0	0.845
Mucinous neoplasia	0	2 (9.5%)	1 (16.7%)	0.283
Fibrous obliteration	1 (5.6%)	1 (4.8%)	0	0.845

*Values are expressed as median [minimum (min)-maximum (max)]. Continuous variables are presented as median (min-max), and categorical variables as counts (percentage). Statistical significance was assessed using the Kruskal-Wallis or Pearson chi-square tests, as appropriate.
PI: Proliferation index, HG: Histological grade, LVI: Lymphovascular invasion, PNI: Perineural invasion, MAI: Mesoappendiceal invasion, CHF: Concurrent histopathological findings

This finding aligns with most published series, which consistently report very low rates of metastatic spread in small, well-differentiated aNETs (typically <1%). Distant metastases are reported in a small subset of patients, often associated with high-grade or deeply invasive tumors.[4,22,23] These results underscore the indolent behavior of aNETs and reinforce the appropriateness of conservative surgical management in low-risk cases.

The majority of patients in this cohort underwent only appendectomy, aligning with ENETS and NANETS guidelines, which recommend simple appendectomy for tumors smaller than 1 cm without high-risk features.[11,12] The necessity of RH remains debated for tumors between 1 and 2 cm, particularly in the absence of adverse features.[17] In our cohort, the observation of negative surgical margins in most cases (90.5%) and a low frequency of adverse histopathological features may support the safety of conservative management in selected patients, which aligns with current guideline recommendations.

Survival outcomes were favorable, with a 93.3% OS rate at last follow-up and no evidence of disease recurrence, comparable to other series reporting 5-year disease-free survival rates exceeding 90%.[3,11,13,19]

Study Limitations

This study has several limitations, primarily its retrospective single-center design, which may limit generalizability. The relatively small sample size and limited number of adverse events also precluded advanced multivariate analysis. Furthermore, although the follow-up duration was substantial, long-term outcomes (>5 years) remain unexplored.

Future Directions

Further prospective multicenter studies are needed to validate prognostic markers and improve surgical decision-making, especially for tumors measuring between 1 and 2 cm. Recent proposals suggest that INSM1 and other novel IHC markers could assist in more precise risk stratification.[24]

Molecular profiling studies also offer a promising frontier for understanding tumor behavior and tailoring therapy, especially considering the biological heterogeneity observed among EC-cell and L-cell tumors.[25,26]

Moreover, with the rising trend toward non-operative management of AA, the potential risk of missing incidental aNETs merits close surveillance and possibly the development of preoperative predictive algorithms.[16,17,27]

CONCLUSION

Our findings reinforce the generally indolent behavior of aNETs, characterized by small TS, distal location, low-grade histology, and favorable prognosis. These results support the current guidelines advocating for appendectomy as the definitive treatment in the majority of cases and highlight the need for vigilance in assessing histopathological features indicative of higher-risk disease. Continued research into the biological diversity of aNETs and longer-term follow-up studies are essential to optimize patient outcomes.

MAIN POINTS

- The majority of appendiceal neuroendocrine tumors (aNETs) in our cohort were small (mean size 0.91 cm), well-differentiated (82.2% grade 1), and located distally (70.5%), reflecting indolent tumor biology.
- Tumor location was significantly associated with grade, size, and pathological stage; distal tumors were more likely to be low-grade and early-stage, while diffuse or proximal tumors showed more aggressive features.
- No distant metastasis was observed during diagnosis or long-term follow-up, even in patients with intermediate-sized tumors (1-2 cm) who did not undergo completion right hemicolectomy.
- Positive resection margins and mesoappendiceal invasion were relatively uncommon (9.5% and 6.7%, respectively), which questions the necessity of radical surgery in most aNET cases.
- Our findings support a conservative surgical approach in selected patients and may contribute to refining risk stratification algorithms in current aNET management guidelines.

ETHICS

Ethics Committee Approval: The study was approved by the University of Health Sciences Türkiye, Non-Interventional Clinical Research Ethics Committee of İstanbul Training and Research Hospital (approval number:99, date: 02.05.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.Y., M.C., Concept: E.Y., M.C., Design: E.Y., M.C., Data Collection and/or Processing: E.Y., Analysis and/or Interpretation: E.Y., Literature Search: M.C., Writing E.Y.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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RESEARCH ARTICLE

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Prevalence and Microbial Etiology of Catheter-Related Bloodstream Infections in a University Hospital in North Cyprus: A Retrospective Study

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Abstract

BACKGROUND/AIMS: This study aimed to determine the incidence of central venous catheter-related bloodstream infections (CRBSI) and to identify specific pathogens in three intensive care units (ICUs) at a university hospital in North Cyprus during 2022-2023.

MATERIALS AND METHODS: A retrospective investigation was conducted using data collected from medical records via the electronic information system. The records provided details on patient demographics, incidence density rates, microbial isolates, and resistance profiles within the ICUs.

RESULTS: In total, 48 cases were analyzed. The overall CRBSIs incidence density was 17.2 per 1000 catheter days. The General ICU had the highest CRBSI incidence at 30.2 per 1,000 catheter days, whereas the Cardiovascular Surgery ICU recorded 0.0 per 1000 catheter days. Among the 48 cases, a total of 49 bacterial isolates were identified, including one case with dual bacterial strains. *Klebsiella pneumoniae* was the leading causative agent, found in 16 isolates (32.7%), followed by *Staphylococcus epidermidis* in 10 isolates (20.4%). Of the 49 bacterial isolates, resistance was observed in 35. Extended-spectrum beta-lactamase production was detected in 12 (24.5%) *K. pneumoniae* isolates, 3 (6.1%) *Proteus mirabilis* isolates, and 1 (2.0%) *Escherichia coli* isolate. In addition, methicillin resistance was noted in 10 *S. epidermidis* (20.4%), 7 *Staphylococcus haemolyticus* (14.3%), and 2 *Staphylococcus hominis* (4.1%) isolates.

CONCLUSION: These findings support continued implementation of protective and preventive measures in hospital ICUs for effective CRBSI management.

Keywords: Catheter-related bloodstream infections, central venous catheter, intensive care units

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INTRODUCTION

Catheter-related bloodstream infections (CRBSIs) continue to be a major problem in healthcare institutions due to their association with increased rates of hospitalization, death, and the high costs related to healthcare.[1] According to recent research, individuals who have either a central venous catheter (CVC) or peripheral venous catheter (PVC) are at risk of central line-associated bloodstream infections or peripheral line-associated bloodstream infections, respectively.[2,3]

Various risk factors are linked to the occurrence of CRBSIs. These include the patient's age, pre-existing medical conditions, and variables related to the catheter itself, such as material, type, insertion location, and length of use.[4,5] Despite numerous preventive methods employed by health institutions to mitigate these risks, clinical data still indicate that a significant proportion of CRBSIs are linked to the use of catheters (CVC and PVC).[6]

The persistence of CRBSIs, despite advanced preventive technologies and protocols, underscores the need for ongoing research into both the epidemiological trends and the effectiveness of different prevention strategies across various clinical settings. Studies have shown that while overall rates of CRBSIs have declined due to infection control measures, certain populations within hospital settings, such as intensive care unit (ICU) patients, remain at high risk. This suggests that factors specific to different ICU environments might influence infection rates, necessitating tailored approaches to infection control.[7]

Moreover, the microbiological landscape of CRBSIs has evolved, with shifts in the prevalence of pathogens and their resistance patterns posing new challenges for treatment and management. The shifts in the prevalence of antibiotic-resistant organisms further complicate the clinical management of these infections, making the timely and accurate identification of causative agents and their susceptibility patterns critical for effective treatment.[8]

Given these challenges, this study aimed to investigate the incidence density of CRBSIs within the general, coronary, and cardiovascular surgery ICUs in a hospital during 2022-2023.

MATERIALS AND METHODS

Ethical Considerations

This study was carried out with the approval of the Near East University Scientific Ethics Committee (approval number: 2023/115, date: 21.06.2023).

Study Design and Setting

This retrospective study was conducted at a University Hospital in North Cyprus, focusing on the incidence of CRBSIs within the ICU departments (general ICU, coronary ICU, and cardiovascular surgery ICU) throughout the years 2022 to 2023.

Participants

The study population comprised adult patients (≥18 years) who were admitted to the ICUs with CVCs inserted. Patients were included if they developed CRBSIs during their ICU stay, as defined by the Centers for Disease Control and Prevention guidelines for diagnosing CRBSIs.[9]

Data Collection

Data were retrospectively collected from electronic medical records, including patient demographics (age, gender), CVC details (type, insertion site, duration), and laboratory results. CRBSIs were identified based on positive blood culture results obtained from samples drawn from peripheral veins and the catheter, in conjunction with clinical signs of infection.

Statistical Analysis

All analyses were performed using descriptive statistical methods. Incidence density rates of CRBSIs were calculated as the number of CRBSI episodes per 1,000 catheter days. Descriptive statistics were used to summarize patient demographics and CVC characteristics, expressing categorical variables as frequencies (n) and percentages (%), and continuous variables (e.g., age) as means ± standard deviation, and medians (minimum-maximum) where appropriate. The standardized infection ratio (SIR) was calculated by dividing the observed number of infections by the predicted number of infections, in line with established national benchmarks.

RESULTS

Demographics

During the study period, 48 cases of CRBSIs were identified among ICU patients. The mean and median ages of the patients were 72.00±11.18 and 74.00 (range: 40.00-89.00), respectively. Male patients were predominant (60.4%).

Incidence

Case Distribution

General intensive care unit: Of the 48 cases of CRBSIs identified during the study period, the general ICU reported the highest number of cases (n=35), accounting for 72.9% of all cases.

Coronary intensive care unit: The coronary ICU reported 13 CRBSI cases, comprising 27.1% of total cases.

Cardiovascular Surgery: the cardiovascular surgery ICU reported no CRBSI cases (Figure 1).

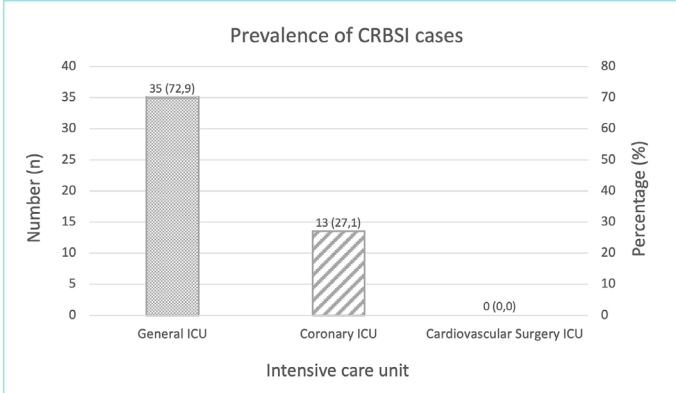

Figure 1. Prevalence of catheter-related bloodstream infections cases in the intensive care units of a New East University Hospital, 2022-2023.

CRBSI: Catheter-related bloodstream infections, ICU: Intensive care unit.

Incidence Density Rates

General intensive care unit: The general ICU had a total of 1,159 CVC days with an incidence density of 30.2 per 1,000 catheter days.

Coronary intensive care unit: With 1,362 CVC days recorded, the incidence density in the coronary. The rate of infection in the ICU was 9.5 per 1,000 catheter days.

Cardiovascular surgery: There were 296 CVC days with no CRBSIs, resulting in an incidence density rate of 0.0 per 1,000 catheter days (Figure 2).

Standardized Infection Ratio

General intensive care unit: The SIR for the general ICU was 7.0, calculated from 35 observed infections against 5 predicted infections.

Coronary intensive care unit: The SIR for the coronary ICU was 2.6, with 13 observed infections compared to 5 predicted infections.

Cardiovascular surgery: The SIR was 0.0, with no observed infections against a predicted 5 infections (Figure 2).

Yearly Overall Incidence Results

Overall, there were 25 CRBSIs in 2022, for a total of 1,319 CVC days and this resulted in a CRBSI incidence density of 18.9 per 1,000 catheter days. In 2023, 23 cases of CRBSI were recorded for a total number of 1,418 CVC days, resulting in a CRBSI rate of 15.5 per 1,000 catheter days. This gave a cumulative duration of 2,737 CVC days and an overall incidence density or rate of CRBSIs of 17.2 per 1,000 catheter days. The overall SIR across all ICUs was 9.6, with 48 observed infections against 5 predicted infections (Figure 3).

Microbial Etiology

In the analysis of CRBSI cases, a total of 49 bacterial isolates were identified. Among these, gram-negative bacteria comprised more than half of the isolates (n=26; 53.1%), with *Klebsiella pneumoniae* being the predominant pathogen (n=16; 32.7%) (Figure 4). On the other hand, gram-positive bacteria accounted for a significant portion (n=23; 46.9%), with *Staphylococcus epidermidis* emerging as the most common gram-positive bacterial isolate (n=10; 20.4%) (Figure 5).

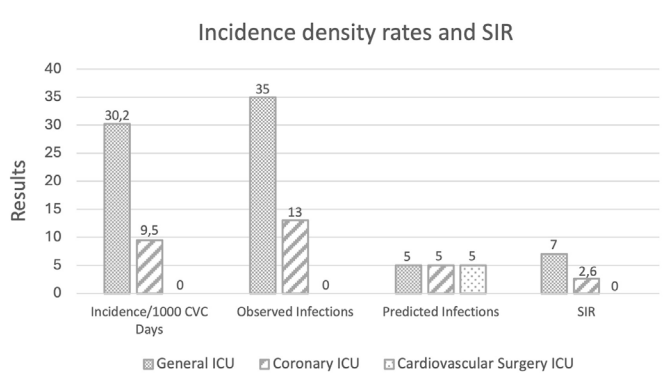

Figure 2. Incidence density rates and standardized infection ratios of catheter-related bloodstream infections at the New East University Hospital, 2022-2023.

SIR: Standardized infection ratio, CVC: Central venous catheter, ICU: Intensive care unit.

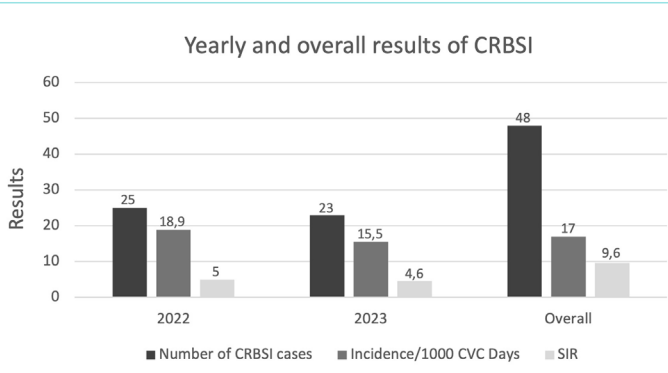

Figure 3. Yearly and overall results of catheter-related bloodstream infections at the New East University Hospital, 2022-2023.

CRBSI: Catheter-related bloodstream infections, CVC: Central venous catheter, SIR: Standardized infection ratio.

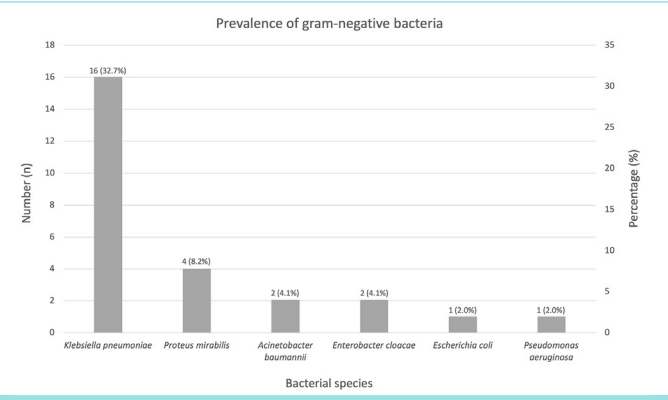

Figure 4. Prevalence of gram-negative bacteria isolated from catheter-related bloodstream infections at the New East University Hospital, 2022-2023.

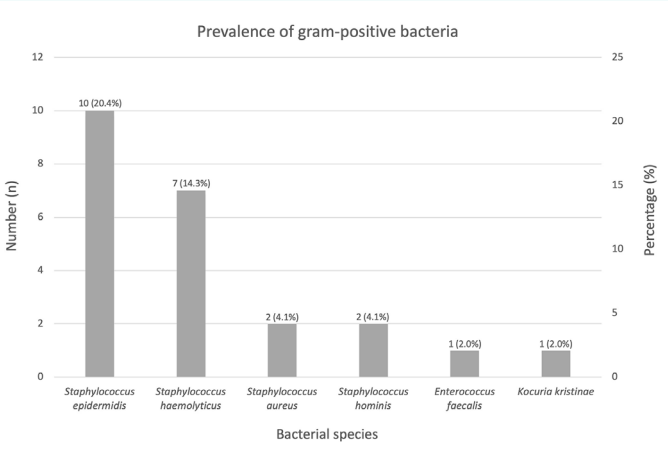

Figure 5. Prevalence of gram-positive bacteria isolated from catheter-related bloodstream infections at the New East University Hospital, 2022-2023.

Antimicrobial Resistance Patterns

Among the 49 bacterial isolates identified, 35 were resistant, categorized as either extended-spectrum beta-lactamase (ESBL) producers, or methicillin-resistant staphylococci. Of these resistant isolates, 16 (32.7%) were ESBL producers, with *K. pneumoniae* being the most prevalent among them (n=12; 24.5%) (Figure 6). On the other hand, methicillin resistance was detected in 19 (38.8%) of the coagulase-negative staphylococci, with *S. epidermidis* being the most affected (n=10; 20.4%) bacterial species (Figure 7). In this study, methicillin-resistant *Staphylococcus aureus* was not isolated from the patients.

DISCUSSION

The study presented here, documented the incidence density of CRBSIs to be 17.2 per 1,000 catheter days. The incidence density reported in this study is higher than that noted in prior research, including the rates of 5 per 1,000 catheter days and 3.52 per 1,000 catheter days reported by Abd El-Hamid El-Kady et al.[10] and Zhang et al.[11], respectively. In the present study, a peak incidence density of 18.9 per 1,000 catheter days was observed in 2022, albeit with a subsequent decline to 15.5 per 1,000 catheter days in 2023. This aligns with findings from Zhong et al.[12]

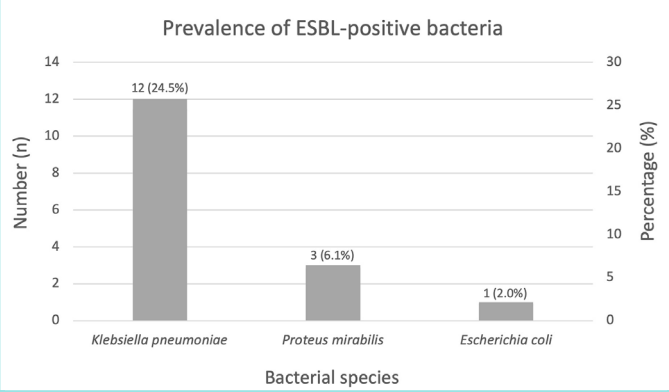

Figure 6. Prevalence of extended-spectrum beta-lactamase (ESBL)-positive bacteria isolated from catheter-related bloodstream infections at the New East University Hospital, 2022-2023.

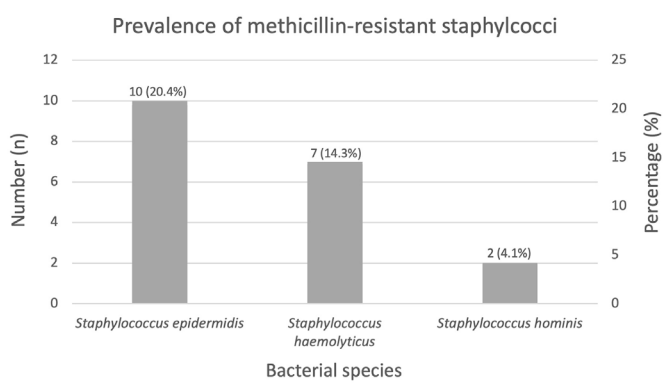

Figure 7. Prevalence of methicillin-resistant staphylococci (MRS) isolated from catheter-related bloodstream infections at the New East University Hospital, 2022-2023.

*No methicillin-resistant *Staphylococcus aureus* isolate was identified in this study.

and Drugeon et al.[13] highlighting the vulnerability of elderly patients due to diminished immune responses, leading to prolonged ICU stays and recovery periods. Moreover, the study population in our research predominantly comprised males, a demographic characteristic that aligns with other studies.[14]

The disparity in CRBSI incidence density between different ICU units, notably between the general ICU and the cardiovascular surgery ICU, may be influenced by several factors. A study by Pronovost et al.[15] showed that targeted infection control interventions can significantly reduce CRBSI rates. In environments like the general ICU, where a variety of invasive procedures are common, the potential for infection might be elevated, thereby increasing CRBSI rates. In contrast, the cardiovascular surgery ICU might exhibit lower or non-existent CRBSI rates as in our study. This lower incidence can be attributed not just to the adherence to strict infection control protocols but also to the relatively low number of patients admitted to this unit, as evidenced by the notably fewer CVC days (296 over the study period). The reduced patient turnover in this specialized unit likely contributes to lower rates of infection, highlighting the impact of patient number on CRBSI rates.

The study identified 49 bacterial isolates associated with CRBSIs, predominantly gram-negative bacteria, with *K. pneumoniae* emerging as the most frequent pathogen. This aligns with the findings of Zhang et al.[11], but contrasts with other reports where Gram-positive bacteria like *S. epidermidis* were more prevalent.[16,17] Notably, *S. epidermidis* was identified as the most common gram-positive isolate in our study, consistent with its known prevalence in CRBSIs, as reported in the literature, often due to its biofilm-forming capabilities, which enhance its persistence on indwelling medical devices.[18]

In the present study, an uncommon gram-positive isolate, *Kocuria kristinae*, was also detected. Although rare, its presence in CRBSIs was documented previously.[19] The characteristics of *K. kristinae*, including its resistance to antibiotics, underline the need for further study in clinical settings.

The observed antimicrobial resistance patterns showed a significant presence of ESBL-producing and methicillin-resistant isolates. *K. pneumoniae* was the most common ESBL producer. The rates of ESBL positivity and methicillin resistance in our study are consistent with increasing trends noted in recent literature; however, the ESBL rate found in the present study is higher than earlier findings.[20] Unlike the previous study, the present report included the patients from the ICU departments; therefore, this explains the increased resistance rates in this study. Yet, the present findings suggest that infection control practices should be continuously implemented in healthcare settings.

Study Limitations

This study was carried out in a single hospital, which may limit how well the results apply to other healthcare settings with different types of patients, infection control practices, or resistance patterns. Additionally, we did not perform molecular testing to identify resistance genes or assess the ability of bacteria to form biofilms. In addition, important risk factors like patient health conditions and previous use of antibiotics were not thoroughly examined.

CONCLUSION

In conclusion, the elevated rates of incidence density and SIR underscore the necessity for preventive measures and continuous monitoring of antimicrobial resistance in the ICU. Our findings highlight the need for more comprehensive studies that search for the molecular characteristics of the bacterial agents isolated from the CRBSIs, particularly in critical healthcare settings.

MAIN POINTS

- The study retrospectively analyzed 48 cases of catheter-related bloodstream infections (CRBSIs) in intensive care unit (ICU) patients during 2022-2023, with an overall incidence density of 17.2 per 1,000 catheter days.
- The General ICU exhibited the highest CRBSI incidence (30.2 per 1,000 catheter days), whereas the Cardiovascular Surgery ICU reported no infections.
- *Klebsiella pneumoniae* (32.7%) was the leading pathogen, followed by *Staphylococcus epidermidis* (20.4%), indicating a diverse microbial etiology.
- High rates of antimicrobial resistance were observed, with *K. pneumoniae* (n=12; 24.5%) having the highest number of extended-spectrum beta-lactamase positive isolates and *Staphylococcus epidermidis* (n=10; 20.4%) having the highest number of methicillin resistant isolates.
- These findings underscore the critical need for continuous and targeted infection control measures in ICU settings to effectively manage and prevent CRBSIs.

ETHICS

Ethics Committee Approval: This study was carried out with the approval of the Near East University Scientific Ethics Committee (approval number: 2023/115, date: 21.06.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: A.P.P.T., H.K.S., E.R., Design: H.C.Y., H.K.S., E.R., Data Collection and/or Processing: S.S.S., H.C.Y., A.T., M.Y., Analysis and/or Interpretation: A.P.P.T., S.S.S., H.C.Y., H.K.S., E.R., Literature Search: A.P.P.T., S.S.S., A.T., M.Y., E.R., Writing: A.P.P.T., S.S.S.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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RESEARCH ARTICLE

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Medical Device-Related Pressure Injuries: Knowledge Levels of Nurses and the Affecting Factors

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Abstract

BACKGROUND/AIMS: This study aimed to determine nurses' knowledge of pressure injuries caused by medical devices and the factors that influence this level of knowledge.

MATERIALS AND METHODS: This was a cross-sectional descriptive study. The study sample consisted of 252 nurses. Data were collected using face-to-face and online data collection methods with the medical device-related pressure injuries knowledge questionnaire.

RESULTS: The mean total score obtained by nurses on the medical device-related pressure injuries knowledge was below 70%, indicating a generally insufficient level of knowledge. The sub-domain "prevention and treatment" was rated with the highest percentage of correct answers, 67.87% (10.86±2.43). The "staging" subdomain had the lowest percentage of correct responses with 31.87% (0.956±0.715). It was determined that age (p=0.001), gender (p=0.025), and working shift in the clinic (p=0.006) affected the total score average of the medical device-related pressure injury knowledge level.

CONCLUSION: The issue of pressure injuries related to medical devices should be given more attention in nursing education.

Keywords: Medical device, pressure injuries, nursing, knowledge

INTRODUCTION

Advances in technology and the increased use of medical devices as an integral part of care have resulted in an increase in the number of incidents of medical device-related pressure injury (MDRPI) in recent years.[1] MDRPI is a localized injury to the skin and tissues caused by the continuous pressure exerted by medical devices used for diagnosis or treatment.[2] MDRPI was first defined in the National Pressure Ulcer Advisory Panel guideline in 2016 and has been effective in increasing awareness of MDRPI.[3]

Pressure injuries caused by medical devices account for over 30% of the total number of pressure injuries in hospitals.[4] It has been found that patients with medical devices are more likely to develop a pressure injury than those without.[5] In one study, the reported frequency and the prevalence of pressure injuries caused by medical devices were 12% and 10%, respectively.[6] In a systematic review of thirteen studies, it was found that the incidence of MDRPI in the intensive care unit (ICU) ranged from 0.9% to 41.2%, and the prevalence ranged from 1-1.4% to 121%.[7] In another study, it was observed that MDRPI occurred seven times more frequently than normal pressure injuries.[8]

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Pressure injury observed in patients causes deterioration in quality of life, increased care costs, and increased mortality and morbidity. Nurses have an important role to play in detecting patients at high-risk of pressure injuries from medical devices and reducing complications.[9] Zang et al.[10] study of critical care nurses' knowledge, attitudes, and practices of MDRPI found that the nurses' acquired knowledge, attitudes, practical skills are at an acceptable level, and that nurses' practices increased with more hours worked in intensive care. The study by Sönmez and Bahar[11] examined the MDRPI knowledge level of nurses and the factors affecting it. It was found that nurses' level of knowledge was inadequate and was influenced by the gender of the nurse, their experience working in the ICU, the frequency of MDRPIs, prior education about these injuries. In a systematic review conducted by Fang et al.[12], it was found that nurses' attitudes towards MDRPI prevention were positive, and their knowledge and practices were insufficient. It was found that nurses' knowledge, attitudes and practices on MDRPI prevention were affected by education level, work experience, having received previous training on MDRPI, caring for MDRPI patients, being a specialist nurse in the ICU, working in tertiary hospitals, and having a wound care certificate.

The limitations of studies assessing nurses' knowledge, perceptions, and experiences of pressure injuries from medical devices prevent the planning of effective interventions in nurse education and clinical practice.[13] It is important to identify the factors that influence nurses' knowledge levels and clinical practice skills in the care and prevention of pressure injuries from medical devices. In this context, not only are the knowledge level of nurses important, but the factors affecting their knowledge level are also crucial in terms of planned practices to prevent pressure injury. After the pressure injury prevention assessment, the identification of patients at risk and the development of a prevention plan will contribute to a healthy solution of the problem.[14] This study differs from previous studies in that it examines the knowledge and attitudes of nurses working in different clinical settings regarding MDRPI. It was also conducted in a different geographical context. It is believed that the results of this study, by highlighting similarities and differences with the literature, will guide the implementation of clinical studies on nurses' knowledge and attitudes towards MDRPI and aid in educational planning.

Nurses play an active role in patient care in wards and ICUs, providing treatment to patients with pressure injuries from medical devices and those patients at risk. Nurses' knowledge plays a key role in preventing pressure injuries associated with medical devices. As pressure injury resulting from medical devices differs from pressure injury due to other causes, it is believed that the assessment of nurses' knowledge levels and factors influencing pressure injury resulting from medical devices will contribute to the planning of in-service training to meet their needs, the development of preventive protocols, and the literature. This study aimed to assess knowledge of pressure injuries caused by medical devices among nurses working in different clinics, and the factors influencing it.

Research Questions

1. What is the level of knowledge of nurses about pressure injuries related to medical devices?

2. What are the factors affecting nurses' level of knowledge about pressure injuries related to medical devices?

MATERIALS AND METHODS

Desing

This study uses a descriptive cross-sectional research design.

Sample

The population of the study consisted of 375 nurses working in internal medicine (neurology, cardiology, oncology, chest clinics), surgery (neurosurgery, general surgery, orthopedics, cardiovascular surgery, urology, emergency) and intensive care (general intensive care, cardiology intensive care, neurology intensive care, neonatal intensive care) clinics of two state hospitals in North Cyprus. There was no sample selection in the study; it was conducted on the population. The study sample consisted of 252 nurses who met the inclusion criteria and who agreed to participate. Inclusion criteria were working in internal medicine, surgery and intensive care and accepting to participating in the study. The exclusion criterion; is working in clinics providing outpatient clinic services. The rate of reaching the population in the study is 67.2%.

After obtaining the relevant institutional and board permissions, the study was carried out with nurses who work in the Dr. Burhan Nalbantoğlu State Hospital and Famagusta State Hospital State Hospitals between October 2022 and November 2023. There was no protocol in the hospital to identify and prevent risk factors for pressure injury due to medical tools and equipment.

Data Collection

The researcher collected the data using face-to-face and online data collection methods. In face-to-face data collection, nurses working in the relevant clinics were informed about the research. Data collection forms were distributed to those whose informed consents were obtained, and the forms were collected after they were answered. Participants took an average of 20-25 minutes to answer the questionnaires. In online data collection, a Google Forms link was sent via e-mail to nurses who could not be reached in face-to-face data collection. The data collection forms used in the study were transferred to Google Forms. Participants were prevented from switching to the next question without answering the current question to ensure the data was completed in the online data collection form. In the online data collection form, informed consent was first obtained from the nurses participating in the study, after which the research questions were answered.

Nurse Information Form

This form was designed by Bahar and Sönmez.[11] and has contained a total of 22 questions.

The first 10 questions of the nurse information form include the sociodemographic characteristics of the nurses, and questions 11 and 12 include professional qualifications, practices to prevent pressure injury related to medical tools and equipment, and educational status.

Medical Device-Related Pressure Injuries Knowledge Questionnaire

The content validity index of the MDRPI knowledge questionnaire (MDRPI-KQ) was 0.99. The Kuder-Richardson internal consistency coefficient (KR_20) was 0.85611. The questionnaire consists of 36 items and four subdomains. From a total of 36 statements in the questionnaire, 20 were positive and 16 were negative. Each statement

in the knowledge assessment form is answered as "true", "false or no idea". The correct answers are each scored as 1, and the incorrect and "no idea" answers are given a score of 0. The total score that can be calculated from the information form ranges between 0 and 36. The increased mean score derived from the questionnaire indicated that the nurses' knowledge of MDRPI had increased. The percentage of correctly answered questions is calculated by dividing the number of correctly answered questions by the total number of questions, and then multiplying by 100. A 70% correct score (25.2 points) is accepted as the cut-off point. The knowledge questionnaire is interpreted as unsuccessful if the percentage of correctly answered questions is less than 70%, between 70% and 79.9% as "moderate level", between 80% and 89.9% (between 28.8 and 32.4 points) as "good level", and above 90% (above 32.4 points) as "very good level".

Statistical Analysis

The data from the study were analysed using the SPSS 22.0 software package (IBM Corp., Armonk, NY). The normality of data (one-sample Kolmogorov-Smirnov test) was tested to determine whether the study data had normal distribution characteristics. It was seen that the data obtained from the measurement tools used in the study did not exhibit a general distribution. The "Mann Whitney U test" was used for the comparison of paired groups, and the "Kruskal-Wallis H test" was used for the comparison of three or more groups. When the results of the "Kruskal-Wallis H test" were significant, the the "Mann Whitney U test" technique was used to determine between which groups significant differences existed. Bonferroni correction was applied when there was a significant difference between two groups. In addition, Spearman's rho correlation coefficient technique, which is the non-parametric equivalent of Pearson's product correlation coefficient, was used to compare continuous variables.

Ethical

This study was approved by the Ethics Committee of Dr. Burhan Nalbantoğlu State Hospital (approval number: 65/22, date: 23.05.2023), and informed consent was obtained from the nurses participating in the study.

RESULTS

Sociodemographic and Professional Characteristics of Nurses

The average age of the nurses participating in the study was 34.61±7.44 years and the mean number of years of employment as a nurse was 11.72±7.49. It was found that 68.7% of the nurses were undergraduate graduates, 48.4% worked in the ICU, and 91.3% worked in day and night shifts (insert Table 1).

The mean duration of employment (years) of the nurses who participated in the study was 11.72±7.49, and the mean weekly working time (hours) was 40.93±6.82. It was found that 92.1% of the nurses did not receive training on pressure injury related to medical devices, 92.1% did not attend in-service training on MDRPI, and 38.5% frequently encountered a patient with MDRPI. It was found that 28.3% of nurses received information on MDRPI prevention and treatments during their nursing education, 97.6% of them thought that a care protocol was needed to prevent MDRPI, 73.4% of them had quite sufficient knowledge about MDRPI, and 97.2% of them wanted to participate in training on MDRPI.

Medical Device-Related Pressure Injury Knowledge and Influencing Factors

The mean MDRPI-KQ total score for nurses was 22.11±3.83, and when analysing the subdomains, it was found that the highest average score of the preventing and treating subdomain was 10.86±2.43 the lowest average score for the staging subdomain was 0.956±0.715. (insert Table 2). The highest correct response in the MDRPI-KQ was 96% for Q27, while the lowest was 18.7% for Q15 (insert Table 3).

A statistically significant difference was found between the MDRPI-KQ total score of the nurses participating in the study and the mean scores of the diagnostic and risk factors subdomains, as well as regarding gender, working status in the clinic, ($p<0.05$, Table 1). It was found that the difference among nurses' age, educational status, working hours, working clinic, and MDRPI-KQ total score and sub-dimensions was statistically significant ($p<0.05$; Table 1).

There was a significantly weak negative correlation between the age of the nurses and the years of employment, the staging subdomains mean scores (r=-0.139; p=0.028; r=-0.140; p=0.027), between weekly work time (hours) and the total knowledge score of the risk factor subdomain (r=-0.193, p=0.002) (insert Figure 1).

DISCUSSION

Although pressure injuries due to medical devices occur at certain intervals in nursing care services, they are usually preventable with holistic nursing care.[13] In this context, it is important for the quality of care to determine the level of knowledge and influencing factors of nurses for the prevention of pressure injuries due to medical devices

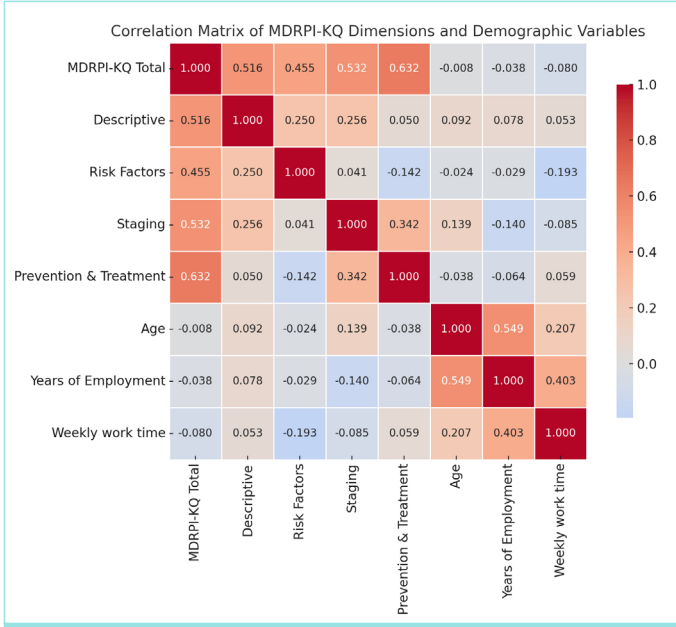

Figure 1. Analysis of the correlation coefficients between the sub-dimensions of the MDRPI-KQ and average total score and age, years of employment in the profession and weekly working hours.

*Correlation is significant at the 0.05 level (2-tailed). **Correlation is significant at the 0.01 level (2-tailed). r: Spearman correlation coefficient. MDRPI-KQ: Medical device-related pressure injury- knowledge questionnaire.

and the application of the most ideal care to the patient during the treatment period.

The study found that nurses were insufficiently knowledgeable about MDRPI, and their knowledge level was below the acceptable limit (≥70%). In general, the level of MDRPI prevention knowledge among nurses is inadequate to moderate.[11,15,16] In a systematic review by Fang et al.[12] investigation of nurses' knowledge, attitudes and practices with regard to MDRPIs, it was found that while nurses generally had a positive attitude, their knowledge and practices were inadequate. In this study, it was found that most nurses did not receive any formal training on MDRPIs. Similarly, in the literature, it is seen that nurses working in the clinic do not receive training on MDRPI and that professional and continuous training is insufficient.[10,17,18] In this context, the study results show that there is a need for nurses to be trained in pressure injuries according to the literature. Lack of knowledge and awareness of nurses about MDRPIs may lead to increased incidence of MDRPIs and negative patient outcomes due to failure to adopt prevention strategies.[19] This is supported by the evidence that the majority of nurses felt that their existing knowledge of MDRPIs was not adequate and stated a need for more training in this area.

Another important finding of this study was that the nurses' score in the "stagings" subdomains of the questionnaire was the lowest score compared to the total score of the MDRPI knowledge level questionnaire and other subdomains According to the National Pressure Injury Advisory Panel (NPIAP pressure ınjury stages), it is recommended that MDRPIs should be staged using the pressure injury staging system.[20]

Mucosal pressure injuries (MMPIs) are seen in mucous membranes with a history of using a medical device at the site of injury. Due to the anatomy of the tissue, these ulcers cannot be staged. Therefore, it is recommended to differentiate between general pressure ulcers and

Table 1. Nurses' knowledge scores according to their demographic and professional characteristics (n=252)

Characteristics	Groups	n (%)	MDRPI-KQ**	D	R	S	P/T
			Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Gender	Female	200 (79.4)	19.87±4.04	4.94±1.39	3.28±1.44	0.93±0.75	10.73±2.58
	Male	52 (20.6)	21.08±2.76	5.06±1.38	3.56±1.55	1.08±0.55	11.38±1.69
	p(α)		0.025*	0.453	0.340	0.101	0.137
Working status in the clinic (title)	Department nurse	242 (96.0)	20.13±3.83	4.93±1.39	3.38±1.46	0.96±0.71	10.87±2.39
	Chief nurse	10 (4.0)	19.70±4.22	5.90±0.57	2.30±1.06	0.80±0.79	10.70±3.50
	p(α)		**0.860**	**0.001***	**0.009***	**0.479**	**0.805**
	Groups	**n (%)**	**M (min.-max.)**	**M (min.-max.)**	**M (min.-max.)**	**M (min.-max.)**	**M (min.-max.)**
Age	22-29[1]	77 (30.6)	21.0 (8-32)	5.0 (0-9)	3.0 (0-6)	1.0 (0-3)	11.0 (0-16)
	30-39[2]	112 (44.6)	20.0 (2-36)	5.0 (0-9)	3.0 (0-8)	1.0 (0-3)	11.0 (0-16)
	40-49[3]	45 (17.9)	21.0 (10-27)	5.0 (0-8)	3.0 (1-7)	1.0 (0-3)	11.0 (7-15)
	50-59[4]	18 (7.1)	17.0 (15-22)	5.0 (4-7)	2.0 (2-6)	0.0 (0-1)	9.0 (7-11)
	p(β)		**0.001*** (1-4.2-4.3-4)	**0.042*** (3-1.3-2)	**0.681**	**0.001*** (1-4.2-4.3-4)	**0.000*** (1-4.2-4.3-4)
Education	Associate degree[1]	10 (4.0)	21.0 (10-27)	7.0 (0.0-7)	3.5 (1-5)	1.0 (0.0-2)	10.5 (8-13)
	Bachelor's degree[2]	173 (68.7)	20.0 (2-36)	5.0 (0.0-9)	3.0 (0.0-8)	1.0 (0.0-3)	10.0 (0.0-16)
	Postgraduate degree[3]	69 (27.4)	20.0 (11-25)	5.0 (2-7)	2.0 (1-7)	1.0 (0.0-2)	12.0 (2-16)
	p(β)		**0.573**	**0.003*** (1-2. 1-3)	**0.000*** (2-3)	**0.216**	**0.000*** (2-3)
Clinic currently worked in	Internal services[1]	50 (19.8)	21.0 (2-36)	5.0 (0-9)	3.0 (0-8)	1.0 (0-3)	11.0 (0-16)
	Surgical units[2]	42 (16.7)	20.5 (9-27)	5.0 (1-7)	4.0 (2-7)	1.0 (0-2)	10.0 (0-15)
	Intensive care units[3]	122 (48.4)	20.0 (8-32)	5.0 (1-9)	3.0 (1-7)	1.0 (0-2)	11.0 (0-16)
	Emergency department[4]	38 (15.1)	20.0 (8-25)	5.0 (0-8)	4.0 (0-6)	1.0 (0-3)	10.0 (7-16)
	p(β)		**0.491**	**0.366**	**0.000*** (2-3)	**0.856**	**0.000*** (1-2.3-2.3-4)
Working shift	Days only[1]	21 (8.3)	17.0 (10-24)	5.0 (1-7)	2.0 (2-5)	0.0 (0-2)	9.0 (4-14)
	Nights only[2]	1(0.4)	20.0 (20-20)	5.0 (5-5)	5.0 (5-5)	0.0 (0-0)	10.0 (10-10)
	Days and nights[3]	230 (91.3)	20.0 (2-36)	5.0 (0-9)	3.0 (0-8)	1.0 (0-3)	11.0 (0-16)
	p(β)		**0.006*** (3-1)	**0.937**	**0.001*** (3-1)	**0.000*** (3-1)	**0.026*** (3-1)

*p<0.05 statistically significant difference; p(α): Mann-Whitney U test; p(β): Kruskal-Wallis H test.
**Medical device-related pressure injuries knowledge questionnaire (MDRPI-KQ).
D: Description, R: Risk factors, S: Staging, P/T: Prevention and treatment, SD: Standard deviation, Min.: Minimum, Max.: Maximum.
Analysis of variance; all descriptive statistics are expressed as arithmetic mean ± standard deviation; M: median (min.-max.).

Table 2. MDRPI knowledge questionnaire mean scores of nurses (n=252)

MDRPIs	Mean ± SD	Median (min.- max.)	Percentage of correct answers %
Total score	20.11±3.83	20.00 (2.00-36.0)	55.87
Description score (9 items)	4.96±1.38	5.00 (0.00-9.00)	55.16
Risk factors score (8 items)	3.33±1.46	3.00 (0.00-8.00)	41.66
Staging score (3 items)	0.956±.715	1.00 (0.00-3.00)	31.87
Prevention and treatment (16 items)	10.86±2.43	11.00 (0.00-16.0)	67.87

MDRPI: Medical device-related pressure injuries, SD: Standard deviation, Min.: Minimum, Max.: Maximum.

MMPIs caused by medical devices. It is thought that the nurses' low level of knowledge about the staging of MDRPIs is due to their low level of knowledge about MDRPIs.

In this study, it was determined that the highest rate of correct answers to the questions with correct answers in the MDRPI was in the "prevention and treatment" subdomains, and the lowest rate of correct answers in the "risk factors" subdomains. Similarly, Sönmez and Bahar[11] found in their study that the nurses' highest rate of correct answers to the questions with correct answers in MDRPI was in the "prevention and treatment" subdomains and the lowest rate of correct answers was in the "risk factors" subdomains. Nursing care is important in preventing pressure injury caused by medical devices and nurses take responsibility in this regard. However, the lack of multidisciplinary work is an obstacle in preventing pressure injuries from medical devices, necessitating combined efforts and teamwork to contribute to successful care. Although MDRPI prevention practices are an integral part of nursing, it is recognized that it is not only the responsibility of nurses and that quality care will be provided if other health professionals contribute. The study shows that nurses have knowledge gaps concerning MDRPI, as the item to which nurses gave the most incorrect answers was related to the risk factors that cause the development of MDRPI. At the same time, the findings of the study support the idea that the frequency of nurses' encounters with a patient with MDRPI affects their level of knowledge about identifying risk factors. This finding shows the importance of focusing on risk factors in training programmes.

In the study, it was determined that nurses' "general" and "overall" scores of the pressure sore knowledge scale related to medical tools and equipment affected the variables of age, gender and clinical working shift, the difference between the general scores of the scale and the mean scores of the variables of age, gender and clinical working shift was statistically significant, and the level of knowledge decreased with increasing age. Similarly, Sönmez and Bahar found that the "general" scores of the pressure sore knowledge scale "general" scores of nurses related to medical tools and equipment were affected by the age variable and the difference between the mean scores of the age groups was statistically significant. In the study conducted by Dalli and Girgin[19], it was reported that the difference between the mean general scores of the scale belonging to the variables of age, gender, education status, the clinic where they are currently working, the status in the clinic, and the working shift in the clinic was statistically significant. According to these findings, it is thought that sociodemographic variables and some clinical characteristics should also be taken into consideration in training and other interventions to increase nurses' knowledge of pressure injury due to medical devices and equipment. In the study, the prevention and treatment subdomain scores of nurses working in surgical clinics were lower than those of nurses working in internal services and ICUs, and their risk factors sub-dimension scores were higher than those of nurses working in these clinics. In a systematic review conducted by Parvizi et al.[16], it was found that knowledge of pressure injuries caused by medical devices is limited and is affected by factors such as age, gender, education level, working status in the clinic, and type of service. Another systematic review determined that nurses' knowledge and practices regarding pressure injuries caused by were affected by variables such as age, gender, education level, working status, and the clinic where they worked.[12] While nurses working in surgical clinics have higher levels of knowledge about the risk factors of pressure injuries due to medical devices and equipment, their knowledge about prevention is lower than in other clinics. This suggests that their interventions for clinical practice are insufficient and that there is a need to address their educational needs and awareness. It is recommended to develop strategies to improve nurses' knowledge and practices in the prevention of pressure injuries related to medical tools and equipment.

It was found that as the age and working years of the nurses increased, the average scores of the staging subdomain of the pressure injury knowledge scale, which is related to medical tools and equipment, decreased. Additionally, the risk factors sub-dimension knowledge scores decreased as the weekly working hours increased. In contrast to these findings in the literature, it has been found that knowledge scores are higher for nurses who are older and have a longer continuous work experience. This contradiction could be explained by knowledge attrition over time, especially in the absence of regular refresher training on updated guidelines. Additionally, burnout, which disproportionately affects experienced nurses in high-demand settings such as ICUs, may diminish motivation to engage in continuous learning or pay attention to evolving practices. Another contributing factor may be reliance on outdated protocols or routines that are no longer aligned with current evidence-based practices, particularly if institutional support for ongoing professional development is limited. These results emphasise the necessity for regular, compulsory ongoing training courses for all staff, including those with experience, to keep up to date with their skills, particularly in areas such as MDRPI prevention, where there is ongoing technological development and new risks related to devices.

Table 3. Nurses' knowledge about MDRPIs (n=252)		
Knowledge items	**True**	**False**
	n (%)	**n (%)**
Dimension 1: description		
1- MDRPIs are pressure injuries caused by medical devices and equipment. (T)	231 (91.7)*	21 (8.3)
2- MDRPIs are caused by constant pressure or friction due to medical devices. (T)	230 (91.3)*	22 (8.7)
3- MDRPIs constitute approximately 1/3 of all pressure injuries that may occur in the hospital environment. (T)	178 (70.6)*	74 (29.4)
4- In MDRPIs. the tissue around or under the device and equipment takes the shape of the device. (T)	227 (90.1)*	25 (9.9)
5- The source of pressure in MDRPIs is the medical device itself. (T)	185 (73.4)*	67 (26.6)
6- MDRPIs usually occur in areas with bony prominences. (F)	104 (41.3)	148 (58.7)*
7- MDRPIs are simple wounds and do not cause serious complications. (F)	30 (11.9)	222 (88.1)*
8- MDRPI is most common in the sacrum. (F)	35 (13.9)	217 (86.1)*
9- There are no differences in the appearance between general pressure injuries and MDRPIs. (F	31 (12.3)	221 (87.7)*
Dimension 2: risk factors		
10- Hypertension is not a risk factor for MDRPIs. (T)	81 (32.1)*	171 (67.9)
11- MDRPIs are potentially caused only by breathing apparatus and feeding tubes. (F)	81 (32.1)	171 (67.9)*
12- Hypoalbuminemia and malnutrition are not causes of MDRPIs. (F)	50 (19.8)	202 (80.2)*
13- All patients with a medical device are at risk of MDRPIs. (T)	224 (88.9)*	28 (11.1)
14- Patients with signs of localized and generalized edema have a higher risk of MDRPIs. (T)	239 (94.8)*	13 (5.2)
15- Patients with swallowing problems are at risk of MDRPIs. (T)	47 (18.7)*	205 (81.3)
16- Face masks used for non-invasive positive pressure ventilation (NIPPV) do not cause MDRPIs. (F)	40 (15.9)	212 (84.1)*
17. Commonly used risk assessment scales do not assess the risk associated with MDRPIs. (T)	78 (31.0)*	174 (69.0)
Dimension 3: staging		
18- The most common stage of encountering a MDRPI is stage 2. (T)	142 (56.3)*	110 (43.7)
19- Considering MDRPIs: if the medical device causes a pressure injury on the mucosa staging is achieved using the "International Pressure Ulcer Classification System". (F)	82 (32.5)	170 (67.5)*
20- Considering MDRPIs: if the medical device causes a pressure injury on the skin no staging is required. (F)	17 (6.7)	235 (93.3)*
Dimension 4: prevention and treatment		
21- Placing the medical device or equipment under the immobile patient should be avoided. (T)	209 (82.9)*	43 (17.1)
22- MDRPIs do not require any treatment and heal spontaneously. (F)	32 (12.7)	220 (87.3)*
23- The skin around and under medical devices or equipment should be observed every 48–72 h for signs of injuries. (F)	87 (34.5)	165 (65.5)*
24- If the patient is at risk of edema or exhibits signs of edema. skin assessment should be performed more frequently than usual. (T)	230 (91.3)*	22 (8.7)
25- Medical devices and equipment should be removed from the part of the body they are attached to as soon as medically possible. (T)	210 (83.3)	42 (16.7)*
26- Relocating the medical devices at regular intervals is the most important method to prevent MDRPIs. (T)	235 (93.3)*	17 (6.7)
27- Relocating the medical devices at regular intervals is the most important preventive method to prevent MDRPIs.	242 (96.0)*	10 (4.0)
28- The skin surface in the area where the medical device is located should be massaged to prevent medical device related pressure ınjuries (MDRPIs). (F)	104 (41.3)	148 (58.7)*
29- If the dietary plan of adult patients at risk of MDRPIs does not meet nutritional requirements, it may lead to poor wound healing. A protein-rich nutritional supplement should be recommended to the patients. (T)	201 (79.8)*	51 (20.2)
30. Using medical devices in a way that minimizes skin damage (soft material, etc.,) reduces the risk of injury development. (T)	235 (93.3)*	17 (6.7)
31. Medical devices and equipment should be firmly fixed in place in order to avoid the risk of dislocation. (F)	56 (22.2)	196 (77.8)*
32. The medical device should be placed directly on the skin. (F)	74 (29.4)	178 (70.6)*
33. The skin on which medical devices are worn should be regularly moisturized with products in order to prevent MDRPIs. (F)	124 (49.2)	128 (50.8)*
34. The skin on which medical devices are worn should be kept clean and dry to prevent medical device-related pressure injuries. (T)	235 (93.3)*	17 (6.7)
35. Medical devices and equipment should be the appropriate size for the patient. (T)	241 (95.6)*	11 (4.4)
36- To reduce the pressure associated with the medical device. specific a dressing/pad should be used under the devices. (T)	222 (88.1)*	30 (11.9)
T: True, F: False.		

Study Limitations

The study was conducted in two public hospital in North Cyprus so that the findings cannot be generalizable.

CONCLUSION

The results of this study showed that the nurses' MDRPI knowledge was at moderate level and lower than the limit for four subdomains of the questionnaire. MDRPI is a growing global concern due to the increasing use of invasive medical devices in care settings. In particular, identified knowledge gaps in the prevention of device-related injuries and device-related complications highlight the need for standardised educational interventions in these critical areas.

These results support the integration of MDRPI-focused content into national nursing curricula and continuing education modules, thereby ensuring that evidence-based prevention and staging practices are taught in a consistent manner. Additionally, adapting in-service education programmes to the specific needs of different clinical units (e.g., surgical services or ICUs) and addressing demographic and experiential factors (e.g., duration of practice or unit type) can enhance knowledge acquisition and improve clinical outcomes. These findings can be used to inform national or international nursing education frameworks to create a broader impact. Integrating these interventions with existing global pressure injury prevention frameworks, such as those promoted by the NPIAP or the European Pressure Ulcer Advisory Panel, could facilitate cross-national comparability, benchmarking, and professional standardisation.

MAIN POINTS

- Nurses' level of knowledge about medical device-related pressure injurys (MDRPIs) is insufficient.
- Inadequate knowledge of MDRPIs may negatively affect patient care.
- Training programmes and standards to increase knowledge of MDRPIs developed.

ETHICS

Ethics Committee Approval: This study was approved by the Ethics Committee of Dr. Burhan Nalbantoğlu State Hospital (approval number: 65/22, date: 23.05.2023).

Informed Consent: Informed consent was obtained from the nurses participating in the study.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: K.Y., G.S.D., Concept: K.Y., G.S.D., Design: K.Y., G.S.D., Data Collection and/or Processing: K.Y., Analysis and/or Interpretation: K.Y., G.S.D., Literature Search: K.Y., G.S.D., Writing K.Y., G.S.D.

DISCLOSURES

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