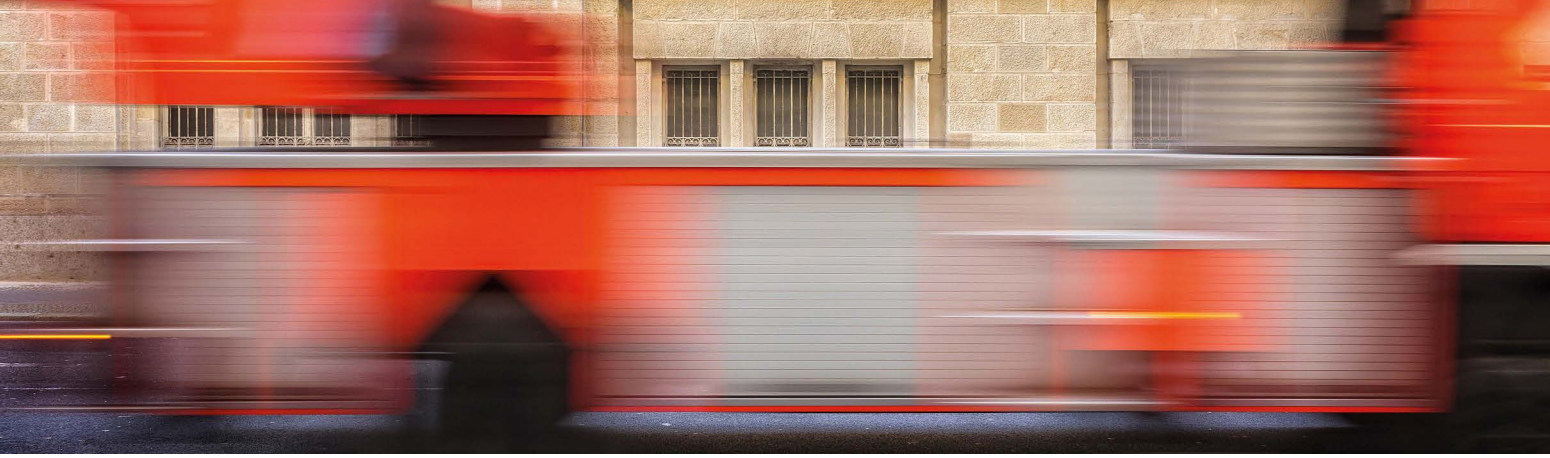

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OMICRON VARIANTS OF THE SARS-COV-2: A POTENTIALLY SIGNIFICANT THREAT IN A NEW WAVE OF INFECTIONS

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KEY WORDS: COVID-19; Omicron variants; SARS-CoV-2

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From the beginning, the COVID-19 pandemic turned out to be a huge challenge and burden for medical services [1]. Currently, humanity is dealing with a new wave of the virus that has evolved and presents a new challenge, mainly due to its ability to avoid immune surveillance. Indeed, our main line of defense — vaccines — may be compromised. Omicron variants are characterized by an evolutionary force unprecedented so far. Among the several sublines that have already emerged, the BA.5 strain exhibit higher transmissibility and demonstrates a worrisome immune evasion. According to several laboratory investigations, vaccination-induced antibodies are less successful at preventing BA.4/5 strains infection as opposed to the infections following BA.1/BA.2 strains exposure [2–6]. The hyper contagious BA.5 variant is mainly responsible for the rise in hospital and intensive care unit utilization we are facing in the current times. Within a few months, BA.5 outperformed its forerunners and became the dominant strain in the United States (US). According to the most recent statistics provided by the Centers for Disease Control and Prevention (CDC), this subvariant was responsible for nearly 2 out of every 3 new COVID-19 infections in the US (3.07.2022–9.07.2022) [7].

The BA.4/5 variants are four times more resistant to sera from vaccinated individuals than other omicron strains [8]. The neutralizing antibody response induced by BA.1 infection, seems to be narrower than anticipated, leaving patients vulnerable to immune evading variants like BA.4/BA.5 [9]. As a result, repeated Omicron infections may affect previously (triple) vaccinated patients. Even patients who developed hybrid immunity via vaccination and prior infection (from Omicron BA.1 or other variants) fail to render BA.4/BA.5 ineffective. This has been linked to the spike mutations L452R and F486V. The new BA.2.75 variant, a sub lineage of the Omicron BA.2 that was first detected in India and has been discovered in other countries, including Japan, Germany, the United Kingdom, Canada, the U.S, Australia, and New Zealand [10]. This may pose a serious

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threat to humankind. Compared to its parent strain, eight more spike protein mutations are present in this strain. Because of the location of these mutations, it is likely that BA.2.75 may overcome immune defense against BA.2 [10]. The ability of BA.2.75 to evade immunity appears to be confirmed by the fact that it was able to expand in at least ten distinct areas of India, despite the previous experience of a BA.2 wave. Immune escape might be made worse by mutations of the novel BA.2.75 sub-variant than what we are now witnessing with BA.5 and BA.4, sub-variants known to escape immunity after both vaccination and prior infection.

The BA.5 variation essentially depicts how this virus evolved to be more infectious and to get beyond human immune defenses against infection, immunization, or both. People have relatively little defense against BA.5 for a mild to moderate illness, regardless of vaccination status, prior infection, or prior infection and vaccination. However, protection against the most severe forms seems to be maintained among healthy individuals as demonstrated by the relatively low incidence of hospitalization, ICU admissions, and death in the number of cases.

Protective measures might also be adapted when dealing with new variants. The Omicron variant (B.1.1.529) has a shorter incubation time and a greater transmission rate than earlier versions [11]. As a result, the CDC advised a shortening of the isolation period for infected individuals from 10 to 5 days following onset of symptoms (or positive test) followed by a 5-day mask wear. When analyzing the replicative capacity of SARS-CoV-2 obtained from swabs of infected patients researchers found that the median time from the initial positive PCR test to the absence of viral infectivity in culture was 4 days (3 to 5) for Delta strain and 5 days (3 to 9) for Omicron. The median time from symptom onset (or initial positive PCR testing) from sterile culture was 6 days (4 to 7) for Delta and 8 days (5 to 10) for Omicron. Considering those observations, it appears that compared to the Delta variant, the infectivity of Omicron lasts longer — on average by at least 2 days (5–10 days). Therefore, the 5-days isolation period seems too short to restrain virus spreading when infected with an Omicron strain. Therefore, the 5-days isolation period seems too short to restrain virus spreading when infected with an omicron strain. In this perspective, strict application of health precautions and physical distancing measures seems mandatory to restrain virus spreading [12].

It's important to keep in mind that vaccinations are based on the original Wuhan strain. Therefore, the vaccine's immunity may not confer enough protection to new variants. Due to the rapid ability of SARS-CoV-2 to evolve and evade, the pharma industry may not be able to develop and provide tailored vaccines fast enough. On this topic, salvation may come from pan-coronavirus vaccines, several of which are in development. Those pan-coronaviruses vaccines may ward off future variants and prevent upcoming waves in an optimistic scenario. However, the emergence of possible antigenic imprinting (or Hoskins effect), a failure of the immune system to mount sufficient effective immune response when encountering a slightly different version of a pathogen, must be taken into consideration [13].

These symptoms will primarily be catarrhal and cold-related. This does not change the fact that owing to the virus's enhanced contagiousness, quite a lot of people may end up needing hospitalization. Due to their capacity to infect individuals who had developed resistance to earlier iterations of Omicron and other variants, BA.4/5 appears to have developed. The rise of BA.4/5, as well as their inevitable decline, will be largely influenced by population resilience because most of the rest of the world outside of Asia is doing little to control SARS-CoV-2. However, we are unable to predict what may happen along the way with potential new varieties. We are also unaware of any more changes that may be far deadlier, especially given the virus's quick mutations — on the bright side, there is less likelihood of a wholly new variety emerging because of infection the longer the Omicron and its branches continue to predominate.

Conflict of interests

The authors report there are no competing interests to declare.

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DESIGNING A DISASTER TRAINING PROGRAM AND EXAMINING ITS IMPACT ON THE LEVEL OF COMPETENCE OF NURSING STUDENTS

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ABSTRACT

INTRODUCTION: Core competencies required for a nurse to be ready for disaster response. The gaps in education make it difficult to recruit nurses prepared to respond to a disaster. The aim of this study was to design a disaster preparedness training program and examine its impact on the level of competence of nursing students.

MATERIAL AND METHODS: A quasi-experimental design was used for 50 nursing students in semester 8 randomly assigned to the experimental and the control groups. A disaster educational program for nursing students was developed based on Harden's model. First need assessment was done and then the goals of the program were determined in the next stage, the educational content was organized based on the priorities of the students and teacher recommendations. In the next stage, the program was implemented and finally, the evaluation was carried out.

RESULTS: The mean age of the participant was 21.4 ± 2.14 and 57.1% of them were women. Compared with the control group, the experimental group showed a significant increase in disaster nursing competency after intervention ($t = 12.37$, $p < 0.001$).

CONCLUSIONS: This study provides evidence of the need and potential positive impact of disaster education opportunities for nurses.

KEY WORDS: training program; nursing student; competence; disaster

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INTRODUCTION

In recent years, the number and intensity of disasters have increased dramatically across the world. Due to its location, Iran is one of the most prone geographical areas for disaster. Disaster can occur at any time and create emergencies for the community, so the preparation of the health care team as an important member of the disaster team to respond effectively to the disaster is essential [1]. Nurses play a key role in providing clinical care and they are essential members of the health care team that responds to disaster events. It is therefore important that nurs-

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es be adequately prepared during their education and graduate with the necessary competencies to effectively respond to disasters [2]. The definition of disaster nursing is currently a topic of discussion because in critical situations nursing is a unique job. Disaster nursing requires new concepts such as disaster care [3]. The international council of nursing (ICN) has defined nursing in disaster as follows: Systematic and flexible use of specific knowledge and skills related to disaster nursing and the expansion of a wide range of activities to reduce health risks and life threats that may arise due to the disaster and in other specific areas [4]. When a disaster occurs, a large number of people in the nursing profession need to provide the necessary support and care to the victims, so nurses must be able to use their skills and speed of action to provide the necessary care for these people, to prevent the aggravation of the problem and the occurrence of complications in them [5]. Therefore, they must acquire the necessary ability to participate effectively in providing services and give a systematic and efficient response to a disaster, since the lack of skills and competence of nurses in playing their role effectively and providing the necessary care to clients in a disaster can lead to aggravation of the problem and irreparable damage to victims and society [6], so we cannot wait for nurses to gradually gain the necessary experience. Also, it is necessary to assess the ability of nurses before being in real situations. Assessing the nurses' competence is crucially important to identify areas on professional development and educational needs, and also to make sure that nurses' competencies are put to the best possible use in disaster relief [7], In spite of attempts to clarify the meaning and different aspects of disaster nursing competence, debates still continues [2].

One task for disaster preparedness is to prepare well-educated nurses to engage in relief operations, therefore, effective preparation of nurses and competency-based education is crucial [8]. One of the best times to improve students' knowledge and skills in this field is before they enter the clinic. In this time education can be more effective and improve their performance after attending the clinic. The clinical aspect of nursing education covers more than half of the training programs of the nursing course [9], and due to the creation of conditions and the real environment, prepares learners for the role of care, education, rehabilitation, and so on. according to the educational goals set for the disaster nursing internship unit, students must have the skill of managing pre-hospital situations related to emergencies and disasters after passing this course [10], and are expected to have a good level of competence in this field after passing the theory course and passing its internship courses in the clinic, but unfortunately in Iran, the results of researchers show that the quality of clinical education is not desirable and there are shortcomings in that field [11].

In Iran, besides mentioned issues, disaster nursing is poorly defined, required competencies have not been clearly stated, and education opportunities are scarce. For example, Salimi et al. [11] state that the clinical skills of nursing students in intensive care units are not at a good level, and Farnia [12] also reports that most nursing students believe that they have not been able to learn the skills needed to work in critical situations during their training. On the other hand, there are problems such as student density, lack of space, reduction of inpatient wards, shortening of hospital stays, student stress in the first encounter and consideration of patients' rights [13], and also in critical hospital situations, students are usually withdrawn and they are invited to remain silent, in which mere observation of such situations does not produce learning [14]. Therefore, in order to teach these skills, new ways must be used so that the student can better deal with real dangerous situations by focusing on dangerous situations without fear of harming the patient. One of these teaching methods is clinical simulation. Clinical simulation is the creation of an educational environment in which learning takes place through the use of a mannequin or group tool without the presence of a real patient. Nursing students in the simulated environment in the clinical skills center acquire the right skills by practicing and repeating and performing well in dealing with patients in a real environment [15]. Various researches have been done on the effect of simulated training by acquiring different skills. In a study, Faraji et al. [16] examined the effect of simulated training on nurses' readiness to perform triage of accidents. They concluded that there was a significant difference between the mean score of nurses' readiness to perform triage (knowledge and accuracy) in the intervention and the control groups.

In contrast, some researchers have concluded that simulated training is not significantly superior to traditional training. Anderson et al. [17] in a study examined the effect of teaching the basics of disaster management in the traditional compared with

role-playing simulation. They conclude that there is no significant difference in the behavior or satisfaction of nursing students in the two groups. So considering that appropriate training programs should be used for nurses before placing them in critical situations to improve their level of preparedness [18], the most important issue that should always be considered by the officials of health care providers is to develop a training program and train students effectively to prepare them to play an effective role in critical situations [19]. Training and acquiring competency in disaster nursing is an important part of students' preparation for disaster. Student courses based on needs assessment and review of graduates' opinions can well identify the various dimensions of the gap in this field and in the next step can be used to plan and design an appropriate program. In Iran, disaster nursing is poorly defined, required competencies have not been clearly stated, and educational opportunities for students, and other nurses, are scarce [20].

This research identifies the areas of required professional development and the associated educational needs of students, and will help to ensure that nursing students' competence is put to the best possible use in disaster relief. Considering the occurrence of disasters in different parts of Iran and the lack of a proper program for the readiness of nurse students to respond to disasters [21]. This study was conducted with the aim of designing a training program for disaster preparedness and investigating the effect of the program on the level of competence of nursing students to participate in disaster situations.

MATERIAL AND METHODS

Study design and setting

This quasi-experimental study was performed on 50 nursing students of Shahrekord School of Nursing and Midwifery in 2020. All students entered the study through a total census sampling method. First, a list of all nursing students was prepared, and all students who met the inclusion criteria (studying in the 7th and 8th nursing semester, and consented to participate in the study) entered the study. Then, the studied samples were assigned to the intervention and control groups using random number assignment software. Before and after the intervention, both groups completed a questionnaire to assess the level of competence of nurses to attend disaster situations. Then the intervention group was educated through the designed training program and the control group received only the routine program. Harden's general step model was used to design the training program. Thus, in the first stage, the needs of the graduates were assessed regarding the gaps in the educational program, and also the professors of the nursing school who were in charge of teaching this course were surveyed. Based on the needs assessment and survey of professors and review of texts, the educational needs of students were determined (Tab. 1). In the second stage, after determining the educational needs, the goals of the program were determined, and in the next stage, based on the set goals, the educational content was organized. In the next stages, the program was implemented and an evaluation was performed [19].

According to the results of the survey, the educational contents were prepared and presented in the form of a three-day workshop program and educational maneuver. The main topics of the training program include: (1) special concepts and meanings related to disasters and the effects of disasters on health (2) disaster management and disaster management stages (3) risk assessment and possible vulnerabilities (4) disaster planning stages and (5) triage. Also, technical and specialized skills were taught to students in the form of working with anatomical models, role-playing simulation, educational videos, and working with pre-hospital emergency equipment. finally, based on students' opinions, techniques that needed more practice were educated in the clinical skills center of the nursing school in a two-hour training session for two weeks.

Regarding moral and legal skills, a four-hour workshop was held for two days on moral and legal challenges in the caregiver in disaster situations, and supplementary contents were provided to students in the form of training files. Also, problem-based training and critical thinking approach were educated. Immediately after and three months after the intervention, both groups completed a questionnaire to assess the level of competence of nurses to participate in the disaster.

Ethical consideration

The present study was approved by Ethical Committee Medical Sciences University of Shahrekord (*Ethics code*: IR.SKUMS.REC.1398.075). Written informed consent was gained from all participants and they were assured that their provided information will remain confidential. After clarifying the

Table 1. Educational need assessment and training activities

Domain	Educational needs	Teaching and learning activities
Teamwork and specific personal competence	• Knowledge about duties and organizational hierarchy, • Unity of command, • Self-management in a disaster situation, • Communication skills, • Skills of coordination and cooperation with the leader, • Ability to communicate and cooperate with relief forces and other team members	• Increase communication skills and self-resilience through a Skill training program, • Lecture for increase knowledge about team working in disaster, • Tabletop maneuver for increase Critical thinking ability
Technical competence	• Ability to perform triage and ongoing assessment, • Ability to use their clinical skills to assist victims during a disaster; • Care of patients with multiple trauma, recognizing the types of shocks and related nursing care, • Providing essential care for a person with life-threatening injuries, • Familiarity with the CAB process, • Implementation of fluid therapy protocol in patients with burns during a crisis, • Ability to sew, provide care to victims of poisoning and bites, • Providing care to injured people suffering from frostbite or heatstroke during a disaster, • Ability to do endotracheal intubation, • Working with medical equipment (electroshock, suction, ventilator, electrocardiography, etc.) in times of disaster, • Ability to collect and record clinical information (reporting, etc.) in disaster, ability to implement or participate in decontamination	Field visit, • Increase knowledge about temporary settlement and tent hospitals through lecture practical exercises for trauma care, triage, and CPR, • Problem-based learning for dealing with problems in floods and earthquakes, • Skill training for: – Prehospital transfer skill – Wound management – Interviewing skill – Psychological first aid and – Need assessment – Skill lab training for working with medical equipment
Legal and ethical competence	• Ethical commitment, • Observing ethics, • Familiarity with the legal requirements, • Observing requirements	• Problem-based learning for ethical value underpinning decision making in disaster, • Lecture for increase knowledge about legal rules in disaster and patient rights
Management competence	• Psycho-emotional stress management • Scene safety, • Assessment of required human and other resources, • Operational coordination and management of resources	• Field visits for hazard assessment in a different disaster situations, • Action learning for distribution of resources in a disaster situation, • Role-playing in practical exercise for psycho-emotional stress management

study purposes and obtaining written consent from nursing students, students were allowed adequate time to complete the competency assessment questionnaire. The researcher reminded students that their participation in the study was voluntary and their information would be anonymous and confidential.

Data gathering

The study data were collected using the disaster nursing competency scale designed by Aliakbari et al. in 2014 [22]. This questionnaire has two parts. The first part collects demographic information and the second part consists of 50 research

Table 2. Sample characteristics

Variable		Control group		Intervention group		p-value
		M ± SD		M ± SD		
*Age [years]		20.85 ± 3.25		12.12 ± 3.48		0.68
Characteristics		N	%	N	%	p-value
**Sex	Male	10	40	12	48	0.39
	Female	15	60	13	52	
**Participation in disaster education	Yes	7	26	10	22	0.45
	No	18	74	15	78	
**History of participating in the exercise and drills	Yes	5	20	8	32	0.61
	No	20	80	17	68	
**History of participating in disaster	Yes	1	4	2	8	0.50
	No	24	96	23	92	

* — based on independent t-test; ** — based on the chi-square test

questions with 4 subscales. These subscales were "management competency (12 questions)", "individual-specific competency (6 questions) and "technical competency (23 questions)" rated on a 5-point Likert scale from very high (5) to very low (1), and "ethical and legal competency (9 questions)" rated on a 4-point Likert scale from rarely (1) to always (4). The minimum and maximum attainable scores in all domains are 50 and 244, respectively; obtaining a higher-than-cut-off point indicates the optimality of nurses' disaster response competencies (The calculated cut-off for the whole tool was 95.91). This questionnaire is a valid and reliable tool. The validity of the tool has been demonstrated by Aghaei et al. [23]. The internal consistency assessed by Cronbach's α coefficient has been reported to be higher than 0.88 for all subscales of the questionnaire and 0.96 for the whole scale. The test-retest method was also used to assess the reliability of the questionnaire. For this purpose, the questionnaire was twice administered to 20 nurses (not included in the main study) at a 2-week interval. The correlation coefficient between the 2 administrations in all subscales of the questionnaire was higher than 0.8.

Data analysis

Data were analyzed by SPSS version 21 (IBM Corp, Armonk, NY) using descriptive and analytical statistical tests. P-value of less than 0.05 was considered significant.

RESULTS

The demographic characteristics of the sample showed that out of 50 participants, 28 (56%) were female and 41 (82%) were single. The mean age of participants was 21.4 ± 2.14. In responding to "disaster training course" (64.3%), did not receive any disaster-related training, in responding to "maneuver training experience" (88.6%) did not attend exercises, and in responding to "history of disaster participation" (71.4%), did not have a history of disaster participation. there was no significant difference between the two groups in terms of age based on the independent t-test ($p = 0.72$) and sex-based on the chi-square test ($p = 0.004$). Other demographic characteristics of nurses in comparison between the two groups are presented in Table 2.

The results showed that nurses' student disaster competence in the control group was (121.58 ± 35.27) and in the intervention group (121.19 ± 16.29). At the beginning of the study, there was no statistically significant difference between the two groups ($p = 0.038$).

The pre-test and post-test difference between the intervention and control groups were assessed using the independent samples t-test. The results revealed a significant difference between the two groups after intervention ($p < 0.001$). Also, based on the analysis of the variance of repeated observations, the interaction between group and time was significant, which shows a different trend in the

Table 3. Comparison of mean competence of nurses in two groups

Variable	Stage	Control group	Intervention group	p-value
		M ± SD	M ± SD	
Nurse Competency	Before intervention	121.58 ± 35.27	121.19 ± 16.29	0.038
	Immediately after intervention	123.21 ± 31.32	137.51 ± 11.57	> 0.001
	3 months after intervention	122.39 ± 29.26	149.19 ± 25.72	> 0.001
p-value between groups		> 0.01	> 0.001	> 0.001*
Changes during the intervention		−1.5 ± 5.13	65.3 ± 28.38	> 0.001

* — Based on independent t-test

competency score of nursing students in the two groups during the study ($p < 0.001$) (Tab. 3).

DISCUSSION

The aim of this study was to design and develop a disaster preparedness training program and to investigate its impact on the level of competence of nursing students to participate in disaster situations. The results of the study showed a significant increase in students 'competency scores after providing education based on students' needs assessment. In the training program of the present study, the courses were organized in such a way as to prepare students to perform tasks in the areas of management, personal, personal, ethical, and *carte blanche*.

At present, in Iranian nursing schools, the curriculum of the disaster, emergencies, and unit is presented in the form of 1.5 theoretical and practical units and the internship unit in the amount of 2 units. A study conducted by Jalalinia and Alhani [24] entitled pathology of disaster education emergencies and unexpected accidents in nursing students indicates there are shortcomings in educational planning and implementation of this curriculum, and graduate nurses schools are not sufficiently prepared for disaster and disaster management, and existing training methods are not sufficient to prepare nurses for clinical practice. Also, Nejadshafiee et al. [25] in their study stated that training and empowering nurses to respond optimally to the needs of injured people by reviewing the current curriculum and paying attention to the required content is emphasized and the current curriculum does not meet the needs of students.

In the recent study, we tried to provide educational materials based on the needs assessment of students because the final year students have passed all theoretical and practical courses and are expected to be ready to work as a nurse in critical situations [26]. The results of the initial needs assessment showed the weakness of students in various fields, which tried to design educational content in accordance with these sections and using skills training methods, practical training and problem-solving processes in a practical way. Findings from a study conducted on the educational needs of undergraduate students in relation to disaster preparedness and response in Turkey and Japan show that nursing students in both regions tend to participate in disaster preparedness training courses are required and it is necessary to include the topics of care in major accidents as well as disaster management skills in the content of the undergraduate curriculum [27].

Also, a study was conducted by Poursoleyman et al. [28] with the aim of designing a training program for mother and infant care in disasters. The proposed program was developed and evaluated by referring to domestic and international sources and according to the results obtained from the needs assessment. The maternal and neonatal disaster care curriculum was developed based on a six-step process. The desirability of the Delphi curriculum was approved by experts in two rounds. During the evaluation of the program developed in this study, it was found that this program has practical features and can play a decisive role in raising the level of knowledge of health service providers of the armed forces to provide services to mothers and infants in disasters.

The results of the current study consist with the other studies that the students believed that it is better to include these contents in their training course in the undergraduate course and also in

the form of in-service training courses so that in addition to holding periodic maneuvers, they can prepare for situations and maintain the critical level [29, 30]. In this regard, Nejadshafiee et al. in Kerman in 2020 [18] conducted a study entitled professional competence in nurses for disasters in which the results showed that the participation of nurses in maneuvers and regular training courses has the greatest impact on the professional competence of nurses in disasters and Participants believed that they did not receive adequate training during their studies, which is consistent with the present study. Chan et al. [31] in a study conducted in 2010 with the aim of designing and implementing a training course for nursing undergraduate students in China, prepared educational content based on the competencies provided in the ICN, and the results showed that the program was useful in increasing students' competency. This is similar to the results of a recent study, but one of the strengths of the recent study was the design of the curriculum based on Harden's planning model and the needs assessment of students and surveys of professors about the educational content.

CONCLUSIONS

Considering that Iran is one of the countries where the occurrence of natural disasters is high and nurses as a member of the medical team should have the necessary qualifications to play a role in responding to the disaster. The findings of this study indicated the effect of educational programs in improving students' competence. Considering that this training program, considering the two important elements of goals and content in the curriculum of nurses' education, has considered various and comprehensive aspects of empowering nurses in the field of disaster, especially the practice and skill aspect, it is recommended that the content of this program be used in the training course for undergraduate students and in-service training course for nurses.

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Conflict of interest

There are no conflicts of interest.

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EVALUATION OF ANXIETY AND PROFESSIONAL COMPETENCE OF PREHOSPITAL EMERGENCY MEDICAL PERSONNEL IN COVID-19 PANDEMICS

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ABSTRACT

INTRODUCTION: Emergency medical services (EMS) are an important part of the health care system. Decision-making is the most important part of their profession because they often have to make quick decisions and act on them despite critical situations. They are often the first to deal with a Coronavirus disease 2019 (COVID-19) patient and experience severe physical, mental, or moral stress. The aim of this study was to investigate the level of anxiety and professional competence of prehospital emergency medical personnel in the COVID-19 epidemics.

MATERIAL AND METHODS: This descriptive-analytical study was performed in 2021. A total of 200 prehospital emergency medical personnel were included in the study. Sampling method was census using a valid questionnaire of Corona Anxiety Scale and professional competence. Data analysis was performed using SPSS statistical software version 21 via descriptive statistics and analytical tests.

RESULTS: Mean and standard deviation of professional competence and anxiety of emergency medical staff were reported as 82.37 ± 65.13 and 98.17 ± 11.11, respectively. The results of the study on the relationship between the scores of the studied variables showed a significant relationship so that the level of anxiety with competence was remarkably related ($p < 0.05$).

CONCLUSIONS: The stress and anxiety of the COVID-19 epidemic might have adverse effects on the professional competence of prehospital emergency medical personnel as well as their mental health. Applying strategies to reduce anxiety and attending disaster-related courses could help the quality of EMS by improving professional competence.

KEY WORDS: anxiety; professional competence; COVID-19; prehospital emergency medical personnel

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INTRODUCTION

Emergency medical personnel receive specialized training to be first-aid workers in dealing with patients in critical condition. Prehospital emergencies are an important and key part of the health care system in society [1]. The important part of its activity is due to the exposure of a wide range of patients with life-threatening situations. The prompt and timely

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action of the emergency medical team leads to the prevention of disability and the saving of lives. Emergency medical services (EMS) are a key component of health care delivery, contributing significantly to the reduction of out-of-hospital mortality. In Iran, prehospital emergency medical personnel consist of nurses, emergency medical technicians (EMTs), emergency medical experts, and other relevant academic disciplines (operating room and anesthesia technicians). In addition, a prehospital emergency medical school has been established in nearly a decade in Iran. Therefore, approximately half of the human resources employed in EMS are nurses. Personnel with different grades and disciplines, such as nursing and medical emergencies, are all within the scope of this study and are considered as a professional collection of out-of-hospital EMS. The duties of each prehospital emergency medical personnel are clearly defined and they act in decision-making based on guidelines and available resources [3].

Given the high importance of the medical emergency profession in the health system, it is important to examine the factors influencing the performance, job satisfaction, and reducing errors [4]. Due to dealing with patients with life-threatening, unconscious, or even death status, prehospital emergency medical personnel are facing daily stress [5]. Prehospital emergency medical personnel are exposed to a variety of stressors and unpredictable threats. As a result, they experience high levels of stress and suffer from chronic stress [6]. Studies have shown that 22% of prehospital emergency medical personnel experience stress-related complications and are more prone to anxiety, irritability, social isolation, sleep disturbance, job dissatisfaction, burnout, post-traumatic stress disorder (PTSD), high-risk behaviors, psychological problems, depression, and medical errors [7]. Stress has significant negative consequences for individuals, including reduced productivity and services, health problems, absenteeism from work, leaving work, and using drugs and psychotropic substances that might severely threaten their mental health [8].

Coronavirus, which has been prevalent in China since late 2019, is a terrifying and highly contagious disease. This virus has become a major crisis in many countries and has severely reduced both labor force and personal protection resources [9]. COVID-19 is a life-threatening virus in people with lung problems such as bronchitis, people with internal diseases, and especially people with weakened immune systems, the elderly, children, and pregnant women. By isolating infected people and using personal protective equipment, N95 mask, and medical gown for people in contact with the virus might be limited. COVID-19 disease is an emerging disease that is now becoming a major health challenge and concern worldwide. The outbreak of COVID-19 has become a worrying international public health emergency [10]. The number of COVID-19 cases and the resulting mortality rate are rising rapidly. COVID-19 is a serious threat to global health and the economy which has raised widespread concerns around the world [11]. Research shows that there is an urgent need for prehospital nurses and emergency staff to be prepared and professionally qualified [12]. In the time of crisis and emergencies, the first referral centers for the injured are hospitals and emergency centers. Emergency medical personnel are often the first to deal with COVID-19 cases and experience severe physical, mental, or moral stress [13]. They also may have doubts about their abilities or priorities, sometimes they may be overwhelmed by the fear of disease and prefer individual interests to collective interests, and be unable to make the right decisions [14]. They also need moral courage and professional competence to escape the stress and tension caused by this global crisis, as well as to strengthen their decision-making power. Moreover, in critical situations such as the outbreak of COVID-19 disease, in addition to stress and anxiety, the burden of responsibility of this group of health care workers has increased, which itself requires the professional competence to provide care [15]. Professional competence refers to the ability to solve complex problems using a combination of knowledge, attitude and practical skills [16]. The need to provide quality care to patients by emergency medical personnel has made the concept of their clinical competence as one of the key issues in educational and clinical centers. Furthermore, the various factors such as a rapid change in health monitoring systems, the need to provide safe and cost-effective services, promoting the public awareness on health-related issues and increasing the expectation of receiving appropriate quality services, along with the willingness of health service providers to employ skilled labor, the clinical competence of health-related professionals has become increasingly important [17]. In order to maintain care standards, it is necessary to know the methods

of development and promotion of clinical competence of prehospital emergency medical personnel. The results of various studies have shown that maintaining and improving the quality of patient care and increasing the capabilities and clinical competence of prehospital emergency medical personnel, is at the top of the plans of managers of EMS centers. To achieve this goal, one of the most fundamental missions of managers is to continuously assess their competence. However, there is still disagreement about the exact meaning of achieving clinical competence. However, the competence includes a wide range of preparations in various dimensions of cognitive, emotional, value, psychomotor and skills in the use of different technologies. Therefore, due to the importance of professional competence and the level of anxiety to provide care in the COVID-19 crisis situation, the research team decided to investigate the level of anxiety and professional competence of prehospital emergency medical personnel in the COVID-19 epidemics.

MATERIAL AND METHODS

Study design

This is a descriptive cross-sectional study conducted in 2021 with the aim of assessing the level of anxiety and professional competence of prehospital emergency medical personnel of urban, road, and urban emergency care units in facing the COVID-19 pandemic. The sampling method was available by sampling and inclusion criteria included a willingness to collaborate on the study, one-year of operational experience in emergency medical bases, and operational presence from the beginning of the period of outbreak of COVID-19 to the time of performing the study.

Methods of measurements

Corona Disease Anxiety Scale (CDAS) and professional competency assessment questionnaire in biological crises were used to collect data.

Corona Disease Anxiety Scale (CDAS) Questionnaire

This tool has been developed and validated to measure anxiety caused by the outbreak of Coronavirus in Iran. The final version of this tool has 18 items and 2 components (agents). Items 1 to 9 measure psychological symptoms and items 10 to 18 measure physical symptoms. This scale is made in the Likert scale (never = 0, sometimes = 1, most of the time = 2 and always = 3). The reliability of this tool was obtained using Cronbach's alpha method for the first factor of alpha 0.879, the second factor of alpha 0.861, and the total alpha of the questionnaire 0.919 [11]. The value of λ-2 Guttman was obtained for the whole questionnaire as λ-2 = 0.922 and Cronbach's alpha coefficient for psychological symptoms as $\alpha = 0.879$), and physical symptoms as $\alpha = 0.861$ [12]. Research data of Alipour et al. (2020) [18] have a suitable fit with the two-factor model. Standard score tables will be drawn and the range of scores of the questionnaire agents and the total score of coronary anxiety severity were divided into three domains of non-anxiety or mild, moderate and severe based on standard T scores.

Professional competency assessment questionnaire in biological crises

This researcher-made questionnaire was prepared based on the competencies extracted from World Health Organization (WHO) and other sources to participate in biological crises and was used after confirming its validity and reliability. Content validation method was conducted with the opinion of ten faculty members and experts in the field of prehospital emergencies including health specialists in disasters and emergencies, emergency medicine specialists as well as emergency medical experts. The results showed that all questions are of Content Validity Index (CVI) = 0.71 and Content Validity Ratio (CVR) = 0.67. The reliability of the questionnaire questions was calculated after a preliminary implementation on 20 prehospital emergency operatives using Cronbach's alpha test calculated as 0.73. After obtaining the agreement and coordination with the relevant authorities, they referred to qualified individuals for sampling. After explaining the objectives of the research and obtaining their written consent for the participation of prehospital emergency medical personnel, the questionnaires were distributed among the studied samples and filled out as a self-report. The researcher provided the necessary information on how to fill out the questionnaires and provided the researchers with their telephone numbers for asking possible questions. The time for returning the questionnaires was also coordinated with them.

Table 1. Determining descriptive indicators of overall professional competence score and anxiety in the study samples

Variables	M ± SD	Min	Max
Professional competence	37.82 ± 13.65	13	56
Anxiety	17.98 ± 11.11	0	46

Data analysis

After returning the filled out questionnaires, data analysis was carried out by SPSS/21 via descriptive statistics including mean and standard deviation for quantitative and chi-square data, frequency and percentage for qualitative data and analytical tests were significant for all tests considered as 0.05%.

Ethical considerations

After selecting the eligible participant, the researcher was introduced to them and the objectives of the study were elaborated for the participants. The informed consent was obtained from the subjects and they were assured that their information will remain confidential. The present study was approved by Ethical Committee Medical Sciences University of Shahrekord (Ethics code: IR.SKUMS.REC.1399.042).

RESULTS

Characteristics of study subjects

Findings of the study on the demographic characteristics of the studied samples showed that a total of 200 prehospital emergency medical personnel facing COVID-19 participated in this study. The age range of the participants was from 22 to 66 years old (33.42 ± 7.14). In terms of work experience, the participants had a history of 1 to 29 years (10.29 ± 6.59). The families of 52% of the participants were involved in COVID-19. Also, 52.5% of the samples were infected with COVID-19. In terms of participating in the exercise, the number of maneuvers varied from zero to forty. In terms of attending in crisis, it varied from zero to twenty. Moreover, in terms of the type of crisis participants attended, epidemic crises such as COVID-19 and floods had the highest and lowest rates of 38% and 8&, respectively. In terms of attendance in training courses, it ranged from zero to one hundred hours. In this study, 134 were married (67%), 124 (62%) had a bachelor's degree, 125 (62.5%) had experience in disaster-related training and 148 (74%) had experience in maneuvering. According to Table 1, the mean and standard deviation of professional competence and anxiety of prehospital emergency medical personnel were reported as 37.82 ± 13.65 and 17.98 ± 11.11, respectively (Tab. 1).

Main results

Furthermore, there is no significant relationship between other professional functions and anxiety with the workplace ($p > 0.05$). There is no statistically significant relationship between education level and mean professional performance score and anxiety ($p > 0.05$). The results of the study on the relationship between receiving training with the mean score of occupational performance variables and anxiety indicate a significant relationship ($p < 0.05$). The results of the study on the relationship between the experience of attending in crisis with the mean score of the variables of professional competence and anxiety revealed a significant relationship between all the studied variables with the history of participating in the crisis ($p < 0.05$). Regarding the relationship between attendance in the maneuver and the average score of the variables of professional competence and anxiety, showed a significant relationship between all the variables studied with the history of participation in the crisis ($p < 0.05$). Also, there was no statistically significant relationship between maneuver training and the mean score of the indicators ($p > 0.05$). The results of independent t-test showed that the mean score of professional competence and anxiety in single employees were significantly higher than married employees being $p < 0.05$, $t = 0.41$ and $p < 0.05$, $t = 0.51$, respectively. In addition, there was a significant relationship between the anxiety variable of the studied samples and COVID-19 symptoms. Anxiety levels were higher in people with COVID-19. But there was no statistically significant relationship between professional competence and COVID-19 symptoms (Tab. 2).

The results showed a significant relationship between the anxiety variable and family infection to

Table 2. Correlation coefficient between having COVID-19 symptoms with the mean score of professional competence and anxiety variables in the study samples

		Having COVID-19 Symptoms			
Variables		M	SD	p	t
Professional competence	Yes	36.96	8.61	0.54	−1.32
	No	38.54	8.27		
Anxiety	Yes	20.47	11.41	0.02	2.91

Table 3. Correlation coefficient between marital status and the mean score of the variables of professional competence and anxiety in the study samples

		Having COVID-19 Symptoms			
Variables		M	SD	p	t
Professional competence	Yes	35.79	8.29	0.62	−3.66
	No	40.03	8.08		
Anxiety	Yes	19.65	12.00	0.01	2.23
	No	16.18	9.81		

Table 4. Correlation coefficient between professional competence and anxiety variables in the study samples

Variables		Professional competence	Anxiety
Professional competence	Pearson Correlation	1*	−0.323**
	Significant (2-tailed)	0	0
	Number	200	200
Anxiety	Pearson Correlation	−0.323**	1*
	Significant (2-tailed)	0	0
	Number	200	200

*Correlation is significant at the 0.05 level (2-tailed); **Correlation is significant at the 0.01 level (2-tailed)

COVID-19; as an individual with an infected member in his/her family experienced higher anxiety. Conversely, there was no significant relationship between the professional competence variable and family infection to COVID-19 (Tab. 3). Moreover, the findings indicated a significant relationship between anxiety and professional competence (Tab. 4).

DISCUSSION

According to the findings of the current study, high severity of anxiety was reported which is in agreement to the previous studies carried out on SARS and Ebola. However, most studies have been performed on nurses and no study has been found on prehospital emergency medical personnel, to our knowledge. In the study of Lai et al. [19], nurses, physicians, and other health care workers experienced high levels of anxiety symptoms during the onset of COVID-19 disease in Wuhan, China (50.4%) which is consistent with the results of the present study. Also in Rahmanian et al. [20] study, he reported the level of anxiety among the treatment staff as 46.91% which is consistent with the current study. However, in Abedi et al. [21] study, there was a significant relationship between receiving training and the mean score of professional competence and anxiety variables ($p < 0.05$) which is in agreement with the current study. Ghaedamini et al. [21] study reported higher level of professional competence for the people who experienced critical and stressful situations which is consistent with the present study. In Rahmati et al. [22] study, it is shown that anxiety following corona is not high but is consistently higher than the average and is higher among employees than students, which differs from the results obtained in the study. The Mutlu et al. [23] study reported moderate to severe anxiety in prehospital emergency personnel,

which is more common among married people. Personnel with chronic diseases have more anxiety, which is consistent with the results of the above study. Vatankhah net al. [24] study reported that psychological factors affect the level of personnel anxiety, which is also consistent with the results of the current study. Faustino et al. [25] study shows that COVID-19 increases anxiety and endangers the mental health of prehospital emergency personnel. In the study of Taghilou and Jafarzadeh Gharajag [26] there is a significant relationship between the effect of COVID-19 on burnout and job and professional performance. Also, they reported the performance of professional competence is reduced by 20% and there is a significant inverse relationship between job anxiety and the practice of professional competence which is in line with the aforementioned study. There was an inverse relationship in both articles and high stress affected professional competence and they reported their competence as moderate. There was no significant relationship between the level of education and professional competence of nurses in response to disasters in the study of Nejadshafiee et al. [27] which is consistent with the present study. In Chen et al. [28] study, the type of exposure and the number of patients with a critical situation affect the level of professional competence of nurses, which is consistent with the findings of the above research. In the study of Slobodin et al. [29] it was reported that the level of cultural competence of nurses is also affected by COVID-19, which online training related to crisis management leads to an improvement in the level of competence of nurses involved. The results of Darminto and Sugandi study [30] show that COVID-19 leads to a decrease in the level of professional competence which is not consistent with the results of the above research.

Limitations of the study

The limitations of this study were the working conditions of the prehospital emergency medical personnel, who were likely to be called up and assigned at any time. Therefore, it sometimes made them difficult to access. Thus, appointments were coordinated with participants as much as possible during leisure and non-working hours. Another limitation of the study was the possibility of transmission of COVID-19 between researchers and study participants. We tried to hold the meetings outdoors as much as possible and in accordance with the health instructions.

CONCLUSIONS

Given that more than two years have passed since the coronavirus outbreak, the various treatments proposed for COVID-19 which are not effective enough and the virus is still mutating. It has put a lot of pressure on the health care providers, especially the prehospital emergency medical personnel. Accordingly, addressing the factors that might reduce the stress and anxiety of these employees is of great necessity and importance. Also, due to the fact that the post-COVID 19 period does not have a specific date and after more than two years, the mental health of prehospital emergency medical personnel has undergone many changes; The Ministry of Health should make decisions to improve the mental health of the country's health care providers. Thereupon, it is necessary to examine the mental health of prehospital emergency medical personnel so as to receive psychological interventions along with training of effective mechanisms and reduction of job stress and psychological strategies.

Conflict of interest

All authors declare no conflict of interest.

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PREHOSPITAL ACUTE STROKE TRAINING APP (PASTAPP) — PROTOTYPE DEVELOPMENT AND INITIAL VALIDATION

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Abstract

INTRODUCTION: Acute ischemic stroke (AIS) is a medical emergency that destroys roughly 2 million neurons each minute, highlighting the importance of treating it with the "time is brain" approach.

MATERIAL AND METHODS: This article will explain the development process of a new smartphone application called PASTApp (Prehospital Acute Stroke Training App) designed to help Emergency Medical Teams diagnose and triage suspected acute stroke patients in the field. We describe the app's features, content, and development and maintenance methods. This smartphone app was developed using a combination of user-centered techniques, including the Information Systems Research methodology and design thinking.

RESULTS: The PASTApp was designed iteratively to satisfy prehospital care workers' preferences.

CONCLUSIONS: Using such an app may improve management, speed, data quality, and communication during patient handover.

KEY WORDS: prehospital care; stroke; mHealth; app

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INTRODUCTION

According to the Global Burden of Disease Study, stroke was the second leading cause of disability-adjusted life-years worldwide in both the 50–74 and 75+ age groups in 2019 [1]sound evidence on trends by cause at the national level is essential. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD .

Acute ischemic stroke (AIS) is a time-sensitive medical emergency that is estimated to destroy approximately 2 million neurons per minute, emphasizing the critical nature of the "time is brain" treatment approach [2].

The key to successful AIS management is early recognition in the prehospital setting (ambulance) and prompt diagnosis in the Emergency Department (ED) [3]. In clinical practice, several features of the clinical history, such as the abrupt onset of focal neurologic symptoms (e.g., slurred speech, asymmetrical facial weakness, asymmetrical arm weakness), suggest a stroke diagnosis. At the same time, it is essential to realize the importance of other conditions which may mimic stroke symptoms — such as metabolic derangements, cardiovascular events, and psychiatric issues [4]. Ischemic stroke is distinguished from hemorrhagic stroke and mimics using neuroimaging modalities such as brain computed tomography and, in some centers, magnetic resonance imaging to obtain a more

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precise assessment of infarcted brain tissues and hemorrhages [5].

The complex diagnostic algorithm used to assess the indication for therapy is so time-consuming in its traditional form that, despite multiple ongoing efforts to optimize pre-and in-hospital processes, thrombolysis rates in regular clinical practice remain poor [6].

Numerous studies have shown that administration of recombinant tissue plasminogen activator (rt-PA) intravenously soon after the onset of symptoms of acute ischemic stroke increases the likelihood of a favorable functional outcome within 90 days [7–9].

Recognition of this fact has prompted providers to improve efficiency in identifying candidates for intravenous thrombolysis and reduce delays in prescribing rt-PA to these patients. Emergency Medical Service (EMS) paramedics are essential partners to more quickly identify ischemic stroke patients who may benefit from thrombolysis administration. In addition, paramedics' prehospital reporting of acute strokes is associated with improved time to care, better imaging results, and overall treatment rates [10, 11].

In the work of medical rescue teams operating based on the Act on State Medical Rescue Service, the necessity of creating electronic medical documentation of a patient in life and health-threatening emergency has been introduced. Documentation in the form of several forms taken directly from the Card of Medical Rescue Actions allows to describe the patient's condition by the description of the incident, determination of the level of consciousness, e.g., using the Glasgow Coma Scale, description of the procedures performed, confirmation of the administration of drugs and medical materials used during medical rescue actions at the place of call and on the way to the hospital ED or the emergency room. However, one of the limitations of the above system is the lack of tools to provide more structured and accurate patient information, depending on the reason for the intervention.

The European Stroke Action Plan 2018–2030 [12] addresses the entire chain of stroke care, from primary prevention to life after stroke, through seven domains: primary prevention, organization of stroke services, management of acute stroke, secondary prevention, rehabilitation, evaluation of stroke outcome and quality assessment, and life after stroke. In addition, this document makes recommendations for digital health solutions that have the potential to improve access to stroke care. The term "digital health" refers to healthcare interventions offered by digital technologies such as telemedicine, Web-based techniques, e-mail, mobile phones, mobile applications, text messaging, and monitoring sensors [13]. Mobile health (mHealth) is a term that refers to the practice of medicine and public health services that incorporates the use of mobile devices [14].

Therefore, we have attempted to prepare a mobile application based on the most recent guidelines of the Expert Group of the Section of Vascular Diseases of the Polish Neurological Society [15] designed to offer paramedics immediate access to the knowledge and resources necessary to excel in prehospital stroke management. An ideal platform should be cost-free to the end-user and be widely and easily accessible with excellent portability while providing a user-friendly interface and decision algorithm that reduces cognitive load. The majority of those characteristics are met by applications designed for smartphones. Indeed, smartphone use has increased significantly among healthcare professionals and is already being used for various purposes in the field of stroke. The purpose of this article is to discuss a new smartphone application named PASTApp (Prehospital Acute Stroke Training App) that was developed to aid emergency medical professionals in the field assessment and destination triage of patients with acute stroke. We detail the application and its content, and the processes involved in its development and maintenance.

MATERIAL AND METHODS

The study was approved by the Institutional Review Board of the Polish Society of Disaster Medicine (approval No. 06.11.2021.IRB). We used a combination of user-centered methodologies, notably the Information Systems Research framework and design thinking, to define and describe the development process of this mobile app (Fig. 1) [16].

RESULTS

Relevance cycle

The objective of the relevance cycle was to ascertain the various groups of end-users and their prehospital stroke treatment needs.

Empathize mode

The target audience was defined by conducting structured interviews with prehospital providers (n = 10) to better understand their practice in taking care of patients in the prehospital phase and the use of mobile medical applications. Table 1 presents the types of questions used.

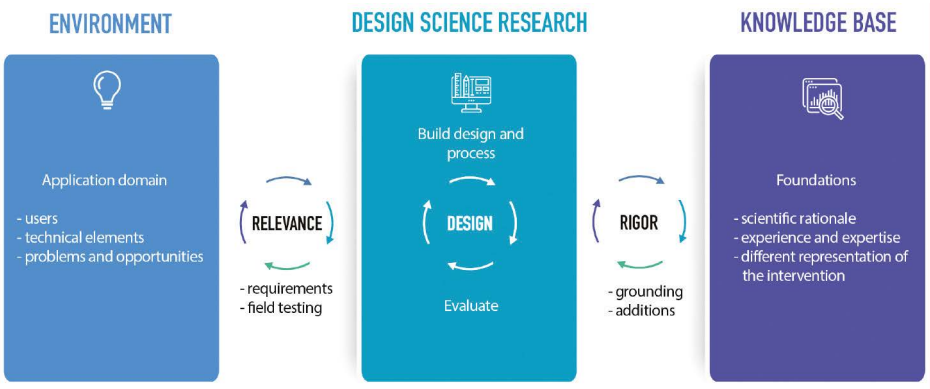

FIGURE 1. The adapted framework for Information Systems Research, incorporating design thinking practices into the relevance, design, and rigor cycles. Adapted from [16] (Creative Commons Attribution License)

Table 1. Questions asked during the semi-structured interviews

Demographic and practice questions
1. I am… a) A physician b) A paramedic
2. Years of professional experience a) Less than 1 year b) 1–5 years c) 5–10 years d) 10–15 years e) More than 15 years
3. Where do you work? a) Ambulance services b) Emergency department c) Air ambulance d) Other
4. What is the number of your duties per month? a) 0–5 b) 6–10 c) 11–15 d) 16–19 e) 20 and more
5. Please specify your confidence in making decisions in the event of emergency treatment of a patient suspected of having a stroke a) 1 — lowest b) 2 c) 3 d) 4 e) 5 — highest
6. How often do you work with a patient suspected of having a stroke within a month? a) Never b) 1–4 c) 5–10 d) > 10
7. Have you participated in workshops/training improving your qualifications on how to proceed in the event of a stroke? a) Yes b) No
8. Do you pre-notify the stroke unit/emergency department about the transport of a patient with suspected stroke? a) Always b) Often c) Sometimes d) Rarely e) Never
9. Do you use the Rapid Assessment Protocol for Suspected Stroke (please tick all that apply)? a) FAST b) LAPSS (Los Angeles Prehospital Stroke Screen) c) CPSS (Cincinnati Prehospital Stroke Scale) d) ROSIER (Recognition of Stroke in the Emergency Room) e) Not using any
Mobile health questions
10. Do you utilize mobile devices daily in your practice for patient-related tasks? a) Yes b) No
11. I avoid using mobile devices for patient-related work because… (check all that apply) c) I am unsure of how to incorporate mobile technology into my daily practice appropriately d) I see no way in which mobile technology can improve my daily practice e) My practice prohibits me from using my personal mobile devices f) Other (please comment)
12. Name medical apps you use for yourself:
13. Please rate the following challenges to integrating medical apps into your regular clinical practice (with 1 being the most significant and 5 being the least significant): a) Insufficient knowledge of practical applications b) Absence of a reliable source for accessing effective applications c) Inaccessibility to mobile devices d) Insufficient practice incentives e) Inability to comprehend the benefits

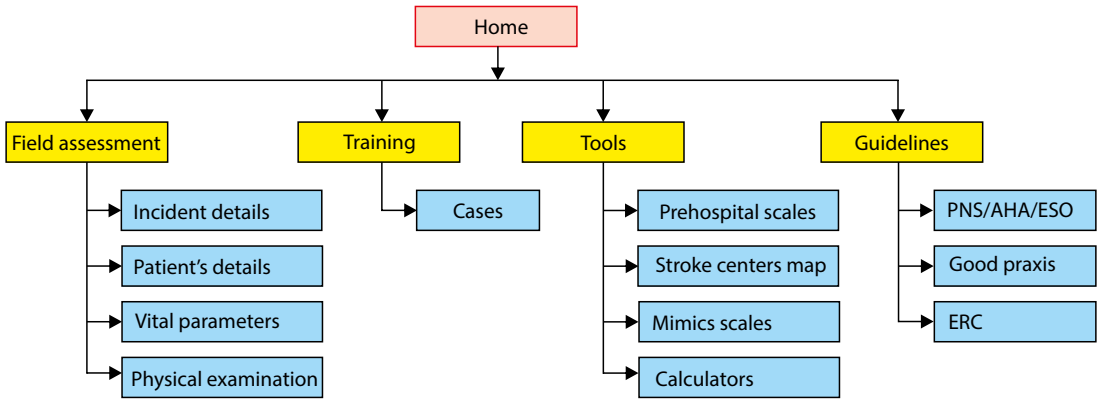

FIGURE 2. Sitemap of the mobile application; AHA — American Heart Association; ASA — American Society of Anesthesiologists; ERC — European Resuscitation Council; ESO — European Stroke Organization; PNS — Polish Neurological Society

Define mode

End-user comments and clinical observations were compiled, processed, and analyzed. This enabled the identification of end-user needs and the assessment of the app's technical requirements.

Design cycle

The design cycle's objective was to compile all of the data obtained in the prior cycle to develop new ideas in the ideate mode. This was utilized to develop a vision for the app prototype's design.

Ideate mode

Ideas were generated in time-constrained intervals, which DT encourages, and represented with sticky notes and pictorial depictions to accommodate the visual nature of creative DT practices. Some of the ideas formulated included: bilingual interface text, using videos and images for instruction, minimal to no text, and visual directives during performing procedures. Most ideas were included in the prototypes, as many of the ideas addressed different themes and problems with the interface.

Prototype mode

We began with a paper prototype to build the application's information flow and incorporate all of the relevant information specified by prehospital providers during the study of the needs. Figure 2 shows the sitemap of the application.

The information flow was later transferred to InVision platform for collaborative development of interface layouts. Figure 3 presents an example user flow diagram applied to the "Field Assessment" module. This particular diagram was developed

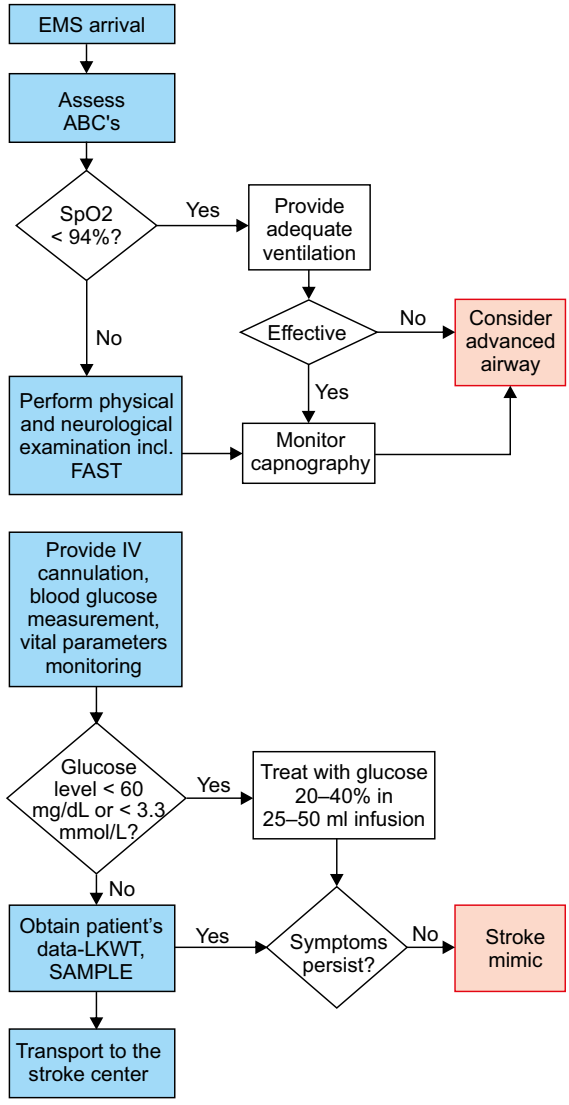

FIGURE 3. User flow diagram applied to the "Field Assessment" module; ABC — Airway, Breathing, Circulation; EMS — Emergency Medical Service; FAST — Field Assessment Stroke Triage for Emergency Destination; LKWT — Last Known Well Time; SAMPLE — Symptoms, Allergies, Medications, Past medical story, Last meal, Events prior to injury

based on three relevant documents — the most recent guidelines of the Expert Group of the Section of Vascular Diseases of the Polish Neurological Society [15], European Academy of Neurology, and European Stroke Organization Consensus Statement and Practical Guidance for Prehospital Management of Stroke [17] as well as guidelines on "Good praxis in treating patients with suspected brain stroke for medical dispatchers and emergency medical services teams" issued on January 24, 2019, by the Ministry of Health, in collaboration with National Consultants in neurology and emergency medicine [18].

We then refined and developed a high-fidelity prototype (Fig. 4) and evaluated it using two types of usability inspection: cognitive walk-throughs to identify potential usability issues with the application's functionality and heuristic evaluations to determine whether the application's screen design adhered to established design principles. Following that, we changed the prototype interface based on the findings of these inspections. In addition, the cognitive walk-through enabled us to ascertain how a novice user would navigate the application.

FIGURE 4. High-fidelity prototype

Rigor cycle

We conducted a study of the available literature for papers that addressed the topic of stroke training for prehospital clinicians, classified them by subject matter, and then tabulated the findings to ascertain knowledge gaps. Examples included the one-hour seminar covering stroke epidemiology, symptoms, diagnosis, therapy, and identifying the start time. The instructional program boosted stroke awareness and increased the precision with which dedicated EMS providers triaged patients [19]. A comparable study conducted in Dubai found that an educational lecture effectively increased stroke awareness [20]. In addition, the online training intervention implemented in Catalonia successfully increased EMS professionals' awareness and compliance with prenotification requirements during stroke code activation and ensured widespread adoption of a new prehospital stroke severity assessment scale (i.e., the RACE scale) [21].

We reviewed the primary relevant publications on similar apps that are available in the literature. Following a review of the relevant literature, a review of the available mobile apps and websites was undertaken. Google Play Store and Apple App Store were utilized to search for mobile applications, as they are the two largest app stores. Our team later evaluated these apps in terms of their strengths and weaknesses. Table 2 summarizes our findings.

Test mode

After finalizing the high-fidelity prototype, we conducted formative evaluations using usability testing. First, we gathered a convenience sample of ten prospective users for the usability testing, consisting of paramedics, medical doctors, and medical students.

To monitor how users navigated the application, one of us provided verbal directions on accessing the application from the home screen. Additionally, the researcher provided the participant with a scenario involving a stroke patient, for which the individual would need to evaluate immediately. We gave no further instructions about application navigation, as the application itself had all the necessary instructions for completing the task of producing a case report.

Following completion of the timed task, we conducted usability testing. Participants were invited to explore the prototype freely and think aloud throughout the interviews to identify usability issues. Interviews were manually recorded, transcribed, coded, and analyzed. Table 3 summarizes the key themes identified during the interviews.

Table 2. Strengths and weaknesses of similar apps

App	Strengths	Weaknesses
Code Stroke Alert [22]	Clinical score calculators and guidelines Instant messaging and reading receipts Interhospital referral Tracked and timestamped data entries for audit Real-time GPS tracking Open-source	Not universally available An early phase of deployment Lacks data on the impact on the outcome
Green [23]	Real-time communication Enables hospital prenotification by EMS Staff is able to create and edit clinic records. Then, the data is automatically entered into the chosen hospitals' electronic clinic records Semi-automated timestamping of events Provides the data to identify weak points in treatment plans and makes comments	The performances of the platform in less populated areas should be examined further Not universally available
JoinTriage (formerly known as FAST-ED [24])	Timestamps events (Last Seen Well, CT, MRI, Angio suite, Reperfusion) Instant messaging platform GPS technology with real-time traffic information Provides information on stroke symptoms, thrombolytic treatment, and prescribed actions when stroke is suspected Computes patient's eligibility for intravenous tissue-type plasminogen activator or endovascular treatment	Not universally available Risk of triage mismatches Lacks data on the impact on the outcome
Stop Stroke Pulsara [25, 26]	Improves communication between staff involved in treatment (EMS, ED, radiology, neurology, and Interventional team) All care team members have real-time access to the most up-to-date patient information Includes stroke scales (LAMS, NIHSS, RACE, FAST/Cincinnati) Keeps running track of LSW, tPA times, and MT times Alerts when images are available Transmits images Allows tPA contraindication review by all Data (limited) on the impact on logistical outcomes	Not integrated to medical records
Stroke 119 [27]	Provides rapid self-screening for stroke Identifies nearby hospitals that provide thrombolytic treatment Facilitates calling emergency services	It is inconclusive that this application can improve patient outcomes in actual practice

EMS — Emergency Medical Service; CT — computed tomography; MRI — magnetic resonance imaging; ED — Emergency Department; LAMS — Los Angeles Motor Scale; NIHSS — National Institutes of Healths Stroke Scale; RACE — Rapid Arterial oCclusion Evaluation; FAST - Face, Arm, Speech, Time; LSW — last seen well; tPA — tissue plasminogen activator; MT — mechanical thrombectomy

Table 3. Summary of topics covered during interviews

Topic	Aspects covered
Appropriacy of an application	Questions concerning the app's scope, audience, and purpose; the app as a learning aid; the app's familiarity and acceptability; and the app's anticipated limitations
Contents	Which prehospital scales should be used; which sources to consult; examination of scientific evidence
Usability	Information presentation; linguistic use; potential decision algorithms; visual design; and familiarity
Safety	Mobile device as a target for theft; data security

DISCUSSION

The article details a step-by-step technique for designing a user-centric mobile health application. PASTApp (Fig. 5) is intended to assist prehospital providers who are confronted with obstacles in caring for acute stroke patients. An early search of the literature found that there are already various solutions accessible in the aforementioned area. However, the bulk of solutions offered makes no mention of user-centered or collaborative design approaches. It is important to emphasize that our application is intended for educational use first.

FIGURE 5. App's welcome screen

Subsequent app development processes will be aimed at preparing the app for use in the management of patients with suspected stroke.

Various educational options based on technology for EMS stroke detection are becoming available. The utilization of online resources and video education for EMS education (e.g., the American Heart Association's FAST-ED video) enables EMS providers to receive education at a convenient time for them and the ability to conduct pre-and post-education testing to determine knowledge retention [28].

Numerous prehospital stroke measures are available, most of which have been field validated against the NIHSS and are streamlined in format, with some, such as the RACE scale, having been field confirmed [29, 30].

Numerous smartphone applications are available to assist stroke patients with self-screening and hospital selection, as well as to potentially reduce hospital arrival time (e.g., FAST-ED [24], Mayo Clinic Acute Stroke Evaluation app [31], Stroke 119 [27], Green [23]).

The apps often include built-in automated decision-making algorithms based on clinical data, a database of all regional stroke centers classified according to their ability to provide Efficient Video Transport (EVT), and Global Positioning System technology with real-time traffic information to determine a patient's eligibility for t-PA or EVT, as well as distances/transportation times to the various neighboring stroke centers to assist EMS professionals in making the most appropriate defibrillation decision.

Currently, data on the implementation of the majority of these applications are in a preliminary phase.

Our study has some limitations. To begin, while our mobile application was successfully constructed, its usability was only tested on a small sample group. Its true impact and safety should now be evaluated and compared to other prehospital stroke treatment delivery methods, first in simulation research and then in the clinical setting.

CONCLUSIONS

The iterative development approach aided in the design of the PASTApp to accommodate prehospital care professionals' preferences. Using such an app may result in improved and faster management and an increase in data quality, which may improve communication during patient handover.

Additional research is necessary to determine the effect of the PASTApp on closing knowledge gaps and enhancing prehospital stroke care in simulated scenarios.

Conflict of interest

All authors have no affiliations or involvement with any organization or entity having any financial or non-financial interest in the subject matter or materials discussed in this manuscript.

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SYSTEMATIC REVIEW AND META-ANALYSIS OF INTRAVENOUS AND TOPICAL TRANEXAMIC ACID IN REDUCING BLOOD LOSS IN KNEE ARTHROPLASTY

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ABSTRACT

INTRODUCTION: The purpose of this review and meta-analysis is to compare tranexamic acid (TXA) administration via the intravenous route (IV-TXA) and topical route (T-TXA), in reducing blood loss in knee arthroplasty.

MATERIAL AND METHODS: A systematic literature search was performed using Medline, EMBASE, Scopus and CENTRAL databases till December 20, 2021. Outcomes of interest included blood loss, hematocrit and hemoglobin drop, and adverse events.

RESULTS: A total of 3,363 patients (n = 1,307 in IV-TXA group; n = 2,056 in T-TXA group) from 23 studies were included. There was no statistically significantly difference between IV-TXA and T-TXA among to: total blood loss (874.8 ± 349.7 mL vs 844.9 ± 366.6 mL, respectively; SMD = 0.13; 95% CI: −9.37 to 85.32; p = 0.15), as well as transfusion needed (10.9% vs 15.4% respectively (RR = 0.79; 95% CI: 0.60 to 1.04; p = 0.09). Blood loss from the drain in IV-TXA and T-TXA varied and occurred 377.9 ± 191.9 vs 302.9 ± 182.6 mL for IV-TXA and T-TXA, respectively: (SMD = 0.52; 95% CI: 0.02 to 1.02; p = 0.04).

CONCLUSIONS: Our clinical findings support that TXA can effectively, safely, and decrease the number of transfusions without severe side effects in patients undergoing TKA. However, given the reports from individual single clinical trials of the superiority of T-TXA, further clinical trials and meta-analyses based on these findings are needed to standardize the approach to TXA use in patients undergoing knee arthroplasty.

KEY WORDS: arthroplasty; knee; replacement; tranexamic acid; intravenous; topical; systematic review; meta-analysis

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INTRODUCTION

Knee arthroplasty (KA) has become a routine orthopedic procedure with tranexamic acid (TXA) used to prevent excessive bleeding [1–5]. Knee arthroplasty may be associated with blood loss of up to 800–1800 mL, making allogeneic blood transfusion necessary with a 10% to 62% [6–8]. This may expose the patient to related complications such as cardiopulmonary embarrassment, disease transmission, immunological reaction, and postoperative infection [9, 10]. Observational studies have reported associations between red blood cell transfusion and increased postoperative morbidity and mortality [11, 12]. Tranexamic acid (TXA) is an anti-fibrinolytic that inhibits fibrin's plasmin-mediated degradation, routinely used in KA but has not yet become the standard of care [12–14]. The absolute contraindications of intravenous TXA are not evident, as well the dose-related effects of TXA on the coagulation system are not clear.

Moreover, the route of TXA application can vary; intravenously (IV-TXA), topically (T-TXA), or orally [13, 15, 16]. T-TXA is considered to be comparable to IV-TXA in reducing postoperative blood loss after primary KA [17]. Topical administration has the theoretical benefits of limiting systemic toxicity and the advantage of locally increased concentrations compared to IV-TXA. It has been investigated as a safe alternative, especially regarding the systemic adverse effects of intravenous TXA [18]. However, most of those studies collectively focus on KA and total hip arthroplasty (THA) [4, 19]. Meta-analyses investigating data from two different procedures fail to capture the differences between the two procedures, their extent, and any differences between the doses of TXA applied topically. Considerations regarding the optimal administration of TXA are still controversial due to the still unclear comparison of the benefits and risks of using TXA by different approaches [16, 20–22].

The purpose of this review and meta-analysis is to compare data from various studies comparing intravenous and topical administration of TXA, which may help guide decisions on the administration of TXA during KA.

MATERIAL AND METHODS

The current meta-analysis was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis statement [23] and the recommendations of Cochrane Collaboration. The study is a continuation of the authors' research on the effectiveness and safety of TXA in orthopedics [24].

Search strategy

To identify all the eligible studies of IV-TXA versus T-TXA in patients with knee arthroplasty, a literature search was performed on the following online databases: Medline, EMBASE, Scopus, and Cochrane Central Register of Controlled Trials (CEN-TRAL) from database inception to December 20, 2021. The following keywords were used as search terms: "tranexamic acid" or "TXA" and "intravenous" or "topical" or "intraocular" and "knee arthroplasty".

Additionally, a manual search of the reference lists of studies and reviews on this topic was performed to identify additional eligible studies. To avoid double data counting, the one with the largest sample size was included when there were multiple publications from the same trial sample.

Eligibility criteria

Studies that were included in this meta-analysis had to fulfill the following PICOS criteria: (1) Participants: patients 18 years old or older requiring knee arthroplasty; (2) Intervention, tranexamic acid treatment administrated intravenously; (3) Comparison: tranexamic acid treatment administrated topically; (4) Outcomes: operative data and adverse events occurrence; (5) Study design: randomized controlled trials and retrospective trials comparing IV-TXA and T-TXA care for their effects in patients with knee arthroplasty. Animal studies, reviews, case reports, letters, conference or poster abstracts, or articles not containing original and not published in English were excluded.

Data extraction

From eligible studies, the following data were extracted into a predefined Microsoft Excel spreadsheet (Microsoft Corp., Redmond, WA, USA): (1) study characteristic (*i.e.*, first author, year of publication, country, study design, inclusion and exclusion criteria, primary outcomes, findings); (2) participant characteristics (*i.e.*, number of participants, age, sex); (3) primary study outcomes (*i.e.*, blood volume loss, operative time, adverse events, hospital length of stay). Data extraction was performed independently by two authors (J.P. and M.P.). Potential disagreements were resolved by discussion with a third reviewer (L.S.).

Quality assessment

The quality of each study was independently evaluated by two authors (J.P. and M.A.-J.) using the RoB-2 tool (revised tool for risk of bias in randomized trials) was used to assess the quality of randomized studies [25], or the ROBINS-I tool (tool to determine the risk of bias in non-randomized studies of interventions) [26]. Any disagreements were resolved by discussion with a third author (M.A.-J.). The risk of bias assessments was visualized using the Robvis application [27].

Statistical analysis

As statistical analyses were performed using the Review Manager, version 5.4EN (RevMan; The Cochrane Collaboration, Oxford, UK) and STATA statistical software, version 17EN (StataCorp LLC, TX, USA). The results for dichotomous outcomes were presented as odds ratios (ORs) or risk ratios (RRs) with 95% confidence intervals (CIs). The standard mean differences (SMDs) with 95% CI were used for continuous outcomes. In case when the continuous outcomes were reported in a study as median, range, and inter-quartile range, we estimated means and standard deviations using the formula described by Hozo et al. [28].

We quantified heterogeneity in each analysis by the tau-squared and I-squared statistics. Heterogeneity was detected with the chi-squared test with n – 1 degree of freedom, which was expressed as I2. Values of I2 > 50% and > 75% were considered to indicate moderate and significant heterogeneity among studies, respectively. A random-effects model was used to pool study results independently of the p-value for heterogeneity or I2 [29]. All the p-values are two-sided, and a $p < 0.05$ was considered statistically significant [30].

To evaluate the potential for publication bias, we plotted values against associated standard errors [31] and used Begg's test to assess the symmetry of the resulting funnel plot [32]. We considered publication bias present when the p-value was < 0.1 in the asymmetry test. However, publication bias was not evaluated when a limited number of studies (< 10) were included in the analysis.

RESULTS

Study selection

Figure 1 depicts the flow diagram for the search process. Overall, the combined search identified 517 articles, of which 470 were excluded (78 were duplicates, and 392 were excluded upon the title and abstract evaluation). The remaining 47 articles underwent full-text evaluation. Finally, 23 eligible articles were found and were included in the qualitative and quantitative analyses.

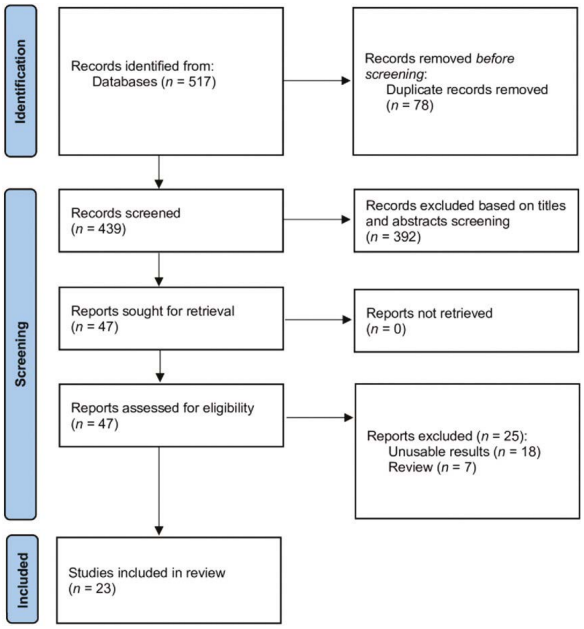

FIGURE 1. Database search and selection of studies according to PRISMA guidelines

Twenty-three trials [8, 9, 13–16, 20-21, including 3,363 patients with knee arthroplasty (1,307 with IV-TXA and 2,056 with T-TXA application) were published between 2012 and 2019. Table 1 displays the baseline characteristics of patients who underwent Knee arthroplasty and were treated with IV-TXA or T-TXA. Twenty-one studies were designed as randomized controlled trials [8, 9, 13–16, 21, 33, 35–42, 44–48]. The risk of bias among included studies is assessed in Figures S1–S4 (see Supplementary file).

There was no statistically significant difference in patient baseline characteristics between IV-TXA and T-TXA (Tab. 2).

Blood loss from the drain was reported in nine studies and was 377.9 ± 191.9 vs 302.9 ± 182.6 mL for IV-TXA and T-TXA respectively: (SMD = 0.52; 95% CI: 0.02 to 1.02; I2 = 92%; p = 0.04; Figure 2).

Fifteen studies reported hemoglobin differences between pre-surgery and post-surgery periods. Pooled analysis of hemoglobin drops in IV-TXA and T-TXA was 2.4 ± 1.1 in each group (SMD = 0.42; 95% CI: = −0.26 to 1.09; I2 = 98%; p = 0.23; Figure 4).

Table 1. Characteristics of included studies

Study	Country	Study design	Intravenous TXA group			Topical TXA group		
			No	Age	Sex, male	No	Age	Sex, male
Aguilera et al. 2015	Spain	RCT	50	72.49 ± 7.68	12 (24.0%)	50	72.53 ± 6.6	18 (36.0%)
Dronos et al. 2016	Greece	RCT	30	69.27 ± 7.21	6 (20.0%)	30	71.10 ± 6.32	6 (20.0%)
Hegde et al. 2013	India	PCS	30	66.57 ± 8.48	NS	30	65.48 ± 6.53	NS
Keyhani et al. 2016	Iran	RCT	40	68.4 ± 10.4	26 (65.0%)	40	67 ± 11.9	23 (57.5%)
Kyriakopoulos et al. 2019	Greece	RCT	41	69.73 ± 6.87	NS	42	70.74 ± 6.55	NS
Lacko et al. 2017	Slovakia	RCT	30	68.4 ± 7.2	12 (40.0%)	30	67.5 ± 7.7	13 (43.3%)
Laoruengthana et al. 2019	Thailand	RCT	76	64.01 ± 7.68	14 (18.4%)	75	64.81 ± 8.06	12 (16.0%)
López-Hualda et al. 2012	Spain	RCT	30	73.1 ± 7.3	24 (80.0%)	30	72.9 ± 7.1	19 (63.3%)
Maniar et al. 2012	India	RCT	40	67.3 ± 9.1	10 (25.0%)	40	67.4 ± 7.9	6 (15.0%)
Mehta et al. 2018	India	RCT	100	62.86 ± 6.08	41 (41.0%)	100	61.85 ± 4.81	44 (44.0%)
Oztas et al. 2015	Turkey	RCT	30	68.56 ± 5.38	5 (16.7%)	30	67.06 ± 6.54	4 (13.3%)
Pitta et al. 2015	USA	RS	202	65.3±10.6	61 (30.2%)	201	65.8 ± 10.9	68 (33.8%)
Sahin et al. 2019	Turkey	RCT	67	66.7 ± 9.5	8 (11.9%)	33	68 ± 7.5	4 (12.1%)
Sarzaeem et al. 2014	Iran	RCT	50	66.9 ± 7.2	7 (14.0%)	50	68.1 ± 6.8	7 (14.0%)
Seo et al. 2013	South Korea	RCT	50	66.8 ± 6.3	6 (12.0%)	50	67.5 ± 6.6	5 (10.0%)
Song et al. 2016	Korea	RCT	50	69.2 ± 6.4	6 (12.0%)	50	69.8 ± 6.8	8 (16.0%)
Tzatzairis et al. 2016	Greece	RCT	40	69.55 ± 6.61	9 (22.5%)	40	69.10 ± 8.68	7 (17.5%)
Uğurlu et al. 2016	Turkey	RCT	40	69.4 ± 7.5	11 (27.5%)	42	70.6 ± 8.6	9 (21.4%)
Wang et al. 2017	China	RCT	50	67.42 ± 8.202	14 (28.0%)	50	67.98 ± 5.971	14 (28.0%)
Wang et al. 2018	China	RCT	60	66.90 ± 9.48	15 (25.0%)	60	63.20 ± 11.75	16 (26.7%)
Yen et al. 2017	Taiwan	RCT	31	69.13 (7.94; 51–85)	4 (12.9%)	32	69.66 (5.53; 59–84)	13 (40.6%)
Yuan et al. 2017	China	RCT	140	63.74 ± 8.05	67 (47.9%)	140	63.26 ± 6.99	63 (45.0%)
Zekcer et al. 2016	Brazil	RCT	30	NS	6 (20.0%)	30	NS	9 (30.0%)

NS — not specified; PCS — prospective comparative study; RCT — randomized controlled trial; RS — retrospective study

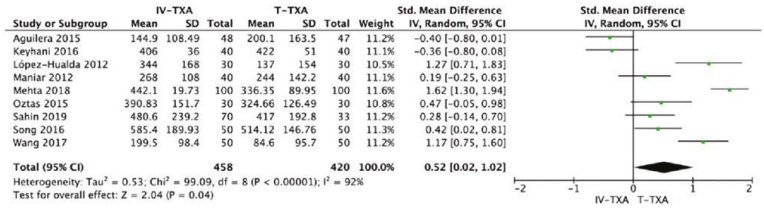

FIGURE 2. Forest plot of blood volume loss from the drain among IV-TXA and T-TXA groups. The center of each square represents the weighted standard mean differences for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds rep-resent pooled results

Hematocrit difference between pre- and post-surgery period was 7.5 ± 2.8% for IV-TXA group compared to 8.0 ± 2.9% for T-TXA group (SMD = −0.08; 95% CI: −1.42 to 1.26; I2 = 94%; p = 0.91; Figure 5).

Pooled analysis of nineteen studies showed that the need for transfusion in the IV-TXA and T-TXA groups varied and amounted to 10.9% vs 15.4% respectively (RR = 0.79; 95% CI: 0.60 to 1.04; I2 = 25%; p = 0.09).

A summary of the individual adverse events observed in the analyzed articles is presented in Table 3. Pooled analysis showed no statistically significant differences in the occurrence of particular

Table 2. Pooled analysis of patient characteristics among included trials

Outcome	No. of studies	Events / Participants or Mean ± SD		Events		Heterogeneity between trials		P-value for differences across groups
		IV-TXA	T-TXA	OR or SMD	95%CI	P-value	I2 statistic	
Age, years	22	66.6 ± 8.5	66.5 ± 8.7	0.00	−0.08 to 0.08	0.94	0%	0.98
Sex female, n (%)	22	327/1,208 (27.1%)	351/1,173 (29.9%)	1.13	0.94 to 1.36	0.80	0%	0.20
BMI	17	28.6 ± 6.2	28.1 ± 5.4	0.07	−0.18 to 0.33	< 0.001	86%	0.59
ASA								
1 class	5	67/321 (20.9%)	56/322 (17.4%)	1.34	0.85 to 2.11	0.92	0%	0.21
2 class	6	240/351 (68.4%)	247/352 (70.2%)	0.91	0.65 to 1.28	0.57	0%	0.59
3 class	5	39/321 (12.1%)	44/322 (13.7%)	0.87	0.54 to 1.41	0.43	0%	0.57
4 class	5	1/321 (0.3%)	1/322 (0.3%)	1.00	0.06 to 16.44	NA	NA	1.00
Pre-surgery hemoglobin, g/dL	19	13.1 ± 1.4	13.1 ± 1.6	0.00	−0.08 to 0.08	0.73	0%	0.99
Pre-surgery hematocrit, %	11	40.1 ± 3.5	40.1 ± 4.1	0.06	−0.09 to 0.22	0.18	27%	0.44

ASA — The American Society of Anesthesiologists physical status classification system; BMI — body mass index; CI — confidence interval; MD — mean difference; NA — not applicable

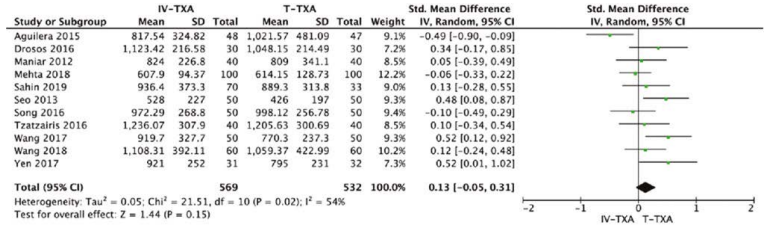

FIGURE 3. Forest plot of total blood volume loss among IV-TXA and T-TXA groups. The center of each square represents the weighted standard mean differences for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results

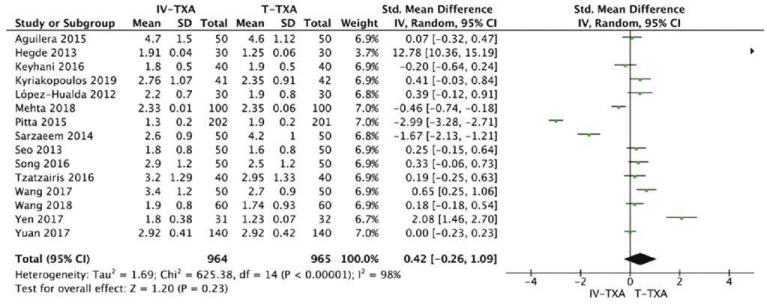

FIGURE 4. Forest plot of hemoglobin difference between pre-surgery and post-surgery period among IV-TXA and T-TXA groups. The center of each square represents the weighted standard mean differences for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results

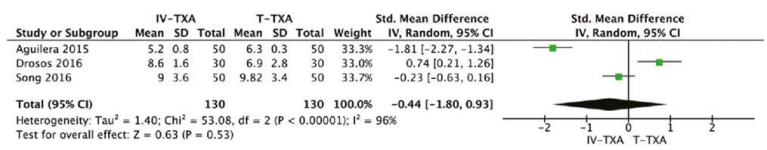

FIGURE 5. Forest plot of hematocrit difference between pre-surgery and post-surgery period among IV-TXA and T-TXA groups. The center of each square represents the weighted standard mean differences for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results

Table 3. Pooled analysis of adverse events occurred among analyzed trials

Adverse event type	No. of studies	Events / Participants		Events		Heterogeneity between trials		p-value for differences across groups
		IV-TXA	T-TXA	RR	95%CI	p-value	I2 statistic	
DVT	6	4/345 (1.2%)	4/342 (1.2%)	1.10	0.26 to 4.62	0.37	7%	0.89
Pulmonary embolus	5	0/331 (0.0%)	0/332 (0.0%)	NE	NE	NA	NA	NA
Wound infection	3	0/230 (0.0%)	1/230 (0.4%)	0.33	0.01 to 8.02	NA	NA	0.50
Atrial fibrillation	1	0/50 (0.0%)	1/50 (2.0%)	0.33	0.01 to 7.99	NA	NA	0.50
Hematoma	2	7/91 (7.7%)	6/91 (6.6%)	1.17	0.43 to 3.19	0.90	0%	0.76
Gastric hemorrhage	1	0/60 (0.0%)	0/60 (0.0%)	NE	NE	NA	NA	NA

CI — confidence interval; DVT — deep vein thrombosis; NA — not applicable; NE — not estimable

types of adverse events between IV-TXA and T-TXA ($p > 0.05$ for every adverse event type).

Both the duration of the operation and the length of hospital stay between examined groups (IV-TXA and T-TXA) showed no statistically significant differences ($p > 0.05$; Figures S5–S6, see Supplementary file).

DISCUSSION

Knee arthroplasty can be associated with significant blood loss. Surgical primary concerns are intraoperative and postoperative period blood loss and secondary acute anemia [7]. Adequate use of antifibrinolytics contributes to decreased blood loss, and TXA has been used widely in total joint arthroplasty through intravenous or topical administration [10]. Routine use of TXA not only appears to increase a patient's prospects for faster and less complicated recovery subsequent to KA but also results in lower direct hospital charges by reducing costs associated with blood transfusion, laboratory testing, and room & board. Gillette et al. [48] report that hospitalization costs for a patient undergoing primary total hip or knee arthroplasty with TXA are lower by nearly $900. However, this study treats THA and KA collectively and refers to a single route of TXA administration. Also, Kyriakopoulos et al. [36] describe the cost reduction of KA with TXA, and the estimated saving is €386 per patient.

In order to compare the efficacy of the routes of administration of TXA used in KA, we conducted a meta-analysis in which eight parameters compared from individual studies were included; total blood loss, blood loss from the drain, hemoglobin drop difference between pre-surgery and post-surgery period, hemoglobin difference between pre- and post-surgery period, need of a transfusion, summary of the individual adverse events, duration of the operation and the length of postal stay.

A meta-analysis of 14 randomized controlled trials conducted by Alshryda et al. [49] in 2014 showed that T-TXA significantly reduced the rate of blood transfusions. Also, in a study by Hamlin et al. [50], it was reported that after T-TXA none of the patients required blood transfusion, while in the IV-TXA group, 2.4% of patients required transfusion. However, these findings are not consistent with our meta-analysis. In 19 analyzed studies, 10.8% of patients in the IV-TXA group required blood transfusion compared to 15.2% in the T-TXA group, and the hemoglobin difference between pre- and post-surgery period was 7.5 ± 2.8% for the IV-TXA group compared to 8.0 ± 2.9% for T-TXA group. These differences, however, must be considered concerning the other data analyzed and cannot unequivocally prove the superiority of IV-TXA because total blood loss in this group was higher than in the T-TXA group (874.8 ± 349.7 mL vs 844.9 ± 366.6 mL). Also, blood loss from drainage reported in ten analyzed

studies indicates an advantage of topical administration (377.9 ± 191.9 vs 302.9 ± 182.6 mL for IV-TXA and T-TXA, respectively).

Topical TXA application has the theoretical advantage of limiting systemic toxicity and benefits of locally increased concentrations, and it can potentially avoid the complications of intravenous TXA [51]. Topical intraoperative applications are easy to perform and therefore seem to be practical. Topical TXA rapidly diffuses into the synovial fluid and synovial membranes until the concentration of the TXA in synovial fluid reaches the concentration of serum, its biological half-life in the joint fluid is about 3 hours [52]. To maintain microvascular hemostasis, it is necessary to reach maximum concentrations at the surgical site. The minimum plasma concentration of TXA needed to inhibit fibrinolysis is 5–10 mg/L [53]. The potential mechanism and advantage of topical application of TXA into the surgical field is to directly reach the bleeding site, attenuating the marked increase in local fibrinolysis associated with a release of the tourniquet [54]. However, as mentioned, the additional costs after TKA are mainly generated by the postoperative need for blood transfusions, and thus analyzing the topic in terms of financial benefits indicates the advantage of IV-TXA again.

It is also valuable to point out that although absolute contraindications of intravenous TXA are not evident, one should remember about relative contraindications for TXA use, such as recent cerebrovascular accidents, deep vein thrombosis (DVT) or pulmonary embolism (PE) [48]. To evaluate the risk of adverse events, we summarized the individual adverse events, including DVT and PE. Pooled analysis showed no statistically significant differences in the occurrence of particular types of adverse events between IV-TXA and T-TXA. No statistical difference was also found in assessing the duration of the operation and the length of postal stay between the examined groups. However, TXA is not considered thrombogenic and prevents the degradation of existing blood clots, and some studies suggest no increase in the incidence of venous thrombosis among patients treated with TXA, even in patients at higher risk, and administration of IV-TXA does not necessarily correlate with an increased risk of venous thromboembolism [55, 56].

There are limitations to the meta-analysis conducted. First, there is a limitation in how results are reported. The different doses and administration times of TXA can contribute to confusion when comparing data. Moreover, there was substantial heterogeneity in the meta-analysis of several outcomes, such as differences in surgical time, technique, approaches, and postoperative measures. The meta-analysis conducted by our team does not allow concluding unequivocally on the superiority of one of the TXA application routes. The analyzed parameters of total blood loss and blood loss from the drain point favors T-TXA; however, the summary analysis of the need for transfusion points in favor of IV-TXA. Considering that the requirement for transfusion reflects the more severe condition of the patient after the procedure and carries the risk of post-transfusion complications, and is associated with additional costs, it seems that intravenous TXA may carry more benefits.

CONCLUSIONS

In conclusion, our clinical findings support that TXA can effectively, safely, and decrease the number of transfusions without severe side effects in patients undergoing TKA. However, given the reports from individual single clinical trials of the superiority of T-TXA, further clinical trials, and meta-analyses based on these findings are needed to standardize the approach to TXA use in patients undergoing TKA.

Author contributions

Conceptualization, J.P. and L.S.; methodology, J.P. and L.S.; software, L.S.; validation, J.P., M.A.-J. and L.S.; formal analysis, J.P. and L.S.; investigation, J.P., M.P., M.A.-J. and L.S.; resources, J.P.; data curation, J.P. and L.S.; writing — original draft preparation, J.P., L.S., MM., M.K. and E.M.; writing — review and editing, J.P., M.A.-J., M.M., M.P., A.M., M.K., E.M., J.S. and L.S.; visualization, L.S.; supervision, L.S.; project administration, J.P. and L.S.; funding acquisition, A.M. All authors have read and agreed to the published version of the manuscript.

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Conflicts of interest

The authors declare no conflict.

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SCREENING ROLE OF COMPLETE BLOOD CELL COUNT INDICES AND C REACTIVE PROTEIN IN PATIENTS WHO ARE SYMPTOMATIC FOR COVID-19

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ABSTRACT

INTRODUCTION: Diagnosis of COVID-19 is through polymerase chain reaction (PCR) or typical involvement of the lung by the virus in computed tomography (CT) scan. However, PCR is not always available, and also CT scan has a high dose of radiation. This study was performed to find the role of complete blood cell (CBC) indices and qualitative C-reactive protein (CRP) in screening of symptomatic patients.

MATERIAL AND METHODS: A diagnostic accuracy study was performed on symptomatic cases in Abadan. Four stepwise logistic regression models were designed that the outcomes were PCR positivity, CT scan positivity, PCR and CT scan positivity, and COVID-19 positivity (*i.e.*, PCR or CT scan positivity). Post-estimation receiver operating characteristics (ROC) curve analysis was performed to report the area under the curve (AUC).

RESULTS: A total of 104 patients were studied. The most accurate model was for the prediction of CT scan positivity (AUC = 0.874) in which the predictors were age [odds ratio (OR) =1.063] and CRP (OR = 2.661 for each plus of positivity). The second accurate model was for the prediction of COVID-19 positivity (AUC = 0.828) in which the predictors were white blood cell count (OR = 0.735 for every 1000 counts per μL) and neutrophil per lymphocyte ratio (OR = 1.248).

CONCLUSIONS: Higher levels of CRP are associated with and predictor of lung involvement in COVID-19 infection. CRP qualitative levels can be measured before a CT scan if there is no other indication for imaging.

KEY WORDS: COVID-19; C-reactive protein; CT scan; clinical reasoning; statistical modeling

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INTRODUCTION

In late December 2019, several cases of pneumonia with unknown symptoms were identified in Wuhan, China, which in February 12, 2020, the International Committee on Taxonomy of Viruses called it acute respiratory syndrome coronavirus 2 (SARS--CoV-2), and on the same date the disease was named as coronavirus disease 2019 (COVID-19) [1, 2].

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This virus is a new strain of β-coronaviruses associated with severe acute respiratory syndrome (SARS) in 2002–2003 and the Middle East respiratory syndrome (MERS) in 2012–2014 [3]. The virus has a longer incubation period and less pathogenicity than SARS and MERS, but its prevalence is much higher. The disease spread rapidly to other parts of China and other countries, so who announced a pandemic [3]. The virus is a common virus between humans and animals and has not been previously reported in humans [2] and is rapidly transmitted from human to human by respiration [2, 4].

Its clinical symptoms are very diverse and include fever, dry cough, shortness of breath, fatigue, and in some patients nasal congestion, runny nose, sore throat, diarrhea, loss of sense of smell and taste, and in some severe cases lead to acute renal failure, acute respiratory syndrome and eventually death [2]. In severe cases, patients have shortness of breath or hypoxia, which usually begins one week after the onset of the disease and progresses rapidly to acute respiratory distress syndrome, septic shock, metabolic acidosis, and coagulation dysfunction, which is also very difficult to improve coagulation function [2, 5].

Infection with the virus has been observed at all ages, as has been observed in children and infants born to infected mothers, in whom children are usually prone to upper respiratory tract infections [4]. However, in the elderly and patients with underlying diseases, complications are also very severe. Also, due to the similarity of the early symptoms of this disease with the flu, its initial diagnosis is not easy, especially in spring and winter [5]. Certainly, cytokine storm and virus escape from the cellular immune system play a key role in the progression and severity of the disease [6].

The definitive treatment for severe cases is not available and different treatment models, as well as its diagnostic methods, are still in the research stages [7]. Therefore, early diagnosis and identification of patients can be of great help in improving and preventing the disease from entering the respiratory phase and reducing mortality, improving the speed of treatment, and also preventing the spread of the disease [1].

Among the diagnostic methods real-time reverse-transcriptase polymerase chain (rRT-PCR) is used as the gold standard to identify and diagnose the disease [8, 9]. However, due to the limitations of rRT-PCR method including sampling, sample transfer, being times-consuming, lack of viral materials in some samples, and lack of diagnostic kits in some centers, other paraclinical tests such as total white blood cell count (WBC), lymphocyte count, neutrophil to lymphocyte ratio (NLR), C-reactive protein (CRP) level, D-Dimer, Fibrinogen, lactate dehydrogenase (LDH), procalcitonin, erythrocyte sedimentation rate (ESR) and computed tomographic (CT) scan are used in the diagnosis and follow-up of the disease [3, 9, 10].

Practically, the diagnosis of COVID-19 is through rRT-PCR or typical involvement of lung by the virus in CT scan. However, rRT-PCR is not always available, and also CT scan has a high dose of radiation. This study was performed to find the role of complete blood cell (CBC) indices and qualitative C reactive protein (CRP) in screening of symptomatic patients to overcome the limitations of rRT-PCR and CT scan. Because of this limitation that our investigated laboratory indices were not specific for COVID-19, the symptomatic patients were selected in order to increase pretest probability to control this limitation.

MATERIAL AND METHODS

A diagnostic accuracy study was conducted on the symptomatic cases of those who were suspected for COVID-19. The samples were collected from 17th Shahrivar Hospital of Abadan, Khuzestan, Iran during the first half of 2021 through convenient sampling. The patients had symptoms such as fever, cough, shortness of breath, and so on. The patients were visited by a physician and then referred for CT scan and rRT-PCR. The inclusion criteria were being symptomatic, lack of underlying disease, and lack of a previous confirmation of COVID-19. This study was approved by the ethics committee of Lorestan University of Medical Sciences with registration number IR.LUMS.REC.1400.224. Informed consent was obtained from the participated patients.

The studied variables were age, gender, weight blood cell (WBC) count, platelet (PLT) count, neutrophil per lymphocyte ratio (NLR), CRP (qualitative from negative to 4+), CT scan positivity, PCR positivity, CT scan or PCR positivity (considered as COVID-19 positivity), and CT scan and PCR positivity. CT scan positivity was defined as a typical pattern of lung involvement by COVID-19 confirmed by a radiologist regardless of PCR positivity.

Stepwise logistic regression was used to predict each of the following outcomes at significance level

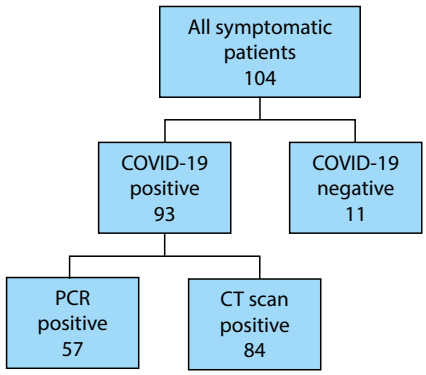

FIGURE 1. Flowchart of the patients based on PCR and CT scan positivity

of 0.1; 1) PCR positivity among the COVID-19 positive patient, 2) CT scan positivity among the COVID-19 positive patient, 3) PCR and CT scan positivity among the COVID-19 positive patient and 4) COVID-19 positivity among the suspected patients. Post-estimation receiver operating characteristics (ROC) curve analysis was performed to report the area under the curve (AUC) for each model. All the statistical analyses were performed in Stata 14 software (StataCrorp LLC, US).

RESULTS

A total of 104 patients were studied. Among them, 93 patients were COVID-19 positive that 57 patients were PCR positive, and 84 patients were CT scan positive (Fig. 1). Among the COVID-19 patients, in 48 patients, both PCR and CT scans were positive. The summary of the descriptive statistics of the variables is shown (Tab. 1).

The mentioned four models were designed with stepwise logistic regression. The most accurate model was for the prediction of CT scan

Table 1. Point estimation and dispersion of the variables

Variable	Frequency [%]/Mean [SD]	95% CI
Outcomes		
PCR positive	57 (54.81%)	45.08–64.53 (%)
CT scan positive	84 (80.77%)	73.07–88.4.7 (%)
Negative for COVID-19	11 (10.58%)	4.57–16.59 (%)
PCR or CT scan positive	93 (89.42%)	83.41–95.43 (%)
PCR and CT scan positive	48 (46.15%)	36.41–55.90 (%)
Total	104 (100%)	
Independent variables		
Gender [male]	58 (55.7%)	46.06–65.47 (%)
Age [year]	55.62 (19.34)	51.85–59.38
WBC [× 1000]	7.46 (3.35)	6.81–8.11
Lymphocyte ratio [%]	22.51 (12.05)	20.16–24.85
Neutrophil ratio [%]	68.31 (14.85)	65.43–71.20
NLR [ratio]	4.68 (4.19)	3.87–5.50
PLT [× 1000]	204.41 (88.55)	187.19–221.63
CRP [0 to 4+]	2.11 (1.19), Median: 3, IQR: 1–3	1.87–2.34
0	17 (16.35%)	
1+	13 (12.50%)	
2+	20 (19.23%)	
3+	50 (48.08%)	
4+	4 (3.85%)	
Total	104 (100%)	

COVID-19 — coronavirus disease 2019; CRP — C-reactive protein; CT — computed tomography; IQR — interquartile range; NLR — neutrophil to lymphocyte ratio; PCR — polymerase chain reaction; PLT — platelet; SD — standard deviation; WBC — white blood cell

Table 2. Stepwise logistic regression modeling for prediction of the outcomes at a significance level of 0.1 for covariate removal

Model		OR	p value	Pseudo *R* square	AIC	BIC	AUC
Outcome	Covariates						
PCR positive	Age [year]	0.977	0.070	0.055	123.369	130.967	0.643
	PLT [× 1000]	0.994	0.030				
	Constant	21.173[1]	0.006				
CT scan positive	Age [year]	1.063	0.026	0.287	48.155	55.753	0.874
	CRP [0 to 4+]	2.661	0.006				
	Constant	0.101	0.095				
PCR and CT scan positive	PLT [× 1000]	0.995	0.072	0.028	129.219	134.284	0.583
	Constant	2.806	0.071				
COVID-19 positive[2]	WBC [× 1000]	0.735	0.003	0.152	65.551	73.484	0.828
	NLR [ratio]	1.248	0.085				
	Constant	46.106	< 0.001				

1) All the constant amounts are in exponential form. 2) For this outcome, all the 104 patients were analyzed while for the other outcomes, only the 93 COVID-19 positive patients were selected; AIC — Akaike information criterion; AUC — area under the curve; BIC — Bayesian information criterion; COVID-19 — coronavirus disease 2019; CRP — C-reactive protein; CT — computed tomography; NLR — neutrophil to lymphocyte ratio; OR — odds ratio; PCR — polymerase chain reaction; PLT — platelet; WBC — white blood cell

positivity among the COVID-19 positive patient (AUC = 0.874) in which the predictors were age [odds ratio (OR) = 1.063] and CRP (OR = 2.661 for each plus of positivity). The second accurate model was for the prediction of COVID-19 positivity among all patients (AUC = 0.828) in which the predictors were white blood cell count (OR = 0.735 for every 1000 counts per μL) and neutrophil per lymphocyte ratio (OR = 1.248). The results of the two other models are also shown (Tab. 2).

As CRP seemed as an available and easy-to-use predictor according to the above findings, another modeling was performed for the prediction of CT scan positivity among the confirmed patients of COVID-19 for clinical use (this model was not multivariable). Briefly, CRP 3+ and 4+ were specific for lung involvement in CT scans while negative CRP was associated with a lack of lung involvement in CT scans. In addition, CRP 2+ was strongly suggestive of the involvement while CRP 1+ was not specific for the involvement. The details of this model are shown (Fig. 2).

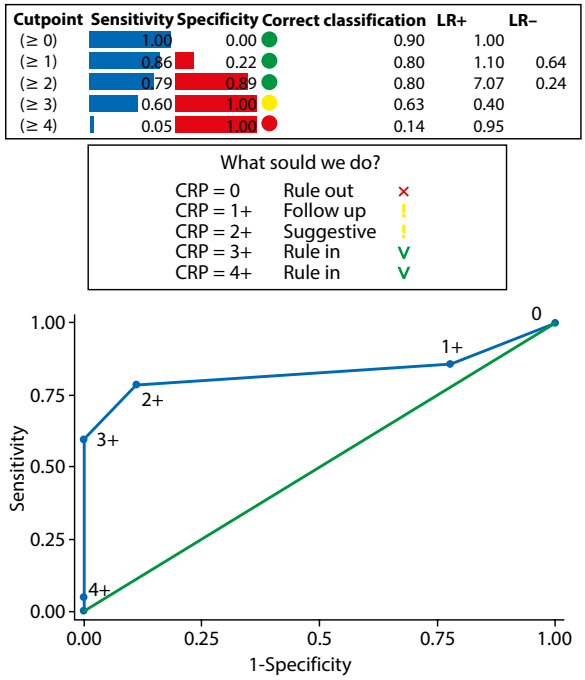

FIGURE 2. Diagnostic accuracy of CRP for CT scan positivity (lung involvement) in confirmed cases of COVID-19 by PCR or CT scan (n = 93). The results of this model should not be generalized to a general population without similar pretest probability; LR — likelihood ratio

DISCUSSION

The present study was designed to show how we can overcome the limitations rRT-PCR and CT scans using available blood tests in a small center. Briefly, lower PLT was associated with PCR positivity, higher ages and higher CRP were associated with CT scan positivity, and lower WBC count along with higher NLR was associated with COVID-19 positivity. The

most accurate model was for prediction of CT scan positivity based on age and CRP. In fact, increased CRP indicated higher inflammatory activity of lung which in turn might be seen as lung involvement in CT scan.

Wang et al. [7] examined CRP levels and CT scan in 27 patients with COVID-19 (including 11 mild, 12 moderate, 2 severe, and 2 critical) in Guizhou, China, and found an increase in CRP levels that was strongly associated with the severity of lung lesions.

Zhang et al. [1] in Hunan, China, by examining 177 patients (99 men and 78 women) with a definitive diagnosis of COVID-19 and dividing them into mild groups with 153 patients and severe patients with 24 patients, found that the laboratory parameters, albumin, total bilirubin, WBC, neutrophil count, neutrophil ratio, D-dimer, aspartate transaminase (AST), alanine transaminase (ALT), LDH, blood urea nitrogen (BUN), creatine kinase (CK), CRP, and CRP to albumin ratio (CAR), in the severe group had a significant increase. lymphocyte count and lymphocyte ratio tests have a significant decrease compared with the mild group, and they showed that high NLR could be a sign of disease progression to a serious condition and also NLR could be used as a very specific and sensitive indicator to predict the severity of the disease.

Wang et al. [11] examined the changes in lymphocyte subtypes in COVID-19 patients by examining 60 patients at Zhongnan Hospital in China and 245 healthy individuals. They showed that the total lymphocyte count in COVID-19 patients had decreased. In severe cases, the lymphocyte count had decreased more than in mild cases, and changes in peripheral lymphocyte subsets were associated with clinical features and treatment efficacy, and TCD8+ cells tend to independently predict the severity and effectiveness of COVID-19 treatment.

Tan et al. [5] with the aim of comparing laboratory markers between COVID-19 and influenza in 27 patients with COVID-19 including 6 severe and 21 mild and 75 patients with influenza A or B without a history of previous underlying disease and pregnancy showed that the increase in CRP, ESR, and neutrophil to lymphocyte ratio (NLR) was positively correlated with disease severity based on CT scan classification and the number of lymphocytes was negatively correlated with disease severity and CRP was increased in the early stages and was directly related to the prognosis of disease severity.

Wang et al. [12] in order to describe the clinical characteristics of patients and analyze related factors and find markers to predict the severity of the disease, studied 209 patients with a definitive diagnosis of COVID-19 and found that CRP could be a valuable marker for predicting the severity of disease and the possibility of needing to be admitted to the intensive care unit.

Mardani et al. [13] with the aim of increasing the accuracy of laboratory parameters in predicting positive PCR cases in Behpooyan Hospital in Tehran, examined 200 patients, 70 of whom had positive PCR, and found that increasing LDH, CRP, AST, and neutrophils could be used in the prognosis of PCR test results and help diagnose patients.

Poggiali et al. [6] in Italy examined 123 patients (91 men and 32 women) to confirm the use of routine laboratory tests, including a set of tissue damage and inflammatory tests for the prognosis of severe respiratory cases, especially in small emergencies where CT scan is not available. They found that LDH and CRP could play an important role in predicting respiratory disorders in COVID-19 patients and that these tests should be used in the initial identification of patients as well as the evaluation of acute respiratory cases and the improvement of treatment methods [6].

Liu et al. [14] with the aim of identifying specific serological methods for the diagnosis and assisting in the treatment of patients with coronavirus, studied 140 patients with COVID-19 (107 mild and 33 severe) and found that serum levels of interleukin (IL)-6 and CRP could be effective in diagnosing and predicting the severity of the disease.

Caruso et al. [10] to compare chest CT scan and rRT-PCR methods in the diagnosis of COVID-19 examined 158 patients with COVID-19 (83 men and 75 women) in Italy. Patients presented with fever, cough, shortness of breath, lymphopenia and increased CRP titers and LDH. They found that chest CT scan was more sensitive (97%) but less specific (56%) compared with rRT-PCR.

In order to find the relationship between hematological parameters and disease severity, Fu et al. [15] examined 75 patients for NLR, D-Dimer, and Fibrinogen in three groups of mild, moderate and severe diseases in China. They found that these parameters had different results in different groups and therefore NLR and D-Dimer could be used in the diagnosis and prognosis of moderate and mild cases conversion to severe cases.

Many of the previously published works supported our findings. The limitation of this study was

being a single center with a low sample size. However, we showed how we could validate our routine evaluations for clinical use in our own centers. In addition, the limitation of routine laboratory indices are their low diagnostic accuracies. Considering these indices within a diagnostic algorithm starting from the samples that have high pretest probability, helps clinician to overcome this limitation. Another limitation was that such indices could not show the causations or explanation of mechanisms. For instance, increased CRP level was supposed to be associated with increased inflammatory activity; but we observed CT scan positivity instead of direct observation of inflammation.

CONCLUSIONS

Higher levels of CRP are associated with and predictor of lung involvement in COVID-19 infection. In addition, leukopenia along with lymphopenia can show COVID-19 infection. CRP qualitative levels can be measured as a simple and widely available method before CT scan if there is no other indication for imaging. The approach of this study design may be suitable to be used in future pandemics of other diseases.

Conflict of interest

The authors declare that they have no conflict of interest.

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OCCUPATIONAL HAZARDS IN THE CONSCIOUSNESS OF THE PARAMEDIC IN EMERGENCY MEDICAL SERVICE

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ABSTRACT

INTRODUCTION: Due to their occupational responsibilities and volatile work environment, paramedics are in constant contact with harmful, dangerous factors, making them vulnerable to a number of occupational health risks. These include harmful biological, chemical, physical, as well as psychophysical factors (musculoskeletal system strain, stress, patient aggression, occupational burnout). The present study aims to evaluate occupational hazard prevalence among emergency medical service (EMS) paramedics, the possibility of occupational illness incidence, and related prophylaxis.

MATERIAL AND METHODS: The participant sample consisted of paramedics employed in five mobile EMS operational areas in the Masovian voivodship. The study involved 238 people, including 223 men and 15 women. The mean age was 39.03 ± 9.27 years for males, and 31.93 ± 7.76 years for females. The study took place between May and September 2019 using diagnostic survey methodology.

RESULTS: Participants ordered the following factors based on a scale of threat: biological factors (47%), psychophysical factors (41%), chemical factors (7%), and physical factors (5%). Health issues included musculoskeletal system discomfort (39%) and mental overload (33%). Participants indicated harmful biological factors to cause illnesses such as influenza (85%), tuberculosis (79%), and hepatitis B or C (70%). The study showed that 73% of the participants are occupationally exposed to patient aggression, while 15% experienced occupational burnout.

CONCLUSIONS: Paramedics are exposed to a number of occupational hazards daily. The ones most significant in terms of serious disease development are harmful biological factors, musculoskeletal risk factors, fatigue, mental overload related to occupational responsibilities.

KEY WORDS: paramedic; work environment; occupational exposure; harmful and dangerous agents; occupational illness

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INTRODUCTION

The protection of employees against the risks caused by occupational factors detrimental to their health, assigning employees to job posts adequate to their psychophysical abilities, and adjusting the labor to the individual and the individual to the labor are all tasks that require a multifaceted approach and knowledge in different fields, as well as satisfying legal requirements in this domain [1].

The work of a paramedic involves saving human life and health. These premises are achieved through the undertaking of medical rescue measures with the aim of stabilizing basic life functions. A paramedic's work is challenging, it is complex and involved a number of different tasks. High physical fitness and dexterity are a necessity. The paramedic is also required to elevate professional competence, record documents, handle medical equipment and devices, collect information regarding patients' health, educate patients and their families about health issues, and promote health. Each of these tasks requires different abilities, predispositions, and skills [2–5].

Paramedics frequently work under the pressure of time. They often face unforeseen situations, such as the sudden deterioration of the patient's condition, or resuscitation, during which minutes can decide whether a patient will live. These kinds of situations lead to progressive fatigue, lower effectiveness of work, and the deterioration of psychological comfort. In numerous cases, they are witnesses of events and personal experiences related to sudden, life-threatening situations which can result in symptoms related to post-traumatic stress disorder (PTSD) [6]. Additional problems for paramedics arise from relations with colleagues, patients, and their families, which can sometimes take place in a situation of high emotional tensions. Due to the nature of their work, this occupational group suffers from circadian rhythm disorders, which consequentially leads to unfavorable emotional and health consequences [7]. The work of a paramedic may carry risks for their health, as they come in contact with various biological factors in their work, including potentially contagious material from the sick (blood, secretions, excretions) [8–11].

In the Polish context, the work of a paramedic is additionally difficult, as the occupation is characterized by low social prestige, low possibility of growth or advancement, and low material satisfaction. Under the current healthcare circumstances, it is one of the occupational groups most vulnerable to stress. The stress sources of this occupational group include: poorly organized work; shift work that disrupts the natural biological rhythm of the organism; unrhythmic work, periodically causing high overload; lack of satisfactory remuneration; lack of recognition from supervisors; lack of growth prospects in their career.

Identification of hazards and their sources

A paramedic is a healthcare professional possessing the required qualifications with appropriate documents as confirmation. An EMS paramedic works in medical entities which are part of the national emergency medical services. They fulfill occupational duties to the local community, in the residential environment, in case of health, illness, or handicap they undertake rescue medical measures in a non-hospital environment in order to save a person in a sudden life-threatening condition. During their occupational duties, they are required to undertake rescue medical measures in accordance with the possessed qualifications and regulations defining good medical care, while cooperating with other members of the team or other services taking part in the rescue operation. In accordance with the nature of their work, they undertake measures related to the promotion of health, disease prophylaxis, nursing, medicating, diagnosis, health improvement, and rehabilitation. Fulfilling the high standards related to their occupation requires the paramedic to constantly educate themselves, and to maintain a constant high physical fitness [5, 12, 13].

The occupation of the paramedic involves exposure to a multitude of factors, which can negatively influence their health. Therefore, the identification of hazards and estimation of occupational risk should be carried out with an accepted methodology [14, 15].

Biological hazards

Biological factors in the work environment are defined as cellular microorganisms capable of replicating or transferring genetic material, including genetically modified cell cultures or internal parasites which can be the cause of infection, allergy, or poisoning. Thus, harmful biological factors in the work environments include not only microorganisms causing contagious diseases, but also micro- and micro-organisms, as well as structures and substances produced by these organisms, whose

existence in the workplace has a negative impact on human health and can be the cause of allergic, toxic, or cancerous occupational diseases, while also functioning as vectors of pathological germs. They cause a heightened risk of contagious and invasive disease contraction due to the direct contact with patients and their contagious material. Very frequently, those are highly virulent and pathogenic microorganisms. Furthermore, they have transmittance pathways that are specific to paramedics [1, 8–13, 16].

The highest risk is posed by biological factors causing negative health effects such as: hepatitis B and C, acquired immunodeficiency syndrome (AIDS), severe acute respiratory syndrome (SARS), methicillin-resistant Staphylococcus aureus (MRSA) infection, and contemporarily COVID-19, which are transmitted through the air or droplets, or from human to human [1, 8–11, 16].

Chemical and physical hazards

Chemical substances in the work environment exist in gas, vapor, liquid, or solid form. In occupational exposure conditions, the intake of chemical substances into the organism takes place in the respiratory and digestive systems, as well as the skin and mucous membranes. The organism's reaction to exposure depends on the physico-chemical properties of the substance, the intake route, dose size, period of exposure, temperature and humidity or the air in the work environment, as well as individual qualities of the employee, such as gender, age, general health, eating habits and the endocrine, immune, genital systems' condition. Such reactions may include exposure effects that are local (irritation and allergic reaction of the skin or mucous membranes) or systemic (affecting the human internal organs), and their intensity may be acute or chronic in nature. The work of a paramedic involves exposure to a number of chemical substances which are harmful to the organism (xenobiotics). Examples with significant impact include agents used in aseptic treatments, meaning cleaning, disinfecting, and sterilizing agents, which contain harmful substances that harm the skin, mucous membranes, and respiratory systems, as well as medical drugs, rubber components, or some metals. Chemical factors can be the cause of incidental or chronic acute poisoning if long-term exposure to small doses takes place (*e.g.*, rescue operations during a fire). Furthermore, long-term consequences may take place due to the effect of chemicals on the genetic material, such as a mutagenic, teratogenic, embryotoxic, cancerogenic or allergenic activity). A paramedic's work is related to the exposure to a number of highly allergizing factors, the most significant of which being natural rubber latex. Outcomes of medical personnel's exposure to chemical factors in the workplace include health consequences such as cancers, allergies, tissue or even organ degeneration, toxic outcomes understood as disruptions of biochemical reactions, immunity and reproduction disorders, including the broad array of teratogenic outcomes, including fetal development disorders, embryonic effects involving specific developmental disorders in the fetal period, and infertility, which is the inability to carry out conception or become pregnant [1, 9, 10, 17–23].

Harmful physical factors that paramedics are exposed to include volatile, adverse microclimate during departures to the patience, noise, light, musculoskeletal overload, limited work area, forced posture, mechanical vibration, or monotype movement at work [1, 9, 10, 24–26].

Psychophysical hazards

In the most general sense, psychophysical factors in the workplace are understood as cumbersome factors capable of deteriorating the worker's physical and mental abilities [1, 13–15].

Employee health in virtually every profession largely depends on their ability to cope with stress. In turn, the quality of the strategies used in stressful situations largely depends on their self-perception and self-appraisal, as well as individual potential abilities in the context of a particularly stressful situation.

The occurrence of violence and aggression are all the more common in the workplace, including that of a paramedic. Lists of aggressive behaviors include various acts of psychological violence: threatening, intimidation, insults, mockery, antagonistic behavior (screaming, yelling, threatening with a fist, spitting), and physical aggression. Paramedics often encounter verbal, or even physical aggression from their patients. Another problem encountered in the work, which involves constant mental and physical strain, is chronic fatigue syndrome, PTSD, and occupational burnout, which are results of their work's nature. The work of a paramedic requires heightened mental effort related to observing the patients' suffering; high engagement in others' affairs, hurting people; high empathy, and understanding for the patient; self-identification with the patient's problems; in-

creased responsibility for the results of their work. All of these factors can in a simple way contribute to the occurrence of serious disorders, at first emotional, and later occupational burnout syndrome [1, 6, 7, 12, 13, 24].

A significant health concern related to the work activities in this occupational group is the strain and its resulting issues with the musculoskeletal system. In this case alike, accidents at work occur frequently, including injuries related to improper posture at work and excessive physical activity during the moving and hoisting of patients. The cause of such incidents is the lack of sufficient knowledge regarding the techniques of safe lifting and moving of patients and not posturing the body correctly during work activities [13, 17, 25–27].

MATERIAL AND METHODS

In 2019, the National Medical Emergency Service System in Poland offered 1577 (100%) mobile EMS, 369 (100%) of which were specialized and 1208 (100%) of which were basic level. In the Masovian voivodship, there were 200 mobile EMS, which constituted 12.7% of all teams [46 specialized (12.5%) and 154 basics (12.7%)] [28].

The sample selection was deliberate, as the Mazovian voivodship has the highest number of EMS on a national scale.

The study was carried out in the period between May and September 2019 amongst occupationally active paramedics in EMS from five operational regions in the Mazovian voivodship: Warsaw, Płock, Ostrołęka, Siedlce, and Radom. Paramedics' participation was voluntary. The research was carried out in accordance with the Helsinki Declaration, meaning it was anonymous and voluntary in nature. Every participant was granted informed consent and was informed of its aims and the ability to withdraw participation at any stage of the study.

The research adopted the diagnostic survey method, using a questionnaire developed for the purpose of the present study, which included a fiche including areas indicated on the occupational exposure evaluation form in relation to occupational disease suspicion [29], and comprised four sections including 23 questions regarding the basic groups of hazards related to the daily work of an EMS paramedic. A majority of the questions were closed, and if another option such as "other" could be marked, participants were asked to specify their answer and give an example. The first part of the questionnaire (questions 1–11) was related to biological hazards encountered at work and focused on assessing the level of knowledge regarding their types, potential exposure routes, the illnesses they may cause, and the knowledge regarding the means of self-protection and behaviors in a so-called emergency situation involving a harmful biological factor. Questions 12–16 were related to musculoskeletal system threats and consequential pain, their frequency of incidence and duration, as well as the evaluation of the consciousness of their existence. The following questions (17–21) dealt with mental strain. These questions raised the issue of aggression from patients, their families, or cohabitants, towards the participants, as well as stress and fear for their own safety. The issue of burnout was also addressed, and respondents were asked if they are aware of what the term entails and whether they experienced it. Finally, questions 22 and 23 asked paramedics which hazards, *i.e.*, biological factors, musculoskeletal pain, mental strain, chronic fatigue, occupational burnout, allergies, or others, do they consider to be the most significant in their work (participants were asked to assign numbers from 1–7 to particular hazards, with 1 — most significant, 7 — least significant). Participants were also asked if they are aware of what occupational diseases they are exposed to in their work. The results were presented in descriptive form.

The study involved 238 participants, including 223 men and 15 women. The mean age of the participants was 39.03 ± 9.27 years for males, and 31.93 ± 7.76 years for females (Tab. 1).

The mean work experience of the participating paramedics showed significant gender differences ($p = 0.000$). It was 12.62 ± 9.41 years for males, and 5.36 ± 7.04 years for females. In both groups, the shortest work experience was approximately half a year (Tab. 2). Participants had further secondary education, or professional/master's degree in higher education (Tab. 3).

RESULTS

According to the gravity of the threat perceived by the participating paramedics, the most dangerous hazards include biological factors (47%), psychophysical factors (41%), chemical factors (7%), and physical factors (5%). Reported health problems included musculoskeletal pain (39%) or mental strain

Table 1. Participant age in years between genders

Gender	n	M	SD	Min	Max	p-value
Male	223	39.03	9.27	23.00	65.00	0.003*
Female	15	31.93	7.76	23.00	50.00	

*Mann-Whitney U Test; $p < \alpha$; $\alpha = 0.05$; SD — standard deviation

Table 2. Years of participant work experience between genders

Gender	n	M	SD	Min	Max	p-value
Male	223	12.62	9.41	0.50	41.00	0.000*
Female	15	5.36	7.04	0.50	28.00	

*Mann-Whitney U Test; $p < \alpha$, $\alpha = 0.05$; SD — standard deviation

Table 3. Level of education between genders

Level of Education	n [%]	Secondary/Further secondary education	Professional higher education	Masters higher education	p-value
Male	223 (100.00)	48 (21.52)	132 (59.19)	43 (19.28)	0.109*
Female	15 (100.00)	1 (6.67)	8 (53.33)	6 (40.00)	

*χ^2 Test; $p > \alpha$; $\alpha = 0.05$

Table 4. Percentage exposure to biological factors during work according to participants

Harmful biological factor	Frequency and distribution
Viruses	97% (231)
Bacteria	94% (224)
Pathogenic fungi	67% (159)
Parasites	48% (114)
Prions	15% (36)

*Results do not add up to 100%, because participants could identify more than one factor

(33%). Among illnesses caused by harmful biological factors, participants pointed toward the possibility of influenza (85%) or tuberculosis (79%) contraction, followed by hepatitis B or C (70%).

The study only references the indicated threats posed by biological and psychophysical factors, due to the fact that participants believe them to be the most important source of their health problems.

A vast majority of the participating paramedics (97%) indicated that their work involves daily exposure to harmful biological factors (Tab. 4), the ones most commonly reported being: viruses, bacteria, and pathogenic fungi.

When asked about their perceived pathways of contracting harmful biological factors at work, participants more or less universally reported four main methods of contagion, such as: inhaling air, *i.e.*, air pathway (81%), contact with items previously touched by sick people (81%), contact with human blood (81%), contact with human secretions and excretions (85%). Meanwhile, 70% of the participating paramedics considered exposure to harmful biological factors to be related to a majority of the activities which are part of their daily work, 36% stated that it was related only to some activities, while 33% additionally reported touching lips and food with unwashed hands to be another pathway of contracting pathogenic microorganisms. Only 6% reported that they are only exposed to them in emergency situations, meaning situations where direct contact is made with infected biological material through a cut or through mucous membranes or the skin.

The answers given to the question regarding the knowledge of diseases that can be caused by harmful biological factors that participants come in contact with during their daily work were rather varied as shown in Figure 1. A majority identified influenza (as much as 85%) and tuberculosis (79%) as diseases with the highest risk of contagion. Hepatitis B and C were also reported (70%). "Other" diseases listed by participants were mostly pediculosis and tetanus.

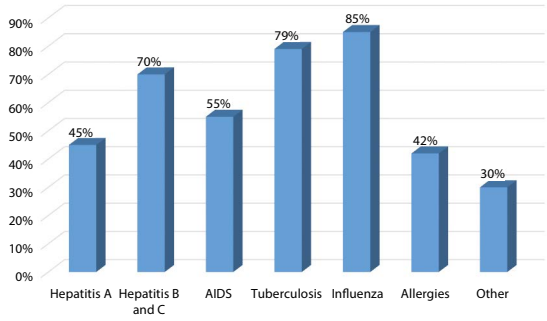

FIGURE 1. Illnesses caused by harmful biological factors at work according to participants

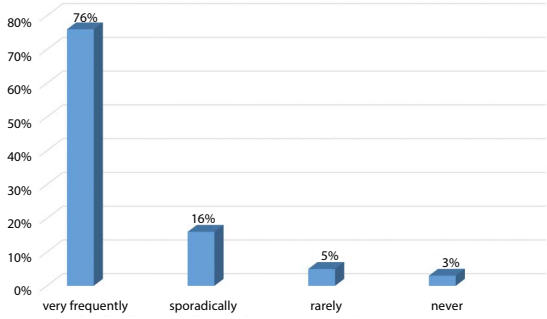

FIGURE 2. Frequency of musculoskeletal pain incidence according to participants

Table 5. Cause of musculoskeletal pain according to participants

Cause of musculoskeletal pain	Frequency and distribution
Forced body posture	64% (152)
Excessive physical activity	58% (139)
Overloading the musculoskeletal system	42% (101)
I do not associate it with work	3% (8)

*Results do not add up to 100%, because participants could identify more than one factor

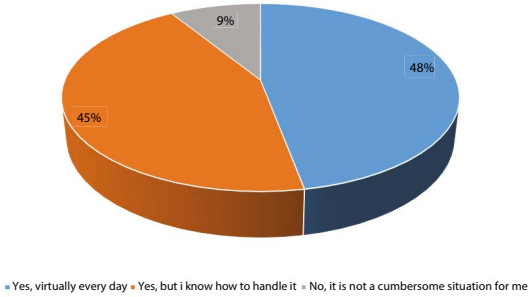

FIGURE 3. Frequency of mental stress according to participants

Musculoskeletal system pain is the second and almost equally significant and important group of threats reported by the participants. Musculoskeletal pain related to the work of the participants was indicated by a majority of the respondents (97%).

Figure 2 shows how serious of a problem this is for paramedics, as it is visible that 76% of the participants report that such difficulties occur very often for them.

As far as the location of the pain is concerned, a vast majority of the participants indicated the sacro-lumbar area (97%), the cervical spine area (52 %), shoulder area (31%), knee area (27%), and arms (24%).

As shown in Table 5, it is worth noting that a majority of the participating paramedics primarily relate their musculoskeletal system pains to improper and forced posture at work and excessive physical activity.

When a paramedic works with people in need of help, it may involve a significant mental strain, the threat of which was reported by 33% of the participants. When asked whether participants encounter aggression from patients in their professional work through verbal aggression, threats, or blackmail, 73% responded that they do. 52% also indicated that they encounter aggression from the families or cohabitants of their patients. The fact that 32% of the participants often face aggressive behavior at work, while 24% do, too, albeit less frequently, is concerning.

Figure 3 shows that high stress and mental strain related to medical rescue services in non-hospital conditions with the aim of saving the life of a person in a sudden life-threatening situation, was reported by 48% of the participating paramedics, and only 9% stated unambiguously that it is not a cumbersome situation for them.

Another serious problem related to the work of providing medical rescue services is occupational burnout syndrome, which affects a relatively large number of mobile ERT personnel. When asked whether they understand what this term means, 82% of the paramedics answered affirmatively, 15% of which admitted that they have experienced this condition. It is quite a large percentage, given that returning to work and one's responsibilities after such an experience can be extremely difficult and requires a significant effort and persistence from the affected individual. The work of a paramedic involves everyday commutes to patients. The stress

related to the fear for one's own safety is also a factor influencing the heightened mental strain among participants. Oftentimes patients themselves, their neighbors, or even cohabitants of the patient do not shy away from alcohol or other addictive substances which make them more aggressive towards their surroundings.

DISCUSSION

The results of the present study indicate that the work of paramedics is tied to the high everyday risk of exposure to harmful biological factors which finds confirmation by other research in the literature [8–11, 16].

Szarpak [9] showed that as much as 80% of the studied paramedics declared coming in contact with patients' blood a couple of times a day, and 16% — a couple of times a week. These results are congruent with the findings of the present study.

Thomas et al. [10] study identified eight significant contagious diseases and transmission pathways. Firstly, those which are transmitted through blood and other body fluids: the human immunodeficiency virus (HIV), hepatitis B, and hepatitis C. Diseases transmitted through air include meningococcal meningitis, and severe acute respiratory syndrome (SARS), influenza, and tuberculosis. The last identified illness was methicillin-resistant Staphylococcus aureus (MRSA) infection, which spreads through direct contact. These findings are consistent with the present results regarding the knowledge of transmission pathways of biological factors during work and the possibility of negative health consequences such as diseases occurring.

The health issue related to the overloading and consequent pain of the musculoskeletal system identified in the present research was also found in other studies [17, 25–27].

Reichard et al. [17] showed that the musculoskeletal disorders experienced by paramedics constituted 40% of all injuries in this group. The injuries related to body movement were most commonly an outcome of lifting, moving, or transporting patients and/or equipment. These findings correlate with the present study.

Friedenberg et al. [27] found that the frequency of back pain ranges between 30% and 66%, while for back injuries and bruising the frequency ranges from 4% to 43%. The frequency of back pain from falling, slipping, tripping, and overloading during lifting and moving patients or equipment ranges from 10% to 56%, with the most frequent injury being overloading. Risk factors included lifting, work in an uncomfortable position, loading patients in the ambulance, and cardio-respiratory resuscitation procedures. The causes of musculoskeletal pain identified in the study are comparable to Friedenberg et al's findings.

Prairie et al. [25] showed that loading stretchers into the ambulance is an activity putting paramedics at high risk of back injury. During interviews, paramedics described a multitude of problems related to the weight of the patients and stretchers. The procedure of loading stretchers into the ambulance requires additional activities (such as raising your hands and extra lifting), which cause additional activity and strain for the musculoskeletal system. The aforementioned finding is consistent with the results of the present study.

Prairie et al. [26] have also found that during work involving medical care and moving patients, paramedics moved their torsos in ways that can significantly increase the prevalence of lower back disorders. The study showed that the professional activities carried out in the transport of the patients in the ambulance were characterized by a significantly bent posture, and during transport, paramedics adopted very twisted postures. According to the authors of the study, the vibrations during the ambulance ride and the uncomfortable back posture adopted during paramedic activities may increase the risk of musculoskeletal disorders. The presented results are comparable to the findings of the present study in terms of the identification of the musculoskeletal pain of the respondents.

The present study identified psychophysical hazards related to professional work leading to negative mental consequences such as stress, PTSD, aggressive behavior, occupational burnout, or depression, which find confirmation in other studies of this occupational group [6, 7, 24, 30].

Roberts et al. [24] research confirmed that the risk of mental injury among medical personnel was the highest for paramedics and was 13 times greater than that of nurses. Their results correlate with the present study, where 33% of the respondents indicated significant mental strain in their work.

In the present study, respondents were asked whether they encounter aggression from patients in their professional work, in the form of verbal aggression, threats, or blackmails, and as much as 73%

answered that it was the case. 52% encountered aggression from families or cohabitants of their patients, meanwhile, 32% of the respondents frequently encounter acts of aggression in their work. These results are similar to the ones obtained in Pękala et al.'s [30]. They showed that 98.1% of the participants experienced aggression in relation to their work. Only 1.9% of the respondents have never experienced workplace aggression. As much as 75% of the participants said that the issue of aggression towards paramedics is frequent.

CONCLUSIONS

As part of the broad category of healthcare medical personnel, paramedics are exposed to a number of occupational hazards in their daily work.

The most significant hazards leading to the development of serious disorders or illnesses primarily include biological factors, threats to the musculoskeletal system, fatigue, and the mental strain related to professional activities.

The identification of occupational hazards is incredibly important for the efficient functioning of EMS, because it enables the incorporation of preventative measures, and employers making competent use of them encourage work safety and protect the health of paramedics. Various protective and prophylactic measures ought to be employed in the work process in order to protect the health and life of paramedics.

The ability to access specialistic help from a psychologist or a psychiatrist in a crisis situation (such as a traumatic event, or an act of aggression) should be regarded as a standard procedure among EMS employers.

Author input

(A) concept; (B) data collection; (C) literature review; (D) study writeup; (E) supervision

Agnieszka Gonczaryk — A, B, C, D; Jaroslaw Chmielewski — A, B, C, D; Agnieszka Strzelecka — C, D; Jarosław Fiks — C,D; Grzegorz Witkowski — C, D; Magdalena Florek-Łuszczki — A, D, E.

Authors' contribution

All authors passed the four criteria for authorship contribution based on the International Committee of Medical Journal Editors (ICMJE) recommendations.

Conflict of interests

None.

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PROGNOSTIC NUTRITIONAL INDEX TO PREDICTING MORTALITY IN SURGICAL INTENSIVE CARE PATIENTS

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ABSTRACT

INTRODUCTION: It is known that immuno-nutritional status affects clinical outcomes in intensive care (ICU) patients. This study aimed to evaluate the relationship of the Prognostic Nutritional Index (PNI) with mortality in surgical ICU patients.

MATERIAL AND METHODS: The single-center, retrospective, observational study was conducted in a 17-bed surgical ICU. Patients over the age of 18 who were hospitalized between May 1, 2018, and May 1, 2019, were evaluated.

RESULTS: 217 patients followed in the surgical ICU were evaluated. The mean age of the study population was 51.84 ± 21.25 years, and 150 (69.10%) patients were male. ICU mortality was calculated as 16.10%. Trauma was the most common reason for hospitalization in both groups, and there was no difference between the two groups in terms of hospitalization reasons. The PNI score was found to be significantly lower in the non-survivor group compared to the survivors ($p < 0.001$). The PNI cut-off value in predicting mortality was found to be 32.01 with a sensitivity of 0.829 and a specificity of 0.956 [AUC = 0.957 (95% CI from 0.929 to 0.984); $p < 0.001$].

CONCLUSIONS: PNI is a cost-effective scoring system that can be calculated with a simple formulation. In our study, in which surgical ICU cases were evaluated, lower PNI values were found in patients with mortality compared to those who survived. We believe that PNI can be used in the prediction of mortality in surgical ICU cases, and our study will shed light on future studies on this subject.

KEY WORDS: Prognostic Nutritional Index; surgical ICU; malnutrition; mortality; intensive care

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INTRODUCTION

It is known that immuno-nutritional status has an effect on clinical outcomes in intensive care (ICU) patients [1]. Malnutrition may occur in critical patient groups due to various reasons. It has been reported that malnutrition is associated with poor outcomes such as the increased risk of infection, delayed wound healing, prolonged ICU length of stay, and increased hospital costs [2]. Early detection of malnutrition risk in ICU patients is important in preventing possible complications. Silently progressing malnutrition is difficult to recognize if it is not suspected and screened.

Many laboratory parameters that can be used in evaluating nutritional status have been studied, since they are associated with poor outcomes up to mortality, and scoring systems that can be used in

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the early detection of malnutrition risk have been developed [3–5]. Numerous scoring systems have been described in the literature. The Nutritional Risk Screening Test-2002 (NRS-2002) and the NUTRIC (Nutrition Risk in the Critically Ill) score are among the most frequently studied screening tests in ICU patients [4, 5]. However, there is still no consensus on which screening test is the gold standard in critically ill patients [6, 7]. The test to be used for screening should be easily applicable, standardized, and cost-effective. Due to the lack of consensus on the method that evaluates the nutritional status from all aspects, studies on scoring systems continue today. One is the Prognostic Nutritional Index (PNI), a combined score reflecting the immunological nutritional status. PNI is calculated using serum albumin and lymphocyte values [8]. It has become a prominent scoring system for using only blood parameters in evaluating PNI, not causing measurement-based differences due to the absence of clinical measurements, and being cost-effective by using laboratory parameters already evaluated in daily practice. It has been reported that the PNI score is significant in predicting prognosis and mortality due to the evaluation of both immunological and nutritional status [9, 10]. Studies on PNI in the literature have generally been conducted in specific patient groups such as infectious diseases, malignancies, and cardiovascular diseases [9–11]. Studies on this subject are generally small population studies evaluating non-critical service patients, and studies with large series evaluating ICU cases are not common in the literature. This study aimed to evaluate the relationship between PNI, which is used in evaluating the nutritional status, and mortality in surgical ICU patients.

MATERIAL AND METHODS

The single-center, retrospective, observational study was conducted in a 17-bed surgical ICU in Turkey. Patients over the age of 18 who were hospitalized between May 1, 2018, and May 1, 2019, were evaluated.

The study protocol was approved by the institutional review board (Approval Date and Number:10.05.2022/E-64106871). The Declaration of Helsinki's principles were followed in conducting this study. All data were obtained from electronic medical records and patient files after ethics committee approval. Patients with ICU hospitalization for less than 24 hours, patients with diseases such as cirrhosis, and acute and chronic hepatitis that may affect serum albumin levels, and patients with sepsis, septic shock, and kidney failure were excluded from the study.

Demographic data of patients including age, gender, comorbidities, Acute Physiology and Chronic Health Assessment-2 (APACHE-II) and NRS-2002 scores, reasons for ICU hospitalization, ICU and hospitalization times, intubation status, operation status, ICU mortality, laboratory parameters including urea creatine, albumin, C-reactive protein (CRP), white blood cell (WBC), neutrophil, lymphocyte and platelet counts were retrospectively analyzed and recorded. The PNI values of all patients were recorded using the formula: $10 \times$ serum albumin (g/dL) $+ 0.005 \times$ absolute lymphocyte count (/mm^3) [8].

Statistical analysis

SPSS 25.0 package program was used for the statistical analysis of the study. In the study, continuous variables were expressed as median (minimum-maximum) and mean $\pm$ SD values, and categorical variables were expressed as frequency and percentage values. The suitability of the data to the normal distribution was evaluated with histogram, probability graphs, and Shapiro-Wilk test. Student t-test or Mann-Whitney U test was used to compare continuous variables according to the normal distribution. The chi-square test was used to compare categorical variables. Receiver operating characteristics (ROC) analysis was performed to predict mortality with PNI. The area under the curve was calculated as the cut-off giving the most optimal sensitivity and selectivity value. A p-value of < 0.05 was considered statistically significant in all analyses.

RESULTS

Between the study dates, 370 patients were hospitalized in the surgical ICU. Two hundred seventeen patients over the age of 18 who met the inclusion criteria and whose data could be accessed were included in the evaluation. The mean age of the study population was 51.84 $\pm$ 21.25 years, and 150 (69.10%) patients were male. ICU mortality of the whole population was calculated as 16.10%. The patients were divided into two groups as survivors and non-survivors. The two groups were similar in terms of age and gender. Trauma was the most common reason for hospitalization in

both groups, and there was no difference between the two groups in terms of hospitalization reasons. ICU length of stay was significantly longer in the non-survivor group ($p < 0.05$). The most common comorbidity in both groups was hypertension. The APACHE-II score on the day of hospitalization was significantly higher in the non-survivor group ($p < 0.05$) (Tab. 1).

When the two groups were compared in terms of laboratory parameters, the albumin level of the non-survivor group was significantly lower than that of the survivor group. There was no difference between the two groups regarding other laboratory parameters (Tab. 2). The NRS 2002 score was 5 (3–7) in non-survivors and 1 (0–4) in survivors ($p < 0.001$). In the evaluation of the NRS 2002 score with the ROC curve to predict mortality, the cut-off value was found to be 3.5 with a sensitivity of 0.914 and a specificity of 0.978 [AUC = 0.991 (95% CI from 0.981 to 1,000); $p < 0.001$] (Fig. 1).

The PNI score was found to be 39.0 (26.0–49.0) in the survivor group and significantly higher than 28.0 (20.0–35.0) in the non-survivor group ($p < 0.001$). In the evaluation of the PNI score with the ROC curve in predicting mortality, the cut-off value was found to be 32.01 with a sensitivity of 0.829 and a specificity of 0.956 [AUC = 0.957 (95% CI from 0.929 to 0.984); $p < 0.001$] (Fig. 2).

Table 1. Baseline characteristics of patients according to groups

	Survivors n (%)	Non-survivors n (%)	p
	182 (83.90%)	35(16.10%)	
Age	53 (17–92)	63 (18–93)	0.112**
Gender			
Female	51 (28.00%)	16 (45.70%)	0.061*
Male	131 (72.00%)	19 (54.30%)	
APACHE-II	15 (3–29)	31 (15–48)	**< 0.001****
Length of hospital stay. days	10 (2–57)	8 (2–36)	**0.042****
Length of ICU stay. days	4 (2–22)	5 (2–27)	**0.033****
NRS-2002	1 (0–4)	5 (3–7)	**< 0.001****
PNI	39.0 (26.0–49.0)	28.0 (20.0–35.0)	**< 0.001****
Reasons for ICU admission			
Trauma	88 (48.40%)	14 (40.00%)	0.225*
Postoperative Follow-Up After Major Surgery	45 (24.70%)	9 (25.70%)	
Hemodynamic Instability	33 (18.10%)	5 (14.30%)	
Respiratory Distress	14 (7.70%)	7 (20.00%)	
Unconsciousness	2 (1.10%)	0 (0.00%)	
Intubation			
Yes	136 (74.70%)	35(100%)	0.052*
No	46 (25.30%)	0 (0.00%)	
Surgery			
Yes	108 (59.30%)	17 (48.60%)	0.320*
No	74 (40.70%)	18 (51.40%)	
Comorbidities			
Hypertension	79 (43.40%)	19 (54.30%)	0.318*
DM	30 (16.50%)	13 (37.10%)	**0.005***
COPD	12 (6.60%)	4 (11.40%)	0.316*
CVD	20 (11.00%)	5 (14.30%)	0.576*

*Chi-squared test, **Mann Whitney U test; DM — diabetes mellitus; COPD — chronic obstructive pulmonary disease; CVD — Cardiovascular disease; NRS-2002 — Nutritional Risk Screening Test 2002; PNI — Prognostic Nutritional Index

Table 2. Laboratory values of patients according to groups

	Survivors (n = 182, 83.90%)	Non-survivors (n = 35, 16.10%)	p
Urea	36.1 (15.5–81.3)	40 (18.7–81)	0.155
Creatinine [mg/dL]	0.97 ± 0.27	1.03 ± 0.29	0.218**
Albumin [g/L]	3.9 (2.6–4.9)	2.8 (2.0–3.5)	< 0.001*
CRP [mg/L]	6.7 (0.3–300.3)	8.9 (0.6–189.6)	0.401
WBC [number/mm^3]	12.8 (3.7–40.0)	11.3 (3.5–25.9)	0.051
Neutrophil [number/mm^3]	8.8 (2.2–36.6)	8.0 (1.4–20.9)	0.228
Lymphocyte [number/mm^3]	2.4 (0.8–6.3)	2.2 (0.8–4.4)	0.197
Platelet, ×10^3/mL	256.5 (42–1407)	230 (61–417)	0.076

*Mann Whitney U test, **Student t test, ortalama ± ss; CRP — C-reactive protein; WBC — white blood cell

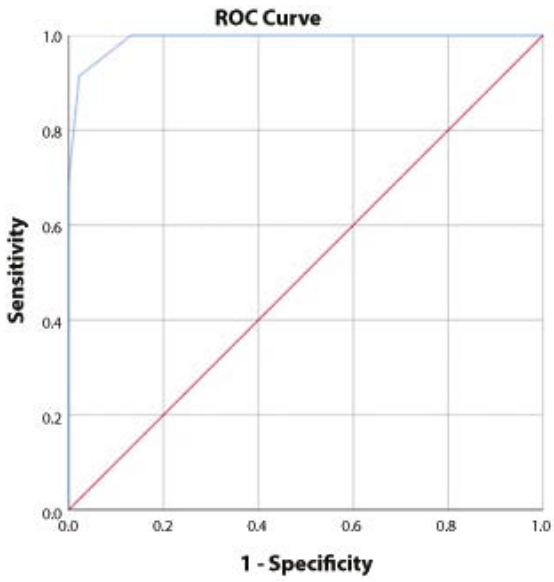

FIGURE 1. Receiver operating characteristics (ROC) curve of Nutritional Risk Screening Test-2002 (NRS-2002). ROC analyses for NRS 2002 to predict mortality, the cut-off value was 3.5 with a sensitivity of 0.914 and a specificity of 0.978 [AUC = 0.991 (95% CI from 0.981 to 1,000); p < 0.001]; AUC — area under the curve; CI — confidence interval

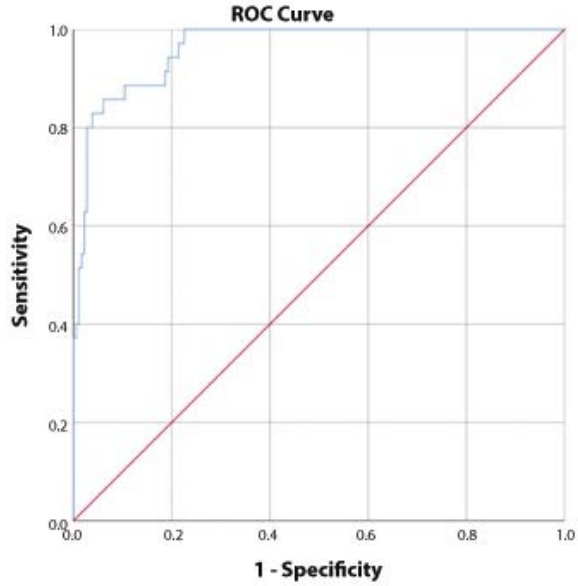

FIGURE 2. Receiver operating characteristics (ROC) curve of Prognostic Nutritional Index (PNI). ROC analyses for PNI to predict mortality, the cut-off value was 32.01 with a sensitivity of 0.829 and a specificity of 0.956 [AUC = 0.957 (95% CI from 0.929 to 0.984); p < 0.001]; AUC — area under the curve; CI — confidence interval

DISCUSSION

The PNI, calculated based on albumin and lymphocyte values, is a combined score used to evaluate the immuno-nutritional status. PNI, the first study in the literature, was in the group of patients who underwent gastrointestinal surgery and was subsequently investigated in a wide variety of patient groups, such as infectious diseases, malignancies, and cardiovascular diseases [5, 9, 11]. Although it has also been evaluated in ICU patient groups such as geriatric patients, COVID-19, and cardiovascular patients, to the best of our knowledge, there is no current study evaluating the relationship between mortality in surgical ICU patients [9, 12, 13].

Patients hospitalized in the ICU have a higher risk of malnutrition than other patient groups for many reasons, such as the developing critical process, hemodynamic instability, accompanying comorbidities, and complications [14]. Surgical ICUs differ from medical ICUs due to the inpatient population, underlying causes of critical illness, surgical, and interventional procedures. In our study, the most common reason for ICU hospitalization was trauma. Trauma cases; It is the patient group in which condi-

tions that may cause muscle loss are more common due to the fact that immobilization is seen more frequently due to various reasons such as surgery, extremity damage, and the developing hypercatabolic state. Numerous scoring systems have been studied to evaluate malnutrition in ICU cases [15]. NRS-2002 is the scoring system frequently preferred in clinical practice to define nutritional risk. BMI is evaluated by questioning parameters such as weight loss in the last three months and food intake in the last week. Cases with an NRS-2002 score of 3 and above are considered to be under nutritional risk [5]. In our study, the NRS-2002 score was found to be higher in the non-survivor group compared to the survivors, and the cut-off value of the NRS 2002 score was found to be 3.5 in the evaluation of mortality with the ROC curve. Fact that the laboratory results are not included in the NRS-2002 scoring, the questions included in the evaluation were obtained from the relatives of the patients who can be reached, not from the patient himself, for reasons such as generally intubated monitoring and unconsciousness; Considering the circumstances such as the inability to reach the relatives of the patients where this information can be obtained in emergency cases and trauma situations, there may be situations where the evaluation of the ICU patient group may be insufficient. There is still no consensus in the literature about a generally accepted method that can be used in surgical ICU cases.

PNI has become a prominent scoring system in terms of being a cost-effective method by saving time using albumin and lymphocyte parameters, which do not include clinical evaluation and measurements, require extra time in ICU practice, and are frequently examined in daily practice routines. It has been reported that a low PNI score is associated with poor outcomes and mortality [15]. In our study, in which we evaluated surgical ICU patients, the PNI score, which is on the agenda to predict prognosis, was significantly lower in the non-survivor group compared to the survivors. The cut-off value was 32.01 in the evaluation of the PNI score with the ROC curve in predicting mortality (with a sensitivity of 0.829 and a specificity of 0.956).

Although studies evaluating various patient groups have shown the relationship between low PNI and mortality, there is no clear consensus about the PNI cut-off value, and there are different results in the literature. Peng et al. [16], in a multicenter study including 494 cases of chronic obstructive pulmonary disease (COPD) followed in the ICU with acute exacerbation, reported the cut-off value of PNI score to predict mortality as 31.8, similar to the results of our study (with sensitivity 62.3% and specificity 64.1%). In a study in which the place of PNI in predicting postoperative outcome was evaluated and 7781 cases who underwent gastrectomy were included, it was reported that when the cut-off PNI was 46.7 in the statistical analysis, significantly higher mortality was observed in cases with a PNI score lower than this value (hazard ratio ¼ 1.383, 95). % CI¼ 1.221–1.568, $p < 0.001$) [10]. Detection of higher PNI cut-off values compared to our study; This can be explained by the fact that most of the cases included in this study were ward patients and that our study was conducted entirely on critically ill patients followed in the ICU. In the recent COVID-19 pandemic, which has affected the world, studies have been conducted on many prognostic and mortality markers. PNI is among the scores evaluated for its use as a prognostic marker [12, 17]. Nalbant et al. [17], in the study in which the efficacy of nutritional indices in predicting disease severity in COVID-19 cases was evaluated, it was reported that PNI $\leqslant$ 36.7% cut-off was significant in predicting disease severity with 73.4% sensitivity and 70.8% specificity, and ICU admissions were 4.4 times higher in the group with low PNI compared to those with high PNI. Although a common result was obtained in these studies in the literature that mortality rates are higher in patients with low PNI, we think that the differences in the PNI cut-off value reported as a predictor of mortality may be related to the fact that the patient groups evaluated in the studies included different populations. Considering that most of the studies conducted with PNI are studies involving specific patient groups in which ward patients are evaluated, we think that it can be supported by studies to be conducted in ICU patients who are at higher risk of malnutrition compared to other patient groups in order to determine the cut-off in critically ill patients.

The value of PNI in predicting mortality, which was defined to assess nutritional risk, can probably be explained by the fact that albumin and lymphocyte count in its formula is associated with many negative prognostic factors. Albumin, one of the components of PNI, is among the laboratory parameters used in evaluating malnutrition [18]. In our study, the serum albumin level was found to be significantly lower in the non-survivor group com-

pared to the survivors. However, it has been reported in recent studies that serum albumin level, which can be affected by various clinical conditions, alone is insufficient to define malnutrition risk [19, 20]. Hypoalbuminemia can be seen in ICU patients for reasons such as increased renal or gastrointestinal loss in critical illness, decreased albumin synthesis due to increased cytokine release with inflammation, and increased escape to the interstitial space due to increased capillary permeability [21]. Peng et al. [16] in their studies in which they evaluated the mortality prediction of the PNI score in critically ill patients, it was reported that the PNI score was more significant in predicting 30-day mortality compared to serum albumin level alone.

It is known that malnutrition can cause negative effects on the immune system and changes in the inflammatory response [22]. Lymphocytes have an important role in the immune system, and in the case of critical illness, changes in lymphocyte numbers can be seen depending on many factors. It has been reported that malnutrition may cause atrophy of lymphoid tissues and a decrease in the rate of lymphocyte production [23]. The development of lymphopenia in critical cases has been associated with negative outcomes, and it has been stated that it can be used in predicting mortality, especially in the case of inflammation [24, 25]. In our study, no difference was found in terms of lymphocyte counts in survivor and non-survivor cases.

Malnutrition, which is associated with poor outcomes up to mortality, progresses silently, especially in ICU cases, and is difficult to recognize when not suspected. Evaluation of nutritional status in critically ill patients in admission to the ICU; It has been reported that it can help prevent bad outcomes by enabling the early detection of risky cases and providing more effective nutritional support [26]. Using a scoring system that is easy to implement and will not cause loss of time, labor, and cost can easily diagnose this patient group and provide a chance for early intervention in ICUs where critical cases are followed.

CONCLUSIONS

In our study, in which surgical ICU cases were evaluated, lower PNI values were found in patients with mortality compared to those who survived. The PNI cut-off value in predicting mortality is 32.01, and this value has generally been found to have higher sensitivity and specificity compared to the studies in the literature that gave PNI cut-off. On the other hand, its retrospective and single-center design are among the limitations of our study. We believe that our study will shed light on future studies to evaluate the use of PNI. Despite its limitations, this cost-effective method can be calculated with a simple formulation and does not require additional measurement and devices used in surgical ICU cases.

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Conflict of interest

The authors have no conflicts of interest to declare.

Ethics approval

The study protocol was approved by the institutional review board (Approval Date and Number:10.05.2022/E-64106871). Because the study was designed retrospectively, no written informed consent form was obtained from patients.

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COVID-19: THERAPEUTIC MISINFORMATION AND INTOXICATIONS

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ABSTRACT

The new coronavirus pandemic alarmed the world. Misinformation regarding prevention and treatment for safeguarding against this pandemic seemed to be life-threatening along with the spreading pandemic. Public health authorities in the world tried to battle this virtual virus by offering true information and correcting misinformation. However, the public misinformation through social media caused toxicological consequences in some parts of the world which provoked awareness, response, and concern of the public health authorities including the Food and Drug Administration (FDA) and the toxicology community. This study analysed the published literature on therapeutic disinformation during the COVID-19 pandemic and its toxicological effects. The electronic databases searched were Scopus, MEDLINE, Scielo. The used keywords were: "COVID-19", "misinformation", "social media", "public health", "drug toxicity", and "education". Finding new strategies for the prevention and treatment of the coronavirus again stresses the role of public education about true drug information. Hundreds of chemicals were/are being tested to be prophylactic medications or healing drugs for the coronavirus. Therefore, spreading accurate information and editing misinformation can be crucial. In summary, this commentary is going to bring attention to misinformation regarding prevention and treatment for safeguarding against the COVID-19 pandemic and its toxicological consequences and the need for public education on the appropriate use of therapies.

KEY WORDS: COVID-19; misinformation; social media; public health; drug toxicity; education

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INTRODUCTION

The 2019 novel coronavirus (2019-nCoV) later renamed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes the disease COVID-19. Despite COVID-19's first appearance in China (December 2019 in Wuhan, Hubei province), it became a contagious pandemic and the declaration of the World Health Organization (WHO) as a Public Health Emergency of International Concern ensued [1]. In parallel with the emergence of the new disease, the people of the world encountered large amounts of correct and incorrect information regarding the strategies for the prevention and treatment of the disease. Since the misinformation on COVID-19 on social media can spread faster than the pandemic, it can bring about panic and confusion in the public and thus decelerate

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the proper response to the outbreak. In this context, misinformation can be regarded as the most contagious component of COVID-19 [2]. Noteworthy, previous research showed that incorrect information can spread faster and reach more audiences in comparison with correct information [3].

Combating misinformation

To countermeasure the toxic infodemic, health authorities and scientific communities started to distribute valid information. WHO launched a platform called WHO Information Network for Epidemics (EPI-WIN) to deliver correct, evidence-based information with the help of experts and consultants of the risk communication team. The team closely is monitoring the common social media and regional authorities in the search for misinformation to neutralize them [4]. Advice through "myth busters" also informs the public to be able to distinguish between rumour and fact. The most prominent points in terms of toxicology are the following: (i) "…Drinking alcohol does not protect you against COVID-19 and can be dangerous… (ii) …Spraying alcohol or chlorine all over your body will not kill viruses that have already entered your body and can be harmful... (iii) …Are there any specific medicines to prevent or treat the new coronavirus? To date, there is no specific medicine recommended to prevent or treat the new coronavirus (2019-nCoV)…" [5].

A very recent study found that the general public in the United States and the United Kingdom suffered from important misunderstandings regarding COVID-19 and thus governmental organizations, scientific communities, and social media need to correct this hazardous misinformation [6]. Recently, an unprecedented mass poisoning and fatality occurred in Iran due to the misinformation distributed by social media just after the first days of the coronavirus outbreak in this country. The rumour started that alcohol consumption can prevent COVID-19 and thus some citizens be persuaded to provide this panacea at any cost. The consumption of fake alcoholic beverages (industrial alcohol tainted with 5% sodium hypochlorite solution, methanol instead of ethanol, an adulterated mixture of ethanol, or methanol and other toxic alcohols plus colour additives) purchased from the black market caused more than 2000 poison cases and more than 200 fatalities in 10 provinces of Iran during a short period of the coronavirus outbreak. The interesting finding was that the death rate from this poisoning was nearly twice as high as the death rate of COVID-19 at that time [7]. Methanol poisoning is a worldwide problem and related outbreaks have been reported in countries that produce and sell the illicit, adulterated alcoholic beverages including India, Uganda, Cambodia, Czech Republic, Kenya, Ecuador, Estonia, Indonesia, Libya, Nicaragua, Norway, Pakistan, Romania, Sudan, Turkey, and Nigeria [8, 9]. Therefore, it is indispensable to consider the risk of abusing alcohol as a pharmacological agent during future infectious pandemics.

Concern toward disinfection

Using disinfectants is another concern that needs proper information dissemination since they are potentially hazardous agents. Two common categories of disinfectants that are used for COVID-19 included alcoholic solutions (*e.g.* ethanol, isopropyl alcohol) and chlorine-based solutions (*e.g.* bleach) [10]. Even though the poisoning reports regarding these chemicals during the current virus outbreak are yet to be fully available in the literature, there was/is a concern about them, since at least 300 calls to the poison control centres attributed to the improper use of these chemicals during COVID-19 [11]. The toxicity of these substances is well documented [12, 13]. Therefore, more endeavours are needed to correct the information and subsequent behaviour of people. The FDA warned about the toxicity of potential drinking bleach releasing the correct information and the "list of products that meet Environmental Protection Agency (EPA) criteria for use against SARS-CoV-2" [14, 15].

Misinformation on therapeutics, toxicological alerts, and future educational demand

Drugs are chemicals that can be used for the prevention or treatment of diseases. In response to the urgent need for establishing a safe drug therapy for the new virus disease, WHO launched a large international clinical trial study known as "Solidarity" to examine the safety and efficacy of drugs including remdesivir, lopinavir/ritonavir combination, Interferon beta-1a, and chloroquine or hydroxychloroquine [16]. However, the delivery of misinformation about the coronavirus treatment, on the TV and the tweeter by a public figure, shortly thereafter resulted in at least one fatal poisoning in the United States [17] and three cases of drug poisoning in Nigeria [18]. Even though, the former case of poisoning resulted from an unpredictable source of an assumed

FIGURE 1. Movie poster, *Colchicum* 2019. Source: http://soureh-cinema.org/movie/219/Colchicum-Sourenjan [access: 14.01.2022]

drug (fish aquarium cleaner contained chloroquine phosphate), it provoked the FDA to communicate the risk to the public by editing the misinformation. The FDA issued a warning letter and at the same time committed to keeping the chemical away from the public. Similarly, the toxicology communities including The American Academy of Clinical Toxicology, The American College of Medical Toxicology, and The American Association of Poison Control Centres jointly released a statement to warn the public about the toxicity and potential fatality of the assumed drugs (hydroxychloroquine and chloroquine) [19, 20]. Moreover, with the help of scientists and clinicians, countries around the world prompting to perform clinical trials to examine the safety and efficacy of preventive therapies and drugs for treatments. A shortcut strategy is the repurposing of the existing drugs. More than hundreds of interventional clinical trial studies are underway (*e.g.* by keyword-based search on the https://clinicaltrials.gov) to evaluate the safety and efficacy of potential preventions or therapies for COVID-19. All these candidate drugs need to be evaluated for their efficacy and safety and that is part of the logic for conducting clinical trials. Again, social media is circulating the news of these promising treatments faster than the official registrations and of course, before the safety evaluation and approval for the treatment by the authorities. For example, the first news about colchicine as a potential COVID-19 drug was released in the middle of March 2020 that was a few days before the first clinical trial registrations (*e.g.*, one first registered the late March 2020) [21]. Collectively, there were few colchicine clinical trials conducted around the world to evaluate the safety and efficacy of this drug toward the virus. Colchicine is an alkaloid that is isolated from plants and introduced as an FDA-approved drug for acute gout flair and Familial Mediterranean Fever in 2009. It is safe when used in the range of therapeutic doses but taking a toxic amount of either drug or plant source can be fatal. Furthermore, the diagnosis of colchicine poisoning is sometimes challenging since it can be misdiagnosed as an infectious disease or food poisoning [22, 23]. Even the plant containing colchicine (*Colchicum Spp.*, dried seeds) can be purchased by online shopping. The plant is composed in the poem of Guillaume Apollinaire, a French poet [24], as below:

AUTUMN CROCUSES
"In fall the fields are poisonous but fair
Where, slowly poisoning, the cattle graze.
The meadow saffron, colchicum, thrives there,
Color of lilac and the circles under eyes.
My life pastures so on the autumn hue
Of your eyes and slowly poisons itself too.
Children in queer jackets come and play
Harmonicas and pick the purple flowers
Which are like mothers, their own daughters' daughters.
When your saffron eyelids raise and lower
They are like flowers that a crazy wind flutters.
The shepherd sings the cattle on their way
As, slowly and flowingly and for all time, they pass
From the broad evil-flowered autumn grass."

Also, the plant recently inspired a drama movie in Iran; with the original title of Sourenjan, a Persian common name for meadow saffron, *Colchicum,* meaning literally as Flower of Regret (Fig 1.).

Interestingly, renowned antidotes such as N-acetylcysteine (NAC) and Desferal are among the candidate lists of repurposing drugs for COVID-19. NAC is considered a mainstay therapy for acetami-

nophen toxicity that is a major cause of liver failure in the United States and the United Kingdom [25, 26]. However, the safety of NAC is dose-dependent meaning that it can cause toxicity when the dose is increased [27]. Desferal is an iron and aluminium antidote but it also has potential toxicity [28]. The last news on social media has stated that ivermectin can be a repurposed drug for COVID-19 [29]. Of course, initial scientific research showed a hope [30] but it is of paramount importance to deliver this fact to the general public that it is not allowed to use before the final approval by the health authorities and at the same time self-medication is a huge mistake that people may commit and thus it is crucial to make aware the public of the risk of misinformation.

CONCLUSIONS AND RECOMMENDATIONS

In conclusion, it is vital to educate the general public about the most important principle of pharmaco-toxicology that the *Paracelsus* has taught since the sixteenth century: "the dose differentiates a poison from a remedy" [31]. A recent infodemiological study evaluating the internet health information regarding preventive measures for the COVID-19 proposed that the use of public health organizations' official websites needs to be encouraged in comparison with other informational websites by the public to the users obtain more correct health information and subsequently increase the chance of sharing by providing the availability on the top list of search engines results [32]. During the pandemic diseases like COVID-19, a lack of awareness and preparedness of the public people may put them at risk of life-threatening conditions. Therefore, disseminating rapid, correct information declared by the official authorities and share via social media is of key importance. Finally, it is recommended to conduct more infodemiological studies about the indiscriminate use of pharmacological agents around the world to be used as a framework for policymakers in learned communities such as scientific pharmacology and toxicology societies.

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