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CANDIDA AURIS AS A SIGNIFICANT EMERGING HUMAN FUNGAL PATHOGEN

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The COVID-19 pandemic has taken resources away from combating and tracking the fungi, which has led to outbreaks [1]. In hospitalized patients, COVID-19 has aggravated various underlying illnesses, leading to a rise in bacterial, viral, and fungal coinfections. Moreover, during the pandemic, shortages of personal protective equipment forced medical personnel to reuse personal protective equipment and masks, which contributed to the spread of fungi [2, 3]. Because of high mortality rates, a lack of diagnostic options, rising levels of antifungal resistance, and severe clinical manifestations, fungal infections provide a particularly difficult challenge [4]. One such fungal disease that causes epidemics in COVID-19 intensive care units and hospitals all throughout the world is *Candida auris* [5]. Therefore, *Candida auris* is not an issue that occurred during the COVID-19 pandemic but was not appropriately recognized at the time, as fungal coinfections were not considered in the first line of diagnostic procedures.

According to the most recent warning published by the Centers for Disease Control and Prevention (CDC) on March 20, 2023, medical professionals are expressing grave concern over the rapidity of *Candida auris*. In 2016, the illness was found for the first time in the United States, since the end of 2021, there were 3,270 confirmed cases of infection and 7,413 confirmed cases of *Candida auris* carrier. The

number of people who did not react to the medicine that was suggested the most (echinocandins) quadrupled in the year 2020–2021, which was the year when the largest number of infections was reported. During this time span, there were also three times as many people who were infected with the virus and who were carriers as there were in 2019. The early data from the CDC indicate that there were 2,377 clinical cases in 2022, which is an increase from the number of 1,471 in 2021 [6]. Such a rapid increase in the population of infected and carriers raises serious concerns about the spread of the disease. It is important to keep in mind that in addition to the individuals who are afflicted by this pathogen, there is also an extremely high percentage of carriers. These individuals can serve as potential sources of infection for the most susceptible populations, or they can become ill themselves if there is a significant reduction in immunity. This group ought to be watched with regard to the strains that they carry, and preventative steps need to be adopted in the form of recommendations with the purpose of eradicating the pathogen. Because traditional phenotypic typing approaches were not utilized in the search for *Candida auris* until very recently, one theory argues that this pathogen was not discovered until much more recently [7]. Some sources claim up to 90% of isolates are misdiagnosed, *Candida auris*

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frequently goes undetected in clinical microbiology laboratories. Problems with identification and misdiagnosis make combating the infection, which is already tough to treat, even more challenging [8]. Additionally, the information that patients with *Candida auris* constantly expel live yeast cells from their skin, which results in the contamination of hospital surroundings, lends credence to the rapid spread of the pathogen. This information demonstrates that patients with *Candida auris* contribute to the rapid spread of the pathogen.

Both *Candida auris* and SARS-CoV-2 were found in a hospital setting, including on IV poles, bed rails, hospital floors, windows, air conditioner ducts, and other hospital surfaces [9]. Moreover, it has been reported that more than 90% of the *Candida auris* isolates are resistant to fluconazole (azole), however, the degrees of resistance might vary quite a little amongst different clades. Many investigations have found that the minimum inhibitory concentrations (MIC) for amphotericin B (polyene) are high, and there is a developing resistance to echinocandins in the isolates of several nations [10]. According to the MIC breakpoints, a significant number of isolates exhibit resistance to numerous types of medicines. It has been discovered that certain *Candida auris* isolates from the United States are resistant to all three kinds of antifungal medication. In the United States, around 90% of *Candida auris* isolates tested positive for resistance to fluconazole, approximately 30% of *Candida auris* isolates tested positive for resistance to amphotericin B, and less than 5% of *Candida auris* isolates tested positive for resistance to echinocandins. These percentages can contain numerous isolates from the same person, and they might shift as more isolates are examined and analyzed [11]. As a result of *Candida auris*, it is essential to research and develop new antifungal medications, as those already available may soon lose all effectiveness against this fungus. In most cases, the fungus does not pose a risk to people who are healthy. Individuals with a weakened immune system or those with lengthy or frequent stays in healthcare institutions are more likely to get it. As COVID-19 attacks the immune system severely, leading to an increased chance of coinfections and increased severity of other diseases, the death rate of coinfection of COVID-19 and fungi is probably very high. *Candida auris* has been linked to bloodstream infections and even fatalities, particularly in people with significant medical conditions who are

residing in healthcare facilities such as hospitals and nursing homes.

The most typical signs and symptoms of a *Candida auris* infection include a high temperature, chills, sweating, and a decrease in blood pressure. Patients of all ages, from premature newborns to the elderly, have been discovered to be infected with various pathogens [12]. Pregnant women also have a weakened immunological response making them potentially susceptible to infection with *Candida auris*. Nevertheless, there have been no reports of infection during the pregnancy. The *Candida auris* infection has a general death rate of 52.5% across the board. The global numbers range from 30 to 59%, while 30–72% of patients pass away due to nosocomial illnesses. Tracheotomy, enteral nutrition, insertion of a venous, urological, or hemodialysis catheter, and stoma are all procedures that increase massively mortality. This percentage is at its maximum when numerous antibiotics are being administered (84.3%), when the patient is admitted to the Intensive Care Unit (78.7%), when they are receiving mechanical ventilation (78.7%), and when they have comorbidities (68.5%) [13]. For this reason, *Candida auris* was included in the World Health Organization (WHO) list of the most dangerous fungi for humans. Even though fungal infections are frequently linked to high mortality rates, they are still not widely recognized as clinically significant etiological factors in the development of infectious illnesses and as the primary cause of fatalities due to these conditions. The issue of fungal illnesses spreading from person to person is still a serious worry from a health, epidemiological, and economic point of view, despite the huge achievements that have been made in modern medicine in recent decades. *Candida auris* is the most recent example of this because it is a species that can rapidly spread, is characterized by wide resistance to existing antifungal drugs, and is equipped with a large number of pathogenic factors. It represents a significant danger to human life and health on account of all that has been discussed thus far. With the discovery of the pathogen in question came the difficult task of formulating an effective plan for combating it. There is a need for more research on this pathogen as well as creature testing that are both quick and accurate in order to identify it before it gets widespread. This also applies to the possibility of self-testing procedures, as was in the case of COVID-19, and which will enable contact

with individuals or relatives of patients to be able to swiftly identify the illness [14, 15]. In addition, in order to prevent the further spread of illness, it is essential to develop and implement care and isolation guidelines.

Conflict of interest

All authors declare no conflict of interest.

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THE EXPERIENCES OF VICTIMS IN THE MASS GATHERINGS: A PHENOMENOLOGICAL STUDY

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ABSTRACT

INTRODUCTION: The mass gathering events are becoming a big source of concern among public health practitioners. These events can affect a population's health in different ways. The study aimed to identify mechanisms associated with morbidity and mortality in mass gathering (MGs) events.

MATERIAL AND METHODS: This is a qualitative study that was conducted under a phenomenological approach. The study population included 21 people who were hospitalized due to injuries in the mass gatherings. Data collection was conducted through semi-structured and in-depth interviews.

RESULTS: A total number of 21 interviews were conducted in this study. Participants included 17 males and four females. Thematic analysis was used to identify 21 different themes and the themes were classified into five main areas. These five areas include Individuals' unpreparedness, unprepared relief organizations, lack of proper response plans, and risky behavior and psychological reactions.

CONCLUSIONS: The lived experiences of MGs victims showed that they need to be better educated at the community level about the potential MGs' health risks. One of the most effective measures to reduce mortality in the MGs is risk governance. Risk governance must be a national policy and priority at the time of holding large gatherings.

KEY WORDS: mass gathering; injury; public health; prehospital care; emergency nursing; emergency medical services

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INTRODUCTION

Mass gathering is a phenomenon that a large number of people (depending on local circumstances, usually up to 25 000 people) gather in a specific location for various purposes, such as entertainment and sporting events, festivals, political and social campaigns, memorials, and religious ceremonies. Mass gatherings have time limits. They can gather people

from various communities or even countries when they become multicultural [1].

Historically, mass gatherings occurred in the form of sports, political and religious events at different locations in the world and sometimes they came along with many lost lives and injuries [2]. In particular, mass gathering disasters take place during religious ceremonies, including Haj in Mecca and Arbaeen in

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Iraq [3]. In the West, the term “mass gathering”: was initially used for gatherings such as football matches and concerts [4]. Also, India, as a country with a large population is the host of many religious mass gatherings [5]. Mass gatherings can be prone to man-made and natural incidences. Therefore, serious attention and planning are required before holding these types of gatherings. According to statistics, religious ceremonies have been the most hazard-prone events [6, 7].

Potential health risks in these events included; extreme weather-related illness, food and water-related diseases, communicable incidents and transportation accidents, injuries, and deaths especially those related to across-the-border gatherings [8, 9].

In recent decades significant numbers of morbidities and mortalities have been caused by mass gatherings all around the world and it has attracted international organizations such as the World Health Organization attention to these events [2]. In many mass gatherings that led to disasters, the population density had reached a critical point. The critical point is when the available space for each person reaches less than 50 cm². Basically, for a moving population in a crowded area, at least 2.3 m² of space should be considered for each person [10]. When the per capita space reaches close to less than 1 m², the smooth movement of the population will slowly be downed. At a density of 50 cm² per person capacity, space is maximized and the possibility of mobility is very limited. In an area of less than 50 cm², people unintentionally push each other. At a *per capita* space of 20 cm² per person, we will see the dangerous force of high concentrations of people and create stress and an unhealthy environment [3].

The mechanisms behind morbidities and mortalities in mass gatherings are not well investigated in the world. Many policymakers and disaster managers do not have accurate and specific information about methods for the prevention of health-related hazards in mass gatherings [11]. It is necessary to identify and develop various dimensions of this phenomenon. Due to the single nature of mass gathering events, phenomenological surveys can help to investigate victims' experiences and to identify potential hazard mechanisms.

Due to the unknown mechanism of damage in mass gatherings as well as the increase in large-scale mass gatherings in our country, this study tries to investigate the experiences of injured people in mass gatherings, to determine the dimension of this

phenomenon. It is hoped that with a more comprehensive understanding of the mechanism of harm to the people in mass gatherings, the preparation and planning will result in none or a lower number of victims in events in the country.

MATERIAL AND METHODS

This was a qualitative study conducted under a phenomenological approach. Phenomenology is studying lived experiences basically. Phenomenology pays attention to the world as lived by an individual, not facts that are separated from human experience [12, 13].

Due to the importance of victims' experiences in mass gathering events and the ability of phenomenological studies in identifying root causes of incidents, we applied the phenomenological approach in this research [14].

The study population included all people who were hospitalized due to injuries in mass gatherings. Being over 14 years old, willingness to participate, and having no mental retardation were selected as the inclusion criteria. Purposeful sampling accompanied by the snowball technique was continued until data saturation was reached. Finally, 21 people were interviewed. In the present study, data collection was done through semi-structured and in-depth interviews. In-depth interviewing is the researcher's intention to penetrate the deep layers of the interviewee's mind and obtain true information. The interview guide was used in this study. A total of 21 interviews were conducted.

A total of 21 interviews were conducted in this study. Participants included 17 males and 4 females. Participants had 3 undergraduate degrees, 6 diplomas, and 12 bachelor's degrees. The average age of participants was 29 years old (Tab. 1).

The duration of the interviews was between a minimum of 13 minutes and a maximum of 1 hour and 17 minutes, depending on the interviewee's willingness to continue. The interviews were conducted individually, to help the interviewee feel privacy while sharing their experiences.

At the beginning of each session, the interviewer explained the aim of the present study and assured participants that all data from the interviews would remain strictly confidential. The interviewees were asked about their anonymous demographic information, including age, education, and. A written agreement was obtained from each of the

Table 1. Demographic characteristics of participants

Gender	Male: 17 persons
	Female: 4 persons
Education	Under diploma: 3 persons
	Diploma: 6 persons
	Bachelor: 12 persons
Type of events	Political gathering: 2 persons
	Religious gathering: 10 persons
	Sport gathering: 7 persons
	Concert and festival: 2 persons

interviewees in order to formalize the consent of the interviewees to participate in the interview. There was a well-designed interview guide following with a list of open-ended questions.

During the interview, additional questions were asked. The interviewees were free to quit the interview whenever they wished. Data analysis was made possible for research based on data collection through selected questions and axes. The interviews were recorded and transcribed, and the sentences, phrases, and quotations that indicated people's understanding of the phenomenon were identified. In the next step, the researcher used important phrases to categorize the meanings that led to the achievement of the sub-themes. These sub-themes were also used to write about what the participants experienced in covering the themes. Eventually, the themes were covered in a wider range called domains. The Collaizi method was used to interpret and analyze the information obtained in this section [15]. To validate the information obtained, the participants were referred to and their compliance with the information was ensured.

RESULTS

By analyzing the study findings and coding the information, 21 different themes were identified by the research team, and the themes were classified into five main areas. These main areas include; psychological reactions were unpreparedness of individuals, the unpreparedness of relief organizations, lack of proper planning for response, and risky behaviors. The first area identified was the area of psychological reactions, which included the three themes of fear of death, lack of access to relief workers, and lack of access to healthcare facilities. Almost all par-

ticipants in the study stated that their first reaction to the incident was fear of death and fear of the unavailability of relief workers and medical staff. For example, participants stated that:

"I could feel too much pressure on my chest. I was scared. My heart was pounding. Every time I looked, there were no emergency-response workers." (P 5)

"I knew my leg bones were broken and I was bleeding heavily. The ambulance was 50 meters away. I asked for help, but the emergency-response workers could not speak because it was so crowded around me that no one could move. I was panicked." (P 11)

The areas of unpreparedness of individuals include four themes lack of education to the community, lack of attention to overcrowding, low risk perception, and physical condition of individuals. Victims of mass gatherings generally criticized their unpreparedness and always blamed themselves for part of the incident.

"I could not believe that the crowd could bother me like this. Although I did not push hard, the crowd pressure was very high." (P 1)

"Our people do not know how to watch games together. They get stuck soon. When the game is over, everyone just rushes out. They do not think that maybe someone has a weak body, maybe someone is crushed under their arms and legs." (P 8)

"I have never watched TV. Teach me how to take care of myself in gatherings. They all advertise that more people should come to the gatherings. The body should not care a bit about people's health." (P 10)

The victims of the mass gatherings in various ways pointed to the underprepared of the relief organizations, especially in the absence of escape routes. They always blamed the congestion on relief organizations' workflow.

"We were stuck in the corner of a three-meter wall. The pressure of the crowd was on the walls. The authorities should have thought beforehand and understood the possible pathways of the moving crowd and plan it for the best option. If people get stuck, they cannot escape anywhere." (P 3)

"There were some soldiers next to us who were very scared. There was nothing they could do. Neither the emergency forces nor the Red Crescent staff. Whatever we shouted, we took the injured out of the crowd, and they did not move. I mean, not knowing anything to do in such situations." (P 19)

Another important but neglected area was the lack of proper planning for the response. In this area, there are a number of problems, such as a lack of quick alert systems, poor population management, poor food distribution, a lack of emergency-response workers, a lack of attention to food quality, and no evacuation plans, poor communication systems, and differences between organizations.

"I do not know if the emergency services were having tea or doing anything else, but there was no word from them. We were all busy watching the game. we were suffocating here. Nothing was happening." (P17)

One of the participants, who had an accident due to the crowd during the food distribution said that the food truck reached the crowd and went to it. "I hardly got hit by the car. I went up from the side of the car. The one who was already on the top fell down". (P10)

An interviewer from the experience of communicating with relief personnel said that (P21): "I went to one of the rescue staff and told him that the crowd should not move, otherwise it will be stocked. At that moment, a policeman came and said, 'No, the crowd has to go out faster, dangerous', and he encouraged the crowd to rush to the door, and then the accident happened" (Tab. 2).

DISCUSSION

Mass gatherings can result in mass casualty incidents. These events attracted thousands of people, which may create more potential health problems such as injuries, infectious diseases, accidents, and deaths. The aim of the study was to identify experiences of mass gathering victims through a phenomenological approach. Results showed that experiences of mass gathering victims can be divided into five categories, including mental and psychological reactions; lack of preparedness in victims; lack of preparedness in responsible organizations; lack of suitable planning for response; and high-risk behaviors. The victims that participated in the study were injured in various gatherings such as religious and sports events, and political and entertainment campaigns. The Arbreen mass gathering is an annual ceremony that gathers millions of people in Iraq. In recent years, many incidents have occurred in the country at Islamic gatherings, sports events, and other religious events [16].

Table 2. Identified areas and themes

Area	Theme
Psychological reactions	Fear of dying
	Lack of access to relief forces
	Lack of access to medical facilities
Unpreparedness in people	Lack of education to the community
	Lack of attention to crowd management
	Low risk perception
	Poor physical condition
Lack of readiness of relief organizations	Uneducated personnel
	There was no escape route
	Lack of proper ventilation
	Insecurity of structures
Lack of proper planning for response	Lack of rapid alert systems
	Improper population management
	Improper distribution of food
	Shortage in relief force
	Lack of attention to food quality
	No plan to evacuate
	Weaknesses in communication systems
	Inconsistency between relief organizations
High-risk behaviors	Drug and alcohol abuse
	Get excited to reach the attractive point

Lack of access to enough medical services at mass gathering events has been identified in various studies. Schwartz et al. [17] pointed out that medical goals in mass gathering events are very important [18]. The goals included assessment and stabilizing people that are injured or unwell, supporting responders; providing medical care to the local population; using the capacity of public health and emergency medical care systems to better prepare for and respond to hazard identification; risk assessment and analysis; risk mitigation; planning for access to those who demand medical services; and transportation of patients to the hospitals. A key decision in mass gatherings is to provide healthcare services such as PHC services and treatment of minor injuries and illnesses [19]. Relief organizations, especially EMS, are typically responsible for providing medical services to those who are injured on a fast track but lack the capacity to triage patients in mass casualties can be seen in this organization [20]. The need for medical services in mass gatherings depends on

various factors, including the temperature and humidity of weather, the duration of a ceremony or event held in outdoor circumstances, the mobility status of the crowd, the type of mass event, the crowd mood, consumption of alcohol and drugs, the crowd density, the geographical situation, past experiences, and the demographical status of the crowd.

Lack of education in people is also an important trigger for potential health risks in MGs. According to studies, low-risk perception and lack of self-protection awareness affected participants' well-being in MGs. Participants must be well educated in hand-washing, wearing masks, and keeping a suitable distance from others. However, maintaining social distance in MGs is difficult. In terms of risk perception and awareness, the people in charge of MGs should collect information from participants before gatherings, such as their age, gender, existing diseases, level of awareness, and education level, so that the right predictions can be made.

One of the most significant issues identified in this study was a lack of cooperation and coordination among respondents. Multi-authority cooperation during the planning is important in order to ensure seamless collaboration between the responders and stakeholders during the event. According to previous studies, planning for mass gatherings is necessary for health authorities [17] and also requires inter-organizational cooperation with police forces and other emergency responders [21]. Previous research demonstrated that having enough medical staff such as first-aid providers available and the use of treat-and-release directives has a significant impact on the required number of patients that are transported to a hospital and, consequently, decreases the workload for the EMS organization and healthcare facilities [22–26]. According to an Australian study by Zeitz et al. [27], the increase in workload for the rescue service in mass gatherings with a total of 5.7 million attendees in a two-year period was only minor. The workload for rescue service consisted of assistance in traffic control and on-call support. The police workload was correlated with the EMS workload. The main determinant for the police force's workload was the weather, while the EMS workload had a wider range of determinants.

Surge capacity planning in human resources decreased the risk of health problems during MGs. The use of adequate physicians, nurses, and emergency technicians not only speeds up medical handling but also prevents unnecessary dispatch of an ambu-

lance to healthcare centers [28]. Security arrangements in MGs result in the prevention of injuries that occur because of population pressure and stampedes. Thus, it must be considered the route for entrance and exit in a one-way flow. Karampourian, who studied religious MGs, proved human resources are essential to good preparedness and response to these events [7]. Allocating and managing human resources should be cost-effective, but it should be noted that sudden changes will reduce the provision of desirable services in organizations with minimal resources. Don't plan for the provision of experts. This can lead to a crisis. Numerous studies in MGs, such as the Hajj, Kumbh Mela in India, and sports games, have demonstrated the importance of managing and providing adequate human resources and equipment before an event [4, 8, 29]. Previous experience and evidence of past events can be used to estimate the manpower and equipment needed to provide appropriate health services during such events. Based on studies of health infrastructure, the size of the accumulation is a key factor in determining the level of readiness of the health system. Inappropriate locations for gatherings, poor facilities, or a lack of infrastructure and medical services can increase the vulnerability of communities. The remoteness of health facilities and the lack of necessary road infrastructure will make medical services and emergency assistance ineffective.

The lack of an early warning system was another case identified in this study. According to studies in mass gatherings, because conventional systems for identifying people in need have problems, it is necessary to consider an early warning system to identify health problems [30]. This system can be related to the surveillance system. Inadequate distribution of water and food is also a risk factor in mass gatherings. Water and food usually attract crowds. Crowds in water and food distribution centers pose a risk of overcrowding and injury [31]. It is necessary for the distribution centers of these materials to be well distributed. Also, the low quality of the food distributed can increase the risk of poisoning and increase the number of medical visits. In addition, in terrorist cases, there is a possibility of more catastrophes and mass casualties.

CONCLUSIONS

Injuries at large gatherings are a one-of-a-kind experience. Most of the responders in mass gatherings

aren't informed about how previous measures can affect an individual's health during MGs. The lived experiences of MG victims showed that we need to better educate at the community level about health risks in MGs. The victims pointed out that MG risk perception is lower than reality in the country. Community education and integration the of disaster risk reduction strategies into social campaigns can promote individual preparedness. At the organizational level, it is necessary to plan for surge capacity and crowd management. Because Iran holds many religious ceremonies each year, public health measures during such events are good, but crude management is poor. In addition, coordination and cooperation between relief organizations is a major challenge. One of the most effective measures to reduce deaths in MGs is risk governance. Risk governance is holding mass gatherings must be a national policy and priority.

Ethics approval and consent to participate

This study was approved by The Research Ethics Committees of Sirjan Faculty of Medical Sciences (approval ID: IR.SIRUMS.REC.1399.010).

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Conflict of interests

The authors declared no conflict of interest.

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DETERMINATION OF FACTORS RELATED TO EMERGENCY RE-REFERRAL IN PATIENTS WITH HEART FAILURE A HOSPITAL IN TEHRAN — IRAN: A CROSS-SECTIONAL STUDY

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ABSTRACT

INTRODUCTION: The re-referral of heart failure patients to the hospital is a significant health problem today and is one of the most costly and preventable events for these patients. The present study aimed to investigate the factors affecting the re-referral of patients with heart failure to the emergency department of Shahid Beheshti University of Medical Sciences in Tehran in 2021. Identifying these factors can lead to the recognition of patients at high risk for re-hospitalization and the design of preventive and effective interventions.

MATERIAL AND METHODS: This descriptive-correlational research was performed cross-sectionally. Ninety patients with heart failure who were re-referred to the emergency department of Masih Daneshvari Hospital entered the study. Sampling was done for 6 months from December 2020 to May 2021. Data collection tools included a researcher-made questionnaire and a European self-care questionnaire for heart failure patients, and the New York Heart Association Classification (NYHA) standard for classifying heart failure class. After completing the questionnaires, the collected data were analyzed by SPSS23 software.

RESULTS: The results showed that age (the mean age of the participants in the study was 69.9 years), duration of disease (77.8% was six months to four years), body mass index (the mean body mass index was 27.2) (demographic characteristics) dyspnea (78.9%), organs edema (47.8%), shortness of breath (pathological factors), high blood pressure (54.4%), diabetes (25%), chronic obstructive pulmonary disease (11.1%), and ischemic heart disease (3.3%), (background diseases), high creatinine (the mean 1.98), (laboratory findings), not using beta-blockers (18.4%) and not taking angiotensin receptor blockers (18.8%) (pharmacological agents), NYHA criteria (89% were in NYHA class 3 and 4) and self-care levels of heart failure patients (the mean self-care score was 37.4) have a statistically significant association to re-referrals to emergency (p-value < 0.05).

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CONCLUSIONS: Identify patients with a high risk of hospital re-referral and decrease additional costs imposed on care centers by recognizing the factors influencing the re-referral of patients with heart failure and design preventive and effective interventions. So, it is possible to increase the patient's self-care level while reducing the number of re-referrals.

KEY WORDS: re-referral; heart failure; patients; hospital cooperation; Iran

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INTRODUCTION

Heart failure is a complex clinical syndrome that results from functional or structural dysfunction of the ventricular or extracorporeal filling, leading to clinical symptoms such as dyspnea, fatigue, and signs of respiratory failure such as edema and pulmonary rale [1]. Besides, this disease is considered one of the most common chronic diseases worldwide and is the final stage of many cardiovascular diseases [2–4].

Today approximately 26 million patients are diagnosed with heart failure worldwide, and this number is likely to increase by 25% in 2030 [5]. According to the Centers for Disease Management, the number of people with heart failure in Iran is about 3,400 per 100,000 [6]. Despite significant advances in diagnostic evaluations and therapeutic interventions, heart failure is a condition characterized by disability, mortality, and high economic burden [7–9]. According to the American Heart Association (AHA), about 7.3% of all deaths from cardiovascular disease are due to heart failure. Studies in Iran have also shown that cardiovascular disease has the highest mortality rate compared to other diseases. The 5-year mortality rate has been reported to be 45% in women and 60% in men [6, 10, 11]. Still, according to the AHA, the prevalence of heart failure between 2012 and 2030 is expected to increase by 46%. So, patients with heart failure will be under 65, and they will have a 6 to 9 times higher risk of sudden death [12].

Heart failure is a significant cause of economic costs in many parts of the world. The main costs are related to referring and hospitalization, followed by medications and social support [13–15]. The admissions and returns of these patients to the hospital are critical health problems today. Despite the advances in political management and numerous studies predicting the re-occurrence of heart failure, it is estimated that more than 50% of patients with heart failure return to the hospital within six months of discharge due to disease-related conditions. Also,

one in five patients with heart failure will return to the emergency room after discharge. Moreover, a re-emergence of heart failure 18 to 24 months after discharge is a poor prognosis for the patient [16–18].

Health care for patients with heart failure occurs mainly in healthcare centers. When these patients need immediate treatment due to the worsening of their symptoms [19, 20], emergency departments are the first line of communication between the patient and the health care system and the patient's main entrance to this system. Due to the unique nature of functional processes in terms of complexity and the number of patients, the emergency has an essential role in reducing mortality and restoring health and satisfaction [21]. Overcrowding in the emergency department is a severe problem in the healthcare system worldwide. Recognizing the causes of this problem will probably decrease the number of patients and improve care quality [22].

Decrease re-referrals to hospitals and emergency rooms after patient discharge is a priority for policymakers, healthcare leaders, and physicians. This reduction is recognized as one of the health care indicators in the United States [23]. The unnecessary use of these resources influences the quality of services provided to patients and the effectiveness of the discharge process. To achieve positive effects on the clinical outcomes reported by patients, heart failure management programs have been developed [24–26].

Despite the number of studies about the rate of re-referrals and hospitalization of heart failure patients, little is known about the cause of returns and re-referrals to the emergency room. Interventional studies inside and outside the hospital have been able to identify factors that decrease the risk of re-hospitalization in heart failure. In general, the reasons for returning to the hospital are divided into three general categories: 1 — Factors related to health care: such as health and subsets of health care; 2 — Factors related to the patient: includ-

ing social and family environment and adoption of treatment measures; 3 — Disease-related factors: such as its natural progression or a combination of all of them [27]. While some of these factors may be avoidable and controllable, the factors related to heart failure are not consistently controlled. Identifying these factors can help identify patients at high risk for re-hospitalization and design effective preventive interventions [28, 29].

Nursing participation is a comprehensive dimension of disease management programs for heart failure and a vital component of this intervention. Some studies have found that a multidisciplinary approach to disease management reduces the duration of hospitalization, and the rate of admission and re-referral improves the quality of life and increases patient survival [30–32]. Nurses have a special place as members of the health team. Their understanding of heart failure patients' re-referral helps develop a strategy to prevent the possibility of re-referral and thus better use of resources and cost maintenance.

To improve heart disease management, it is necessary to understand the factors associated with re-referral [29, 33, 34]. Recognition of these factors plays an essential role in increasing the life expectancy of patients while identifying the unmet medical, educational, and psychological needs of patients, which will reduce their re-referral rate [34]. Therefore, this study was conducted to investigate the factors related to emergency re-referral in patients with heart failure in the selected hospital of Shahid Beheshti University of Medical Sciences in Tehran.

MATERIAL AND METHODS

Study design

This descriptive-correlational research was performed cross-sectionally. The research population includes patients with heart failure referring to the selected hospital emergency department of Shahid Beheshti University of Medical Sciences in Tehran. Sampling was done for 6 months from December 2020 to May 2021. Accordingly, based on the Heydari et al. study [35], the sample size was estimated to be 81, including the possibility of 20% sample loss. Ninety patients with heart failure were selected and studied as available samples which were qualified and referred to the emergency room of Masih Daneshvari Hospital. Inclusion criteria: the ability to answer questions, age over 55, at least six months

after diagnosis, congestive heart failure grade 2 or 3 or according to the New York Heart Association (NYHA) classification, and absence of mental problems such as Alzheimer's and mental retardation. After obtaining a Shahid Beheshti University of Medical Sciences license, they referred to the research fields. Sampling began in this center after introducing and obtaining permission from the competent authorities of Masih Daneshvari Hospital. At the beginning of the study, the patient was informed about the research, and the confidentiality of the questionnaire information was emphasized. Data collection tools included a researcher-made questionnaire and a European self-care questionnaire for heart failure patients, and the NYHA standard for classifying heart failure class.

Statistical analysis

After completing the questionnaires, the collected data were analyzed using SPSS23 software. Descriptive statistical tests were used to analyze the frequency of data and determine the factors affecting patients' re-referral. Independent parametric T-tests, one-way analysis of variance, and nonparametric Spearman correlation tests were used.

The tools used in this study included the following three questionnaires: Questionnaire related to patient information, NYHA criteria for classifying heart failure and severity of illness and European self-care questionnaire for patients with heart failure.

Questionnaire related to patient information

According to previous studies, this questionnaire examines patients with heart failure in 5 dimensions:

- **Demographic dimension:** Demographic characteristics of people were measured, including age, sex, marital status, income status, insurance status, employment status, level of education, patient referral, caregiver, heart failure detection time, body mass index, and body surface area.
- **Pathological factors:** The pathological causes of the patient's re-referral to the emergency room were evaluated, including dyspnea, weakness, lethargy, chest pain, general body pain, limb edema, shortness of breath, and fever, cough, abdominal asthma.
- **Background diseases:** Background diseases were examined along with heart failure, including cases such as acute coronary syndrome, heart attack, open-heart surgery, chronic

obstructive pulmonary disease, having a pace-maker, atrial fibrillation heart rhythm, peripheral vascular disease, diabetes, hypertension, stroke, malignancies, hyperlipidemia, anemia, gastrointestinal diseases, chronic renal failure, dialysis, pneumonia, asthma, ischemic heart disease, pleural effusion, and pulmonary emphysema.

- **Pharmacological factors:** The patient's medications were questioned based on group therapy and included the following: beta-blockers, renin-angiotensin system inhibitors, diuretics, nitrates, statins, insulin, calcium channel blockers, and alpha-receptor inhibitors.
- **Laboratory and paraclinical findings:** The laboratory findings were available to patients (blood sugar, biochemical tests, liver tests, arterial blood gas results), and findings from echocardiography were evaluated (ejection fraction and pulmonary vein pressure).

The validity of the questionnaire was confirmed by experts and was given to professors and 10 patients with heart failure to determine the reliability of the questionnaire, and its overall reliability was estimated at 0.73.

NYHA [36] criteria for classifying heart failure and severity of illness

The New York Heart Association has divided heart failure into four categories based on the amount of activity that causes these symptoms:

- **Class one:** The patient performs regular physical activity without causing fatigue, dyspnea, palpitations, or chest pain. Lack of lung congestion or peripheral blood pressure, the patient is asymptomatic. There is no limit to daily life activities, and the prognosis is good.
- **Class two:** The patient has low limitations in daily life activities. The patient does not report symptoms during rest but will experience symptoms with increased physical activity. The rale and S3 murmur may be heard at the base of the lungs, and the prognosis is still good.
- **Class three:** The patient has clear limitations in daily life activities. The patient feels comfortable at rest but suffers from dyspnea with less activity than usual, and the prognosis is poor.
- **Class four:** The patient also has symptoms at rest, which is a sign of heart failure, and the prognosis is poor.

European self-care questionnaire for patients with heart failure

The European questionnaire on the self-care behavior of patients with heart failure was developed by Jarasma et al. [37]. The questionnaire has 12 items. Furthermore, the items are based on a five-point Likert rating: that is totally true 1 point, that is true 2 points, to some extent 3 points, that is not true 4 points, and not at all 5 points. This questionnaire's overall score was calculated by adding the scores of all items together. The score range will be between 12 to 60. Scores between 12 and 28 were considered good, 29 and 44 average, and 45 and 60 poor. The lower the score obtained in this questionnaire, the better the self-care behavior level of people and vice versa. The formal and content validity of the self-care questionnaire in Khoshtarash et al. [38] research was approved by ten nursing and midwifery professors. Its reliability was calculated at 0.71 by Cronbach's alpha method.

Ethics considerations

This study was drawn from a research project (No. IR.SBMU.PHARMACY.REC 1397.095) sponsored by the Deputy of Research and Technology at Shahid Beheshti University of Medical Sciences. Participants were aware of the purpose of the study and provided informed consent prior to accessing the questionnaire and participated voluntarily. No compensation was provided, and all collected data was stored securely.

RESULTS

Sociodemographic profiles results of the data analysis from the questionnaire related to patients' information and the European self-care questionnaire for heart failure patients, and the NYHA standard for classifying heart failure class, showed that most of the participants were men (62.2%), married (76.7%), and had primary education (24.4%). The duration of diagnosis in the majority (77.8%) was six months to four years. Meanwhile, most of the samples (90%) were in Classes 3 and 4 of the American Heart Association. The mean age of the participants in the study was 69.93 years, the mean body mass index was 27.25, and the mean number of emergency referrals was 11.33.

Most participants (78.9%) re-referred to the emergency room due to dyspnea followed by hands

and feet edema (47.8%) and 25.6% by chest pain. Cough, palpitations, and nausea are other common symptoms that have caused CHF patients to re-refer to the emergency room. Some symptoms such as loss of consciousness, imbalance, and dizziness were not reported in any samples.

Among the background comorbidities, most patients with heart failure who participated in the study had high blood pressure (54.4%). Cardiac angioplasty (34.4%) and diabetes mellitus (25%) also appeared, and other background diseases associated with heart failure include chronic kidney failure, smoking, hypothyroidism, and heart attack.

The frequency of patients with different drugs shows that most samples participating in the study (67.7%) use beta-blockers. Followed by antiplatelet drugs, diuretics, and booster medications. Insulin and levothyroxine were also evaluated as diabetes and hypothyroidism were among participants.

The minimum ejection fraction of participants of the study is 10%, and the maximum is 65%. In terms of blood sugar, the mean blood sugar in participants was 131.76. Other important biochemical experiments that influenced the study results are given in Table 1.

In addition to Table 1 shows the demographic and self-care characteristics of patients with heart failure referred to Masih Daneshvari Hospital. The minimum self-care score is 23, the maximum is 50, and the average self-care score is 37.44. Only 6.7% of the participants had an excellent self-care score. Most patients with heart failure who were re-referred to the emergency room of Masih Daneshvari Hospital (83.3%) had a moderate self-care score.

In relation to related laboratory and paraclinical factors, since the distribution of data was normal, Spearman's non-parametric test was used to correlate them with re-visits, and the results showed that only creatinine of heart failure patients has a statistically significant relationship with their re-visits. The results of the data analysis are shown in Table 2.

The result of the study showed that some of the factors raised in the questionnaire can have a direct effect on emergency re-referral in patients with heart failure, which is shown in Table 3.

DISCUSSION

The study results showed that some of the factors mentioned in the questionnaire could directly affect re-referral, which is fully shown in Table 1. In the results

Table 1. Questionnaire related to information of heart failure patients re-referred to the emergency room of Masih Daneshvari Hospital

Demographic specifications		
Age (average)	69.9	
Body mass index (average)	27.2	
Body surface area (average)	1.9	
Emergency re-referrals (average)	11.5	
Gender		
Man (frequency)	56	62.2
Woman (frequency)	34	37.8
Marital status		
Married	69	76.7
Single	5	5.6
Dead spouse	16	17.8
CHF diagnosis time		
Less than 6 months	4	4.4
4 months to 4 years	70	77.8
More than 4 years	16	17.8
NYHA classification		
1 class	2	2.2
2 class	7	7.8
3 class	40	44.4
4 class	41	45.6
Income		
Enough	25	27.8
Somewhat enough	46	51.1
Insufficient	19	21.1
Level of education		
Illiterate	18	20
Elementary	22	24.4
High school	14	15.6
Diploma	17	18.9
University	19	21.1
Pathological factors	Number	Percent
Dyspnea	71	78.9
Chest pain	23	25.6
Limb edema	43	47.8
Shortness of breath	3	3.3
Palpitations	11	12.2
Fever	2	2.2
Cough	14	15.6
Abdominal ascites	4	4.4
Nausea	11	12.2
Background comorbidities		
Acute coronary syndrome	2	2.2
Heart attack	16	17.8
Coronary artery angioplasty	31	34.4

→

Table 1 (cont.). Questionnaire related to information of heart failure patients re-referred to the emergency room of Masih Daneshvari Hospital

Open heart surgery	2	2.2
Chronic obstructive pulmonary disease	10	11.1
Blood pressure	49	54.4
Diabetes	25	27.8
Pacemaker	6	9.7
Stroke	1	1.1
Chronic renal failure	11	12.2
Dialysis	3	3.3
Pulmonary embolism	4	4.4
Pleural effusion	5	5.6
Malignancies	3	3.3
Addiction	3	3.3
Smoking	18	20
Hypothyroidism	9	10
Ischemic heart disease	7	7.8
Medicinal agents		
Beta-blockers consumption	60	66.7
Taking angiotensin receptor blockers	37	41.1
Using angiotensin II receptor antagonists	38	42.2
Diuretics consumption	61	67.8
Digital consumption	30	33.3
Statins consumption	37	41.1
Nitrates consumption	19	21.1
Insulin consumption	15	16.7
Alpha-blockers consumption	6	6.7
Calcium channel blockers consumption	11	12.2
Taking consumption	9	10
Antiplatelet drugs consumption	64	71.1
Laboratory factors	Average	Standard deviation
Urea	76.03	64.1
Creatinine	1.98	1
CPK	81.13	70
CKmb	19.81	8.6
Na	135.51	3.38
K	4.19	0.61
Ca	9.33	0.97
LDH	285.12	193.4
Alk.p	303.54	265.7
AST	33.2	38.6
ALT	48.7	110
WBC	8.84	3
RBC	4.52	0.70
Hb	12.60	2.1
Plt	209.24	99.3

Table 1 (cont.). Questionnaire related to information of heart failure patients re-referred to the emergency room of Masih Daneshvari Hospital

INR	1.45	0.44
PT	15.41	2.9
PTT	35.78	9.5
BS	131.76	59.6
HCO ₃	55.56	3.3
PaCO ₂	44.44	5.9
PH	7.39	0.06
Para clinical agents		
Ventricular ejection fraction	38.67	11.6
Pulmonary vein pressure	46.34	10.7
Self-care agent		
Self-care		
Good	6	6.7
Medium	75	83.3
Weak	9	10

INR — the international normalized ratio; PT — prothrombin time; PTT — partial thromboplastin time; BS — blood sugar; HCO₃ — bicarbonate/hydrogencarbonate; PaCO₂ — partial pressure of carbon dioxide; PH — potential of hydrogen; CPK — creatine phosphokinase; CK-mb — creatine kinase-MB; Na — Na sodium; K — potassium; Ca — calcium; LDH — lactate dehydrogenase; Alk.p — alkaline phosphatase; AST — aspartate aminotransferase; ALT — alanine transaminase; WBC — white blood cells; RBC — red blood cells; Hb — hemoglobin; Plt — platelets; PAP — pulmonary artery pressure

of this study, most patients with heart failure (77.8%) were re-referred to the emergency department more than six times. Comparing, Heydari et al. [35] found that 57% of heart patients were hospitalized again. Bhatia et al. [39] study, the re-referral rate of heart failure patients during the six months after discharge was 61.8%. Dharmarajan's et al. [40] study reported that the re-referral rate in patients with heart failure was 24.8%. In the Hamner et al. [41] study, performed retrospectively, 40% of heart failure patients were re-admitted six months after the first hospitalization.

In contrast, the percentage of patients with heart failure in European countries was lower than in the research conducted in Iran. Perhaps more advanced medical centers and more attention to home care systems in Western countries can be attributed to this difference. In the case of demographic factors, the study results showed three age variables, body mass index, and duration of disease diagnosis as factors related to re-referral. No study has been found on the duration of the disease and its relationship to re-referral, but it can be argued that the longer the duration of heart

Table 2. Results of quantitative variables correlation in the study with re-referrals based on the Spearman test

Variables	Re-referral	
	The correlation coefficient	Significance level
Body area level	−0.017	0.87
Ejection fraction rate (EF)	−0.022	0.83
PAP	−0.175	0.09
Urea	0.009	0.93
Creatinine	0.042	0.00
CPK	−0.116	0.27
Sodium	−0.121	0.25
Potassium	0.024	0.82
Calcium	0.008	0.94
LDH	−0.095	0.37
Alkaline phosphatase	−0.085	0.42
AST	0.031	0.77
ALT	−0.147	0.16
White blood cells	0.017	0.87
Red blood cells	0.016	0.88
Hemoglobin	0.059	0.58
Platelet	−0.059	0.58
PT	0.022	0.83
PTT	0.085	0.42
INR	−0.106	0.32

INR — the international normalized ratio; PT — prothrombin Time; PTT — partial thromboplastin time; BS — blood sugar; HCO₃ — bicarbonate/hydrogencarbonate; PaCO₂ — partial pressure of carbon dioxide; PH — potential of hydrogen; CPK — creatine phosphokinase; CK-mb — creatine kinase-MB; Na — Na sodium; K — potassium; Ca — calcium; LDH — lactate dehydrogenase; Alk.p — alkaline phosphatase; AST — aspartate aminotransferase; ALT — alanine transaminase; WBC — white blood cells; RBC — red blood cells; Hb — hemoglobin; Plt — platelets; PAP — pulmonary artery pressure

failure, the patient has more time to refer. Different studies have shown different results regarding age. In some studies, age has been suggested as a strong predictor [42–44]. However, in other studies, such as the study by Roohani et al. [45], there is no significant statistical relationship between re-referral and re-hospitalization with age. Explaining whether age can be statistically related to the number of re-referrals, it can be examined that with increasing age, heart rate decreases.

On the other hand, the elderly are more prone to disease progression. Therefore, age can affect re-referrals. Regarding the body mass index and its relationship to re-hospitalization, the results of Hekmatpour et al. and the Ravi Shah study also showed that body mass index effectively re-hospitalization of patients with heart failure [46, 47], and is consistent with the results of the present study. In the Arora study, the results showed that obesity is one of the factors influencing re-

-hospitalization [48]. Obesity in patients with heart failure can add extra pressure to the heat load and, therefore, be more effective in their re-referrals to medical centers. Another variable examined concerning re-referral was the American Heart Association's classification of heart failure. The study results showed that the NYHA classification level was consistent with the re-referral of heart failure patients [49].

The results showed a statistically significant relationship with re-referral, consistent with some studies, including the Farasat. The results showed that most participants were referred to the emergency room due to dyspnea, followed by Hands and feet edema. In contrast, in the Retrum study, limb edema and shortness of breath were reported as the most common causes of re-referrals in patients with heart failure [50]. Gheorghide's study also showed that orthopnea (dyspnea while lying down) is one of the main factors in the re-referrals of patients with heart

Table 3. Factors associated with emergency re-referral in patients with heart failure

Demographic factors
Age
Body mass index
Diagnosis time
Pathological factors
Dyspnea
Limb edema
Shortness of breath
Factors related to background diseases
Blood pressure
Diabetes
Chronic obstructive pulmonary disease
Ischemic heart disease
Laboratory and para clinical agents
High creatinine
Medicinal agents
Not using beta-blockers
Not taking angiotensin receptor blockers
Self-care level
Poor self-care level
NYHA classification
Classes 2 and 3 based on the NYHA classification

failure [51] and is consistent with the results of the current study. Also, in a study by Heydari et al. [35], some patients were re-hospitalized for more than one underlying cause. Others were re-referred due to the exacerbation of the disease (with symptoms such as chest pain, dyspnea, palpitations, edema, weakness, and lethargy). So, patients with heart failure experience many symptoms due to the inefficiency of the heart system; and dyspnea and limb edema are the most common symptoms. Examining the causes of early recurrence in patients with heart failure, Muzzarelli et al. [52] showed that angina, limb edema, and dry cough were associated with re-referrals of these patients.

Furthermore, Moser [53] showed that 94.4% of heart failure patients had shortness of breath during the month after discharge, 81.7% reported some degree of limb edema, and 88.7% reported fatigue during the day. According to this study and other similar studies, pathological symptoms associated with heart failure are considered one of the leading causes of these patients' re-referrals, including dyspnea, limb

edema, and fatigue. Therefore, more attention to the control of these symptoms can moderate the re-referral and re-admission of these patients.

When the heart cannot function correctly, it affects other systems in the body, including the lungs, nerves, kidneys, and other organs. On the other hand, defects in any body system can affect the severity of symptoms associated with heart failure, so paying attention to background diseases and heart failure is fundamental in re-referrals and plays an essential role in treatment plans. The current study results showed that chronic obstructive pulmonary disease, hypertension, diabetes mellitus, and ischemic heart disease are the four most common background diseases affecting the re-referral of patients with heart failure. In a study, Lim et al. [42] showed that chronic obstructive pulmonary disease and hypertension could affect the re-referral of patients with heart failure. However, ischemic heart disease and diabetes mellitus did not predict re-referral, which contradicts the results of this study. In Aranda's et al. [54] study, background diseases, high blood pressure, and diabetes mellitus had a statistically significant relationship with the re-referral of heart failure patients six to nine months after discharge. However, it should be noted that chronic obstructive pulmonary disease has not been considered in this study. In Pierre-Louis's [55] article, diabetes mellitus and chronic obstructive pulmonary disease have been cited as the leading causes of heart failure patients' re-referral to the hospital. However, high blood pressure did not have a statistically significant relationship with re-referrals. In Western countries, healthcare systems are more focused on prevention and treatment at home. Maybe high blood pressure has no significant relationship in this study because the factor influencing the re-referral of patients with heart failure was poor health care in Iran. No attention is paid to home care and prevention principles in this treatment category. Based on the results of this study and other studies, it can be concluded that the background diseases associated with chronic obstructive pulmonary disease, hypertension, and diabetes mellitus are the major causes of patients with heart failure re-referrals to medical centers. Therefore, these centers and relevant specialists should consider the control of these diseases.

The goal of drug therapy in patients with heart failure is to prevent exacerbation of the disease, improve the heart's contractile strength, and reduce the pressure on the heart. Medications such

as beta-blockers, angiotensin receptor blockers, and digoxin are among the drug groups used. Suppose medication is prescribed based on the level of heart failure. In that case, better treatment will undoubtedly be given, and the subsequent side effects will be diminished, and a decrease follows this in re-referrals. The association of medications with re-referral was assessed. The current study results showed that most samples received beta-blockers, angiotensin receptor inhibitors, and diuretics.

On the other hand, the T-test results showed a statistically significant relationship between the re-referral of patients with prescription or non-prescription beta-blockers and angiotensin receptor inhibitors. In this way, patients with heart failure who did not receive these drugs had a higher average refer to the emergency room. Similar studies were reviewed: in Moser's study [53], the considered samples (79%) used beta-blockers, and 77% of them received ACEI, which confirms the present results. Lim et al. [42] showed that the administration of beta-blockers and angiotensin receptor inhibitors after discharge was significantly statistically associated with re-referrals in patients with heart failure and is consistent with the current results. Pierre Louis et al. [55] concluded that prescribing beta-blockers and ACEIs did not have a statistically significant association with re-hospitalization, which was inconsistent with the current study results. The results of the Sanam et al. [56] study showed that prescribing ACEI after discharge reduced the re-referral of patients with heart failure. Setoguchi et al. [57] also found that not prescribing beta-blockers after discharge increased the re-referral rate in patients with heart failure.

Disruption of laboratory findings, in turn, can cause signs and symptoms that can lead to re-referral in patients with heart failure. Water and electrolyte disturbances, heart enzyme disturbances, and disturbances in arterial blood gases can affect the severity of heart failure symptoms. Therefore, the attention and elimination of these causes and their treatment can affect the subsequent patients' re-referrals. Pearson's correlation in Table 2 showed that the only laboratory parameter associated with the re-referral of patients with heart failure was creatinine. Decreased cardiac function, which leads to heart failure, will affect kidney function.

On the other hand, heart failure is one of the main symptoms of limb edema, and now if the kidneys are underactive, these symptoms will intensify.

The explanation was physiological, but it is necessary to examine the studies to prove or disprove this claim with more substantial reasons. In the study of Gheorghiade et al. [51], which looked at the factors associated with re-hospitalization in patients with heart failure, the results showed high creatinine, high urea, sodium, and B-type natriuretic peptide (BNP) were statistically significant in association with re-referrals [50]. In the present study, only high creatinine had a statistically significant relationship. In the study of Muzzarelli [52], the results showed that re-referral in patients with heart failure had a statistically significant relationship with high creatinine past thirty to ninety days after discharge.

Sodium disorders did not have a statistically significant relationship with re-hospitalization, which confirms the current study results [51]. Instead of using creatinine, Pierre Louis et al. [55] used glomerular filtration to relate kidney function to re-hospitalization. The study results showed that the lower the kidney function, the higher the re-referral rate of patients with heart failure, which is consistent with the results of the current study [54]. Regarding the para-clinical findings based on extracted echocardiography from the patient, ventricular ejection fraction and pulmonary artery pressure did not significantly correlate to re-referral. Muzzarelli's study showed that the mutation ejection fraction was not consistent with the re-referral of patients with heart failure and was consistent with the current study [52]. However, the study results by Gheorghiade et al. [51] showed that EF had a statistically significant relationship to the re-referral of heart failure patients, so that the lower the rate of ventricular mutation ejection fraction, the lower the rate of ventricular mutation ejection fraction, the higher the mean hospitalization and re-referral [50].

The study results showed that the average self-care score of patients with heart failure was 37.44. Most patients with heart failure who were referred to the emergency room of Masih Dane-shvari Hospital (83.3%) had moderate self-care scores. ANOVA test revealed that the self-care status of patients with heart failure was statistically significant when they were re-referred to the emergency room, which means that patients who had better self-care had lower referrals to the emergency room and vice versa. In the study of Khoshtarash M et al. [38], the results showed a significant statistical relationship between the self-care of patients with heart failure and hospitalization and re-referrals, which is

consistent with the results of the current study [33]. Retrum's study showed that good self-care alone could not moderate re-referral, but both good and practical self-care can moderate the number of re-referrals [50]. In his study, Ditewig et al. [58] showed that good self-care could reduce the number of re-referrals and even deaths of patients with heart failure. However, it should be noted that in Western countries, more attention is paid to increasing self-care because most Western studies have reported higher rates of patient self-care. However, the results of this study and the studies that were examined confirm the principle that more self-care in patients with heart failure can moderate re-referrals.

Limitations

The psychological state of the research units when answering the questions can affect the way they answer and therefore it is considered a limitation of the research. In this research, all the cultural-social aspects of the patients cannot be examined, and considering the possible impact of the cultural and social status of cardiac patients on the occurrence of re-hospitalization, this issue can be considered a limitation of the research. Considering the hemodynamic status and clinical conditions of the patients and the many questions in the questionnaire, the assessment of the patient's mental status, including depression and anxiety, and its effect on re-visits could not be measured, so it should be investigated in separate studies. The reason for conducting the study in a hospital may reduce the generalizability of the study results.

CONCLUSIONS

The emergency room has always been known as the heart of hospitals and a symbol of the whole hospital. The hustle and bustle of the emergency department can overshadow the quality of nursing care, and planners should always keep in mind that they need to reduce the number of emergency referrals in the future. Patients with heart failure experience a complex and chronic condition, and a variety of factors can exacerbate the disease and its symptoms, leading to re-referrals. A general understanding of the factors and risk factors affecting the re-referral of patients with heart failure can identify patients at high risk of re-referral. Nurses, who have consistently been recognized as the critical elements of health care systems, can reduce the number of emergency

re-referrals by modifying these symptoms. This study provides a comprehensive review of the factors associated with the re-referrals of patients with heart failure in hospital emergencies, and planners are expected to use the results of this study in future planning of treatment systems, especially emergencies.

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Conflict of interest

All authors declare no conflict of interest.









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PARAMEDIC STUDENTS NEED MORE TRAINING IN LEFT VENTRICULAR ASSIST DEVICE — A PILOT SIMULATION STUDY

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ABSTRACT

INTRODUCTION: Mechanical Circulation Systems are a promising therapy for patients with end-stage of heart failure. Left ventricular assist device (LVAD) enforces using of concomitant anticoagulant therapy. This may lead to severe complications. LVAD patients are more and more frequent users of the emergency department. There are several differences in cardiovascular function in these patients, as well as on examination. Its interpretation may be challenging and result in potentially fatal conclusions. The aim of this research was to assess the skills of paramedic students in assessing patients with LVAD.

MATERIAL AND METHODS: The study was designed as a simulation study. The aim of this scenario was to provide a full primary survey of an unconscious, spontaneously breathing person with an LVAD pump implanted. Ten groups of paramedic students from Polish medical universities took part in this study.

RESULTS: Four teams started chest compressions unnecessarily. Of them, only one had contacted LVAD local coordinator and discontinued after short instructions. Four teams completed the driveline and device check and six checked only the line without moving the controller. No major errors were noted in the field of airway assessment and management as well as assessment of consciousness, breathing, and circulation.

CONCLUSIONS: More attention should be paid to educating paramedic students in LVAD therapy. Educators should focus mainly on differences in cardiovascular function and pay attention to complete perfusion assessment. Medical simulation seems to be a good tool for assessing difficult clinical cases rarely encountered in practice.

KEY WORDS: mechanical circulation systems; resuscitation; physical examination; simulation study; paramedics

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INTRODUCTION

Due to the aging population, more and more patients suffer from heart failure (HF) [1]. Recent meta-analyses have shown, that almost half of the patients

with HF will die within 5 years [2]. Mechanical circulatory systems bring back hope that the quality of life can be restored for patients in the end-stage of this disease. Left ventricular assist device (LVAD) is

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increasingly being used in patients as a bridge to heart transplantation or as a destination therapy [3]. Left ventricular assist device recipients create a specific group of patients. This therapy forces the use of anticoagulation agents continuously. This in turn increases the risk of bleeding. Gastrointestinal hemorrhages and intracranial hemorrhages are the most common complications of LVAD therapy [4]. Shore et al estimated that 16% of patients required hospitalization within the first month and even 98% in the first 2 years after implantation [5]. There is a number of differences in the examination of a patient with implanted LVAD pump [6]. These differences relate primarily to the interpretation of the cardiovascular system examination. Blood flow generated by an LVAD centrifugal pump is different from the physiological. LVAD patients may be pulseless despite adequate perfusion. Conventional methods of assessing blood pressure, pulse, and saturation levels may be misleading. Therefore, their use may contribute to misdiagnosis and poor treatment. European Resuscitation Council recommends beginning chest compressions in every unconscious person without normal respiration [7]. Chest compression related injuries are usually harmless, but also potentially life-threatening may occur [8]. The lack of a correctly conducted primary survey, as well as the incorrect conclusions drawn afterward, can lead to misdiagnosis in many fields. Therefore we believe that emergency healthcare providers must have the appropriate knowledge to provide safe and efficient care. However, the subject of LVAD therapy is not discussed in the Polish paramedics training program.

This study aimed to assess if paramedic students can correctly conclude the results of the initial examination of LVAD patients.

MATERIAL AND METHODS

Legal aspects

According to Polish law, this study did not meet the criteria of a medical experiment and therefore consent from the Bioethical Committee was not required.

Study design

The authors designed a simulation scenario. The goal of the scenario was to correctly examine an unconscious, spontaneously breathing patient with a properly working LVAD device. The scenario was

run by 10 teams comprised of paramedic students from 3 different Universities in Poland. The core curriculum for paramedic training in Poland does not provide LVAD skills. The simulation was carried out during outdoor paramedic students, multi-university joint exercise as one of the competitions. The simulation was performed on the Baltic Sea shore. The composition of each team was random and students from different facilities were mixed. The weather conditions for each team was the same. The length of the scenario was 10 minutes. The scenario time was counted from the moment the team entered the room. There was only one evaluator and one simulation technician present during the scenario.

Simulator and devices

MegaCode Kelly (Laerdal Medical AS, Stavanger, Norway) advanced patient simulator was used in the study. The simulator was allowed to provide a complete ABCDE examination including an assessment of breathing, pulse, and electrocardiogram (ECG). All advanced airway management techniques as well as ventilation using bag-valve-mask were possible. Lifepak 12 defibrillator (Physio-Control, Redmond, Washington, USA) was used to monitor the patient's heart. Vital signs of the manikin were set as follows: ventilation rate 24/min; SpO₂: 98%; heart rate: 90/min; ECG: normal sinus rhythm; blood pressure: 0/0mmHg (undetectable), pupils: anisocoria (left pupil dilated). The simulator was prepared by the authors to play the role of an LVAD patient. The HeartMate III centrifugal pump (Thoratec Corporation, Pleasanton, California, USA) was prepared and placed in a sealed glass jar containing water. The power line was then led through the skin between the chest and abdomen and connected to the controller. The controller as well as battery supply were placed in a dedicated bag and secured with a belt. The unit was set at 5400 rpm. A flow rate of 2.8 l/min was provided. Sounds of the pump humming could be heard during auscultation. The telephone number of an LVAD local coordinator was clearly presented on the device. Dialing this number connected directly to another instructor playing the role of coordinator.

Scoring form

We prepared our own scoring form for the evaluation of this scenario. Performance of the following interventions was evaluated: consciousness level,

airway assessment, breathing assessment (including rate, depth, auscultation, SpO₂), circulation assessment [including heart rate (HR) and noninvasive blood pressure (NIBP), perfusion assessment (including skin and capillary refill time), disabilities assessment, full body exposure, contacting the LVAD coordinator]. There were two critical errors defined: 1) initiation of chest compressions and maintaining this decision for at least 30 seconds, 2) Cutting the driveline. Each team was evaluated by the same instructor.

RESULTS

All teams performed and completed the scenario on time. Six teams did not start chest compressions. All of them had contacted the LVAD coordinator. Four teams started chest compressions. Of them, only one had contacted the LVAD coordinator and discontinued after instructions. For the students who

took part in the study, no major errors were noted in the field of airway, breathing, and circulation. All teams achieved full or nearly full results in these categories. The only exception was the perfusion assessment, Only one team performed a full evaluation. Four teams completed the driveline and LVAD device check and six checked only the line without moving the controller. The scoring form as well as the exact scores for each team were presented in Table 1.

DISCUSSION

The aim of this study was to perform an analysis of paramedic students' skills in the examination of a patient with LVAD. This therapy is becoming more widely used today. According to recent European Society of Cardiology recommendations, LVAD should be considered as bridging or destination therapy for patients with advanced heart failure.

Table 1. Scoring checklist and results of the study

Evaluated procedures	Team number									
	1	2	3	4	5	6	7	8	9	10
Examination and interventions										
Assessment of consciousness (0 for none, 1 if completed)	1	1	0	0	1	1	1	1	1	1
Assessment of airway (0 for none, 1 if completed)	1	1	1	1	1	0	1	1	1	1
Assessment of breathing (rate, depth, auscultation, SpO ₂) (0 for none, 1 for one or two items, 2 if completed)	2	1	2	1	2	2	1	1	2	2
Assessment of circulation (HR, BP) (0 for none, 1 for one item, 2 if completed)	2	0	1	0	2	2	1	1	2	2
Assessment of perfusion (CRT, skin) (0 for none, 2 for one item, 5 if completed)	5	0	0	0	0	1	0	0	2	0
Assessment of disabilities (glucose level, pupils, AVPU) (0 for none, 1 for one item, 2 for two items, 3 if completed)	3	1	2	1	3	3	1	1	1	2
Exposure (driveline, alarms) (0 for none, 1 for one item, 3 if completed)	1	1	3	3	1	3	1	3	1	1
Contact with LVAD coordinator (0 for none, 2 if completed)	2	0	2	2	0	2	0	2	2	0
Interview with bystander (0 for none, 1 for one, two or three questions from SAMPLE, 2 for full SAMPLE interview)	2	1	2	2	1	2	2	1	2	2
Airway management (0 for none, 1 for basic interventions, 2 for advanced interventions)	1	2	1	1	1	1	2	1	1	2
Critical errors										
Compression started and continued for at least 30 sec.	Y	Y	N	N	N	N	Y	N	N	Y
Driveline cut	N	N	N	N	N	N	N	N	N	N

AVPU — level of consciousness scale; CRT — capillary refill time; HR — heart rate; LVAD — left ventricle assist device; N — no; NIBP — blood pressure; SAMPLE — medical interview; SpO₂ — oxygen saturation; Y — yes

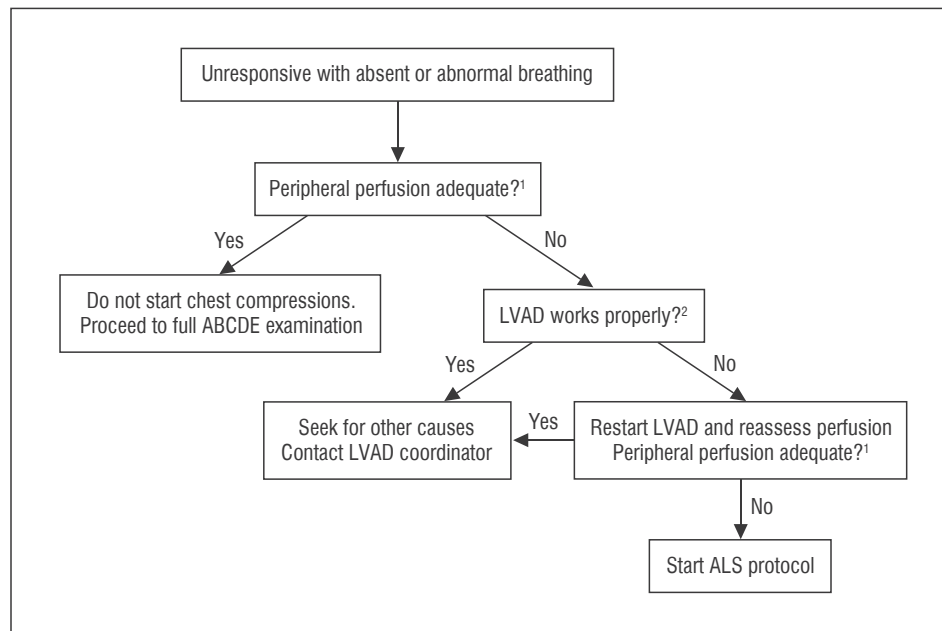


FIGURE 1. Management of unresponsive left ventricle assist device (LVAD) patient with absent or abnormal breathing; ALS — Advanced Life Support; ¹assess skin colour, moisture, temperature, capillary refill time; ²check pump humming, power source, line, alarms

Kirkling et al. [9] estimated the overall; the survival rate of LVAD patients as high as 80% in the first year after implantation. These results are encouraging, especially at a time when the demand for transplantation is greater than the availability of transplants.

Stroke is a major cause of death in patients with LVADs. According to the literature, about 10% suffered at least one hemorrhagic stroke and one-third of cases are fatal [10–11]. It is therefore essential, that providers focus on ruling out stroke in any patient with neurological manifestations, and with altered mental status as well as unconscious.

The main role of any emergency clinician is to provide the best possible care to every patient. The recognition of a life-threatening condition is usually a result of a thorough physical examination and medical history. Assessing vital functions in a patient with an LVAD can be confusing, especially for an inexperienced provider. There are some major differences when examining the cardiovascular system. This is a result of the implanted pump providing continuous blood flow. Hence, the absence of a normal pulse, the difficulty in blood pressure measurement, and unreliable saturation readings should be taken into account when assessing cardiovascular function.

The results of this study revealed that students demonstrated good patient examination skills. Nonetheless, their decisions were incorrect. Most groups did not perform a perfusion assess-

ment. In the absence of a palpable pulse, resuscitation was undertaken — according to standard protocol. During the scenario, the authors carefully observed the students. There was widespread discussion about the doubts regarding the need to perform chest compressions. Some groups interrupted cardiac compressions even a few times. In our opinion, this may be due to insufficient knowledge or lack of experience. Although no high-quality clinical trials assessing the efficacy and safety of chest compressions in LVAD patients were published, retrospective studies have shown that performing this procedure is safe and no significant pump or internal organs are observed [12–14].

In the literature, a number of protocols for examining a patient with LVAD can be found [6]. When analyzing these papers, one can see that the indications for resuscitation are the absence of normal breathing and the absence of pump humming. This modification of the standard algorithm, in our opinion, requires appropriate training. It is important to emphasize the role of assessing perfusion in a comprehensive manner and not just by evaluating the presence or absence of a pulse. As differences regarding the initiation of chest compressions may raise concerns, especially for less experienced professionals, in Figure 1 we have proposed an algorithm that clearly presents the procedure. In this study, only four of ten teams assessed both the driveline and the device itself. In one of our previous pa-

pers, we proposed a protocol to modify the entire ABCDE survey with an emphasis also on assessing critical technical aspects [15]. Although, as written in the introduction, the number of patients will increase, at the moment exposition of paramedics to LVAD patients is still low. Support of the dispatcher and medical control may be crucial for ambulance teams. Clear information on the device and contact with the coordinator as well as emergency reference cards are recommended [16].

In the study by Municino and colleagues, only 4% of paramedics presented knowledge concerning the influence of LVAD on the circulatory system and its impact on findings in the examination. In another study it was found that more than 40% of respondents have never heard about LVAD and more than 80% have never had any training. Interestingly, this research was done in the USA, where the number of LVADs was relatively high with 2,500 implants per year [17]. Therefore, it is to be expected that in countries where fewer devices are used, the level of knowledge may be even lower.

High-fidelity medical simulation is not the only effective method of education. It is also used for verifying new strategies of treatment, and multi-level procedures before implementation in real life [18, 19]. Therefore, in our opinion, training through medical simulation also in this field is needed. Students who took part in our study were previously unfamiliar with LVAD devices, but knew simulation as an education technique. By using simulation, we were able to identify gaps in knowledge and investigate how these affect the management compliant with standard protocols. This suggestion stands in agreement with other authors who have studied the feasibility of medical simulation in improving adherence to critical processes of care and reducing errors in management [20]. Regardless of the poor results of most teams, we received very positive feedback on this scenario. Participants expressed their appreciation for this scenario, as it allowed them to get acquainted with a previously unknown device and algorithm.

CONCLUSIONS

More attention should be paid to LVAD patients in the undergraduate training of paramedics. Medical simulation may be a useful educational tool in the implementation of previously unknown subjects and procedures into paramedics practice.

Conflict of interests

The authors declare no conflicts of interest.

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ACCIDENTAL HYPOTHERMIA AND RELATED FACTORS AMONG BURNED PATIENTS

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ABSTRACT

INTRODUCTION: Early diagnosis, control and management of hypothermia are decisive in the outcome of burns. Various factors play a role in creating or aggravating accidental hypothermia in these patients. This study was conducted with the aim of determining accidental hypothermia prevalence and related factors among burned patients referred to Shahid Motahhari Hospital in Tehran, Iran in 2021.

MATERIAL AND METHODS: In this prospective observational study, 151 burn patients who were transferred to the emergency department by EMS were selected through available sampling from February 2021 to August 2021. Data was collected and recorded in three areas (pre-hospital, emergency ward, and burn center) through observation and interview of patients and their relations and review of records from admission to discharge. The ambient temperature and core body temperature (CBT) of the patients was measured by a calibrated tympanic thermometer at the time of arrival. Individual, clinical, environmental, and care variables were investigated as factors related to hypothermia. The research data were analyzed using descriptive and inferential statistics such as Pearson correlation, chi-square, and multiple linear regression by SPSS software version 22. A significance level of less than 0.05 was considered.

RESULTS: Forty-seven percent of patients had a CBT of less than 36 degrees Celsius at arrival. Through multiple linear regression, 15 independent variables were entered with the backward model. Only the kind of airway management ($\beta = -0.296$, $p < 0.001$), and volume of fluids received ($\beta = 0.144$, $p = 0.082$) were as predicting factors for accidental hypothermia in burn patients.

CONCLUSIONS: About half of the patients were hypothermic at the time of admission. Optimizing care in pre-hospital and burn departments and empowering the healthcare team in the assessment of burn patients, and early detection, prevention, and proper management of accidental hypothermia are highly expected.

KEY WORDS: accidental hypothermia; burn; pre-hospital care; core body temperature (CBT); risk factors; Iran

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INTRODUCTION

With an incidence of 9 million and a prevalence of 90 million cases in 2017, burns are considered one of the most frequent incidents worldwide [1]. Due to the high prevalence of burns and their unpleasant consequences, costs, and association with high mortality, care measures should be

based on preventing burns and their resultant complications [2, 3].

One of the common complications of burns is hypothermia caused due to extensive skin damage. Various studies have reported the prevalence of hypothermia between 34 and 79.2% [3–7]. These patients become hypothermic during transfer to the

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burn center or during wound care [2]. Hypothermia is expected to be associated with increased mortality and unpleasant consequences, but the evidence is limited in this regard [3].

Hypothermia is classified into two types: therapeutic and accidental [8]. Accidental hypothermia generally refers to the reduction of CBT to less than 35 [9]. In patients with burns and skin tissue damage, a temperature of less than 36°C in some studies [10–13] and less than 36.5°C in others has been defined as hypothermia [5, 14]. Hypothermia or CBT below 36°C can lead to dangerous complications for burn patients [15]. Hypothermia is physiologically known as hemodynamic instability, suppression of the immune system, mild metabolism of drugs [4], and homeostasis disorder, and it forms a deadly triad in trauma and burns patients with blood coagulation disorder and acidosis [4, 6, 7, 16–19].

Some studies have suggested various factors such as cooling the burn wound at the scene, injecting a lot of fluids, and the long distance to the burn ward as factors involved in hypothermia [20]. Some other studies have introduced variables such as age, gender, percentage of burn surface, type, mechanism and degree of burn, injury location, injury season, trauma severity, the way of temperature measurement, rapid pre-hospital treatment, fluid injection, endotracheal intubation, level of consciousness, instability of the physiological state, and the duration and the way of transfer to the burn ward as the risk factors for hypothermia [5, 16, 21–23].

Although hypothermia is a serious threat to pre-hospital patients, especially injured patients [24, 25], the evidence in this regard is limited [3]. Weak evidence and information regarding pre-hospital measures and guidelines [26], insufficient knowledge of the healthcare team about hypothermia, and neglect to implement hypothermia management guidelines [20, 27, 28] emphasize the need for more studies in this field. This study was conducted to investigate accidental hypothermia and its related factors among burn patients referred to Shahid Motahari Hospital in Tehran.

MATERIAL AND METHODS

This prospective observational study was conducted on eligible burn patients referred to Shahid Motahari Hospital in Tehran. Before being conducted, this

study obtained permission from the Research Ethics Committee of Zanjan University of Medical Sciences (IR.ZUMS.REC.1399.183).

Data were collected from patients referring to Shahid Motahari Hospital in Tehran. This hospital, with a capacity of 112 active beds, includes outpatient and inpatient emergency, ICU, operating room, internal, infectious, surgical, pediatric, sub-specialized reconstructive surgery, orthopedics, physiotherapy, and occupational therapy wards and admits burn patients referred from all over Tehran province and other parts of Iran.

One hundred and fifty-one patients with burns above 20% of body surface area (BSA) who were transported by EMS staff to the hospital's emergency ward were included in the study through convenience sampling from February to August 2021. Patients sent from other medical centers and patients transported by private vehicles were excluded from the study.

CBT upon admission, ambient temperature upon admission, level of consciousness in the pre-hospital stage, type of burn, degree of burn, age, gender, transfer time, cooling at the scene, underlying disease, percentage of arterial oxygen, the volume of fluids received, response time, drug intake, BSA, and airway type were checked and recorded.

The CBT variable using a tympanic thermometer (model Gp-300 iso9001, identification code of Manufacturer: Harbin XianDe, with a measurement accuracy of 0.1 and measurement error of 0.2°C) and the ambient temperature varies with a thermometer (ATA.152. DI. 39 with an accuracy of 1°C) were measured and recorded at the time of entering the burn emergency ward. The data was collected through the researcher's datasheet using observation and interviews with patients and their companions and patient files. BSAs were calculated using Lund Broder's chart (the gold standard for BSA calculations), which was calculated by the burn emergency department nurse and documented in the patient's medical record. The study included patients with a BSA of 20% or higher. In this study, the cut point for accidental hypothermia was determined to be 36°C.

Data analysis was performed using descriptive statistics and Pearson's correlation coefficient test, analysis of variance (ANOVA), and multiple linear regression analysis and analyzed with SPSS version 22 software. A significance level was considered less than 5%.

RESULTS

The study findings are the result of analyzing the data of 151 burn patients meeting the inclusion criteria. The majority of patients were male (67.5%). The mean and standard deviation of the individuals' age was 36.44 (13.58) years. The lowest BSA was 20%, the highest was 100%, and the mean and standard deviation of the BSA was 47.04 (20.96) (Tab. 1, 2).

The thermometer present in the pre-hospital area was of mercury type and did not have the ability to measure the CBT. About half of the patients (47%) were hypothermic upon admission (Tab. 3).

CBT of burn patients upon admission showed no significant association with the quantitative variables of age ($r = -0.063$, $p = 0.443$), BSA ($r = -0.086$, $p = 0.294$), arterial oxygen percentage ($r = 0.052$, $p = 0.529$), the volume of fluids received ($r = 0.055$, $p = 0.503$), the response time ($r = -0.015$, $p = 0.853$), the transfer time ($r = 0.026$, $p = 0.753$), hospitalization days ($r = 0.057$, $p = 0.485$), and ICU hospitalization days ($r = -0.012$, $p = 0.882$) (Tab. 4).

CBT upon admission showed no significant association with qualitative variables such as cooling at the scene ($p = 0.79$), degree of burn ($p = 0.75$),

Table 1. Patients' characteristics

Individual and burn-related variables		Number	Percentage
Gender	Male	102	67.5
	Female	49	32.5
Underlying disease	Yes	113	74.8
	No	38	25.2
Place of burn	Home	81	52.6
	Out of home	64	42.4
	Out of the city	6	4
Type of burn	Thermal	116	76.8
	Inhaler	23	15.2
	Electrical	5	3.3
	Chemical	7	4.6
Burn degree	Grade 2	54	35.8
	Grade 3	22	14.6
	Grade 2 and 3	75	49.7
Burn site	Head, face and neck	9	6
	Organs	18	11.9
	Combined	124	82.1
Cooling at the scene	Yes	54	35.8
	No	97	64.2
Level of consciousness (GCS)	Conscious	136	90.1
	Lack of consciousness	15	9.9
Intubation	Yes	12	7.9
	No	139	92.1
CPR at the scene	Yes	1	0.7
	No	150	99.3
Taking warm IV fluids	Yes	68	45
	No	83	55
Taking medication	Yes	17	11.3
	No	134	88.7

CPR — cardiopulmonary resuscitation; GCS — Glasgow Coma Scale;

Table 2. Frequency distribution of some quantitative variables of patients

Variable	Mean	Standard deviation	Minimum	Maximum	Number
Age	36.44	13.58	12	75	151
Burn percentage (BSA)	47.04	20.96	20	100	151
Response time	20.23	6.168	6	40	151
Transfer time	20.66	6.43	7	38	151
Ambient temperature upon admission	23.58	1.1	21	27	151
CBT upon admission	36.61	0.62	35	39.3	151

BSA — body surface area; CBT — core body temperature

Table 3. Frequency distribution of patients with normal temperature and hypothermia

CBT	Number	Percentage
Hypothermia (equal to and less than 36°C)	71	47
Normothermia (more than 36°C)	80	53

CBT — core body temperature

Table 4. Correlation of quantitative variables with CBT of burn patients upon admission

Variable	CBT		
	Pearson correlation coefficient	p-value	Number
Age	−0.063	0.443	151
Burn percentage (BSA)	−0.086	0.294	151
Blood oxygen saturation	0.052	0.529	151
Volume of IV fluids received	0.055	0.503	151
Response time	−0.015	0.853	151
Transfer time	0.026	0.753	151

BSA — body surface area; CBT — core body temperature

type of burn ($p = 0.23$), and gender ($p = 0.45$). CBT upon admission showed a significant association with the level of consciousness ($p = 0.009$), and intubation ($p = 0.002$) (Tab. 5).

Fifteen independent factors (ambient temperature of the emergency ward upon admission, level of consciousness in the pre-hospital stage, type of burn, degree of burn, age, gender, transfer time, cooling at the scene, underlying disease, percentage of arterial oxygen, volume of fluids received, time response, drug intake, BSA, and airway type) were entered into the regression model with the CBT of the patient upon admission as a dependent variable. In the multiple linear regression analysis, among the 15 independent or predictive variables included in the backward model at the 14th stage, only the two variables of airway type ($\beta = -0.296$, $p < 0.001$) and the volume of fluids received ($\beta = 0.144$,

$p = 0.08$) were identified as effective in triggering hypothermia and played a role as independent predictors of hypothermia upon admission of burn patients (Tab. 6).

DISCUSSION

The findings of this study showed that accidental hypothermia in burn patients was highly prevalent (47%). Multiple linear regression analysis identified two factors of airway type (intubation) and volume of fluids received in the pre-hospital stage as effective factors in accidental hypothermia upon admission of burn patients.

One of the serious reasons for the drop in the CBT of burn patients in the present study seems to be the lack of serious attention to the evaluation of the CBT of burn patients and the inability to de-

Table 5. The difference in the mean CBT on admission according to the variables of cooling the burn site, burn degree, type of burn, gender, consciousness, and intubation in the pre-hospital

Variable	status	Mean (SD)	Number	F	P-value (ANOVA)
Cooling at the scene	Yes	36.60 (0.59)	97	0.06	0.79
	No	36.62 (0.69)	54		
Burn degree	Grade 2	36.65 (0.58)	54	0.25	0.75
	Grade 3	36.61 (0.84)	22		
	Grade 2 and 3	36.57 (0.59)	75		
Type of burn	Thermal	36.65 (0.62)	116	0.73	0.23
	Inhalation	36.63 (0.68)	23		
	Electrical	36.58 (0.420)	5		
	Chemical	36.57 (0.61)	7		
Gender	Male	36.58 (0.61)	102	0.56	0.45
	Female	36.66 (0.65)	49		
Level of consciousness	Conscious	36.65 (0.58)	136	6.97	0.009
	Lack of consciousness	36.21 (0.84)	15		
Intubation	No	36.65 (0.61)	139	10.10	0.002
	Yes	37.07 (0.59)	12		

Table 6. Multiple linear regression analysis of independent variables with CBT at the beginning of admission of burn patients (step 14 of Backward model)

Variables	B	S.E.	t	β	Sig.	95 % CI	
						Lower	Upper
Airway type (intubated)	-0.684	0.191	-3.58	-0.296	< 0.001	-1.062	-0.307
volume of IV fluids received	0.000	0.000	1.748	0.144	0.082	0.000	0.001

CI — confidence interval

tect individuals at risk of hypothermia early. Lack of awareness or failure to follow clinical guidelines, as well as insufficient facilities and equipment for assessing CBT in patients and not reheating them, are other reasons. Failure to provide proper temperature care in the pre-hospital area and even burn emergency wards, such as not using heaters to heat injection fluids, can be one of the reasons for the high prevalence of hypothermia in the studied patients.

Numerous studies have reported the prevalence of hypothermia between 34 and 79.2%. In a retrospective study of 57 patients, Alonso et al. (2020) reported that 79.2% of patients were hypothermic during admission [17]. Ehrl et al. (2018) mentioned the prevalence of hypothermia during admission among 52 patients as 65.4 [4]. Also, Ziegler et al. (2019), in their study on 141 patients, estimated the prevalence of hypothermia at 60.3% [3]. Steele et al. (2016) reported a 42% prevalence

of accidental hypothermia in patients with large burns during admission and hospitalization [5]. Based on Weaver et al.'s (2014) study, among 277 patients, about 42% were hypothermic [7]. Hostler et al. (2013) also conducted a study on 12097 patients and reported the prevalence of hypothermia to be 39.67% [18]. In a retrospective study on 301 patients, Lukusa et al. (2021) also reported the prevalence of accidental hypothermia to be 34% [6].

The main reasons for the variation in the prevalence of hypothermia in different studies seem to be related to the differences in the selection of the cut-off point for hypothermia, inclusion criteria (degree and extent of burn), temperature recording methods (peripheral or CBT recording thermometers), study times (cold and hot seasons), different geographical regions (cold or tropical), and the type of studies (retrospective or prospective).

In most studies, the cut-off point for hypothermia has been defined as less than and equal to 36°C [3, 27, 29–31]. In a few studies, including Weaver et al. (2014) and Hostler et al. (2013), hypothermia has been defined as below 36.5°C [7, 18]. The results of two studies, in which hypothermia had been considered less than and equal to 35°C [19, 27] were contrary to the present study's findings. This difference can be justified according to the cut-off point of 36°C used in the present study.

The results of multiple linear regression analysis showed that the volume of injected fluids in the pre-hospital stage was related to hypothermia upon admission. Of course, this relationship is such that with an increase in the volume of injected fluids, the CBT of the patients also increases. In many studies, hypothermia is usually aggravated by increasing the volume of intravenous fluids in patients, while this study showed contradictory results.

Ehrl et al.'s (2018) study showed that hypothermia enhanced with the increased volume of injected crystalloid fluids [4]. Steele et al.'s (2016) study also reported the association of excessive administration of intravenous fluids in the pre-hospital phase with exacerbation of hypothermia [5]. In Reynolds et al.'s (2012) study, the prevalence of hypothermia in massive transfusions was also high [32].

However, some studies, including Lim et al. (2016), Lapostolle et al. (2012), and Ziegler et al. have not reported any relationship between the volume of fluids received and causing hypothermia [3, 31, 33].

The discrepancy between the finding of the present study and other existing studies can be argued for various reasons. One of the specific reasons for this study is to provide low volumes of intravenous fluids in the pre-hospital stage for burn patients in such a way that the average volume of fluids received by these patients was about 780.46 ± 335.50 mL, which does not seem to be enough to reduce the CBT of patients significantly. The second reason can be related to the relatively fast time (20.66 minutes with a standard deviation of 6.428) of transferring burn patients by ambulance to the medical center, which is not enough to cause temperature changes due to receiving the volume of intravenous fluids. Of course, the temperature of the injected fluids is also an important factor, which in the present study was not possible to check accurately in the pre-hospital stage. The temperature of intravenous fluids is a risk

factor for hypothermia [7, 21, 34] and has negative effects [35].

Another independent risk factor for the prevalence of hypothermia in the present study was the airway type so that the body temperature upon admission was lower in intubated than in non-intubated patients, and this difference was statistically significant. Many studies have reported the association between tracheal intubation and the prevalence of hypothermia [3, 4, 7, 20, 33, 36, 37]. However, Lukusa et al.'s (2021) study was inconsistent with the present study, showing that intubation in children is not a suitable indicator of hypothermia [6].

Since patients with tracheal tubes are often unconscious or have a low level of consciousness, lose the ability to regulate their body temperature, and their intubation at the scene is also a factor in wasting time in transportation, and they will have more opportunity to lose temperature. In addition, changing the natural path of breathing and replacing it with artificial tracheal tubes distorts the possibility of warming the breathing air temperature.

Among other findings of the present study was the exacerbation of hypothermia with a decrease in the level of consciousness, although this finding was not identified as an effective factor in multiple linear regression analysis. Studies have also shown that hypothermia increases with a decreased level of consciousness [7, 38–40]. This phenomenon can be due to the non-observance of temperature care protocols for burn patients in the pre-hospital stage, such as not heating the injection fluids, insufficient coverage of patients, and patients' prolonged intubation at the scene. In addition, temperature regulation mechanisms are disturbed in unconscious or low-consciousness patients.

The pre-hospital field information recorded in the datasheet may not have sufficient validity. Another limitation of the study was the investigation in different seasons (cold and hot), which was considered a confounding factor. Recording the body temperature of some patients inside the ambulance cabin with a mercury thermometer was another limitation of the study. The present study was conducted only in a burn center and on patients referred by ambulance. In order to accurately check the prevalence of hypothermia, it is better to conduct other studies on patients who are referred from other hospitals and by private vehicles as well.

CONCLUSIONS

In the present study, nearly half of the burn patients were hypothermic. Among the numerous variables evaluated as risk factors related to hypothermia in this study, patients with endotracheal intubation and the volume of fluids received effectively contributed to creating or aggravating hypothermia. One of the different findings of this study was the correlation of CBT in patients upon admission with the volume of fluids received, which contradicted the existing research evidence and therefore needed further study and exploration. The role of factors such as lack of assessment or inappropriate assessment of core body temperature, neglect of temperature care instructions, and weakness of diagnostic and interventional equipment for managing accidental hypothermia in burn patients should not be ignored. Empowering the pre-hospital and hospital care team and improving their knowledge and skills in evaluating burn patients and early diagnosis, prevention, and optimal management of accidental hypothermia is expected seriously. Also, the application of research evidence and clinical guidelines on how to manage accidental hypothermia in burn patients in emergency wards and the commitment to evidence-based practice along with the optimization of temperature care in the pre-hospital field and burn centers can be effective in the management of accidental hypothermia and related consequences.

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Conflict of interest

The authors declare no conflicts of interest.

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PULMONARY INVOLVEMENT IN LASSA FEVER: A SCOPING REVIEW

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ABSTRACT

INTRODUCTION: Lassa fever (LF) affects all body systems, however, inadequate knowledge exists on the involvement of the pulmonary system in LF infections. This scoping review, therefore, aimed to describe the pulmonary involvement of LF.

MATERIAL AND METHODS: We conducted an extensive search of the literature on two databases, namely PubMed and Google Scholar. Overall, 5,217 articles were retrieved from a database search, out of which 107 duplicates were removed. Overall, 12 articles were included: four review articles, three case reports, three experimental inoculation studies, one retrospective study, and a prospective case-control study.

RESULTS: Symptoms experienced included fever, pharyngitis, retrosternal pain, respiratory distress, and proteinuria. Complications included unique pulmonary arteritis, pulmonary embolization, mucosal bleeding, pleural or pericardial effusion, pulmonary edema, and interstitial pneumonitis. Consequences of the effect of Lassa virus infection were impairment of the immune system alongside continual replication of Lassa virus infection in affected tissues and death of affected individuals. LF has varied but serious effects on the pulmonary system.

CONCLUSIONS: These symptoms, particularly in areas where LF is known to be endemic, should prompt clinicians to request LF polymerase chain reaction for confirmatory diagnosis. These features should promote the provision of respiratory support for patients in need of such.

KEY WORDS: Lassa hemorrhagic fever; lungs; *Mastomys natalensis*; pulmonary involvement in Lassa fever; Lassa virus

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INTRODUCTION

Lassa fever (LF) is an acute hemorrhagic illness caused by Lassa virus (LASV), a member of the *Arenaviridae* family [1]. Outbreaks of the LF have been reported in Nigeria, Liberia, Sierra Leone, Guinea, and the Cen-

tral African Republic, but it is believed that human infections also exist in the Democratic Republic of Congo, Mali, and Senegal [1]. Imported cases of LF have also been reported from around the globe because of exposure to the vector transmitting LF [2].

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Lassa fever is associated with occasional epidemics, during which the case-fatality rate can reach 50% among hospitalized patients [3]. Eighty percent of LASV-infected persons do not develop the disease, and 1% of infections overall result in death thus corroborating the fact that disease also depends on variations in host susceptibility due to concurrent infections or genetic differences [4, 5]. Among 20% of LASV-infected individuals however, LF may progress to more serious symptoms including hemorrhaging (in gums, eyes, or nose), respiratory distress, repeated vomiting, facial swelling, pain in the chest, back, and abdomen, and shock.

Death can occur within two weeks after the onset of symptoms due to multiple organ failure [3, 6]. Compared to HIV/AIDS, LF is more infectious to close associates and of a high fatality. In all instances, fatality occurs among 15 to 20 percent of all LF hospitalizations, however, only 1% of all LASV infections result in death. A single case of LF is termed an outbreak of LF. Its predominance among the elderly and reproductive age group constitutes a lot of public health concern and economic hazard, however, LF has been grossly underestimated [1]. So far, ribavirin is the only available therapy for LF [7].

The primary transmission route of LASV from its host to humans is by direct exposure to the virus, which may occur via the respiratory tract, through inhalation of infected particulates [8]. During the infection process, LASV makes contact with the epithelial layers of the body and, after breaking through the epithelial tissue barrier, exploits dendritic cells for further dissemination [8]. It has been shown for LASV, as well as for other arenaviruses, that during infection, infectious virus particles are released from epithelia into body fluids and urine [9–12].

All systems in the body could be affected by LF. Neurological effects of LF include hearing loss, tremors, and encephalitis [13, 14]. The pulmonary (respiratory) system is also not spared and has been shown both clinically and pathologically to be involved in LF [12–14]. When affected by LF, the compromised pulmonary system could cause a crash in the entire makeup of an individual [12]. However, there exists limited synthesis of the available evidence, and insufficient knowledge on the involvement of the pulmonary system in LF infections as it relates to mortality and the disease outcome. Scoping reviews are aimed at an unbiased summary synthesis of available evidence on the subject matter under investigation. The pulmonary manifestation of

LASV has not gained much reporting over the years, hence the need for the scoping review method in this study. A review of this nature is also important to initiate syndromic case management of LF while confirmatory diagnosis is expected. The review is also important in raising the index of suspicion of physicians working in endemic areas to facilitate the diagnosis and management of individuals affected by LF. This scoping review therefore aimed to assess the pulmonary involvement of LF among confirmed LF cases.

MATERIAL AND METHODS

We searched for articles on the pulmonary involvement of LF on PubMed and Google Scholar databases. A purposive selection of the two databases was done because they are indexed in many journals. OSI and AAA served as independent reviewers in the data extraction from the databases. In instances where both OSI and AAA could not agree on the inclusion of an article, CU assisted in decision-making. This, therefore, helped to eliminate bias in the data collection. Data collection was conducted in two periods; April–May 2022, and December 2022.

Keywords used in the search strategy included: “Lassa fever” OR “Lassa hemorrhagic fever” OR “Hemorrhagic fever” OR “Lassa” AND “Pulmonary system” OR “Respiratory system” OR “Respiration” OR “Lungs” OR “Breathing” OR “Inhalation” OR “Exhalation”.

Studies that focused on the involvement of the pulmonary system in LF infection were included in this review. All articles which have been published in the English Language were included in the study for ease of understanding by the authors. All articles that described the pulmonary involvement of LF in human and/or animal models for included to yield robust data. No date restriction was applied because only a few studies had been published on the pulmonary manifestation of LF. Articles that were not specifically tailored to the pulmonary involvement of LF were screened as ineligible literature. Overall, 5,217 articles were retrieved from a database search, out of which 107 duplicates were removed. Of the remaining 5,110 articles, 2,242 articles were excluded for describing the epidemiology and transmission of LF only, 1,209 articles were excluded for describing only the general pathogenesis of LF, 1,213 articles were excluded for comparing general systemic effects of LF with other viral hemorrhagic fevers, and 434 articles were excluded for describing

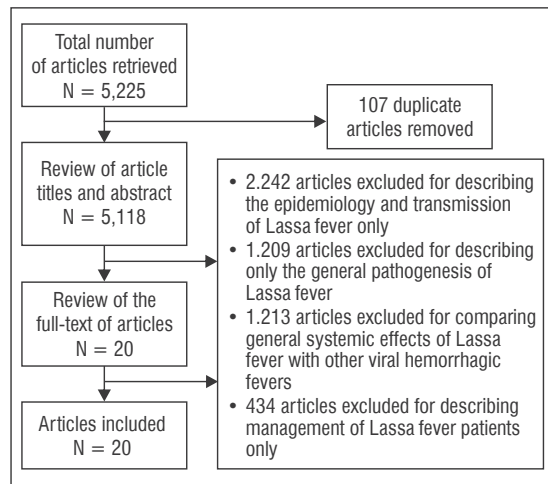


FIGURE 1. PRISMA flowchart showing the article search strategy

the management of LF patients only. Twenty articles were thereafter included in the review: six reviews, six case reports, five experimental studies, one retrospective study, and prospective case-control study, and one qualitative research (Fig. 1).

A three-step method proposed was adopted in the search strategy as follows:

Step One: A search of PubMed and Google Scholar databases was used for index terms and text words contained in the title and abstract.

Step Two: Identified keywords and index terms were used to prompt search on included databases.

Step Three: The reference lists obtained from the articles were searched for additional literature.

Registration

This review was not registered on any public repository. The protocol for the study was prepared and can be accessed upon reasonable request from the corresponding author. No amendment was made to the protocol.

RESULTS

Table 1 summarizes the literature retrieved from a database search. There are limited studies that have outlined the prevalence or mortality associated with the pulmonary manifestations of LF.

A retrospective cohort study conducted among 65 LF patients at Irrua Specialist Hospital, Edo State, Nigeria documented the pulmonary involvement of LF in 10 cases, with pneumonia reported among five

of them, pneumonia with pleural effusion among three cases, and acute respiratory distress present among two cases [12]. Among the ten patients with pulmonary involvement, seven died yielding a CFR of 70% [12]. Among LF cases without pulmonary involvement, 21 died out of 55, generating a CFR of 38.2%. Overall, the CFR was 44.6% (29/65). Death (Fatal outcome) was associated with non-administration of ribavirin; the presence of cough, hemorrhage, and being elderly [12]. Pulmonary manifestations of LF can be classified as mild, moderate to severe presentation [12]. Mild to moderate presentation includes retrosternal chest pain and cough. Retrosternal chest pain could occur as a result of the inflammation of serous surfaces (serositis) which could account for the severe retrosternal or epigastric pain seen in many patients [12]. Severe presentation of LF on the pulmonary system includes breathlessness or acute respiratory distress. Focal interstitial pneumonitis has also been reported in LF. It could result from direct respiratory infection or from viremia (Fig. 2).

A case report of a 56-year-old Nigerian seen at the Emdee Medical Center in Jos, Nigeria, because of a 2-week history of fever (38.2°C) and diarrhea. Treatment with antibiotics was initiated. On 23 March, he was admitted to the Life Camp Clinic, Abuja, Nigeria. His temperature was 39.6°C; he was drowsy and intermittently disoriented. The patient later developed signs of pulmonary embolism, which ultimately resulted in his death [14].

A prospective case-control study of LF was conducted in Sierra Leone to measure the case-fatality rate of LF among febrile hospital admissions and to better delineate the clinical diagnosis and course of this disease [15]. Lassa fever (LF) was responsible for 10–16% of all adult medical admissions and for 30% of adult deaths in the two hospitals studied. The CFR for 441 hospitalized patients was 16.5%. Symptoms experienced included fever, pharyngitis, retrosternal pain, and proteinuria. Among the documented complications, pleural effusion was seen in 3% [15]. Others included mucosal bleeding (17%), bilateral or unilateral eighth-nerve deafness (4%), and pericardial (2%) effusion [15].

In an experimental study of nine Rhesus monkeys with LASV and a closely related *Arenavirus*, Mozambique virus, symptoms such as fever, conjunctivitis, and a reduction in the intake of food and water were reported. Interstitial pneumonia and unique pulmonary arteritis were the reported

Table 1. Summary of literature on the pulmonary involvement of Lassa fever

S/N	Title	Study design/ type	Sample size	Inclusion criteria	Signs/symptoms	Case Fatality Rate	Parts affected	Complications	Outcome
i.	Pulmonary manifestation of Lassa hemorrhagic fever and the impact on mortality (Nigeria) [12]	Retrospective Study	65 persons; 34 males 31 females		Cough and/or breathlessness	70%	Lung parenchyma	Hemorrhage	Death
ii.	Lassa fever encephalopathy: Lassa virus in cerebrospinal fluid but not in serum (Emdee Medical Centre, Jos, Nigeria) [14]	Case report	A 56-year-old Nigerian male		Two-week history of fever and diarrhea, drowsiness, intermittent disorientation		Pulmonary vasculature	Pulmonary edema Pulmonary embolism	Death of the patient
iii.	A case-control study of the clinical diagnosis and course of Lassa fever (Sierra Leone) [15]	Prospective case-control study	441 hospitalized Lassa fever patients of 1,087 febrile adult medical admissions	i. Age: > 10 years ii. Presentation with a febrile illness iii. Admission to the medical ward of either of the two hospitals used in this study	i. Elevated respiratory rate ii. A combination of fever, pharyngitis, retrosternal pain, and proteinuria (pooled predictive value together: 0.81)	16.5%	Sternum, pericardium, and throat	i. Mucosal bleeding: 17% ii. Bilateral or unilateral eighth-nerve deafness: 4% iii. Pleural effusion: 3% iv. Pericardial effusion: 2% v. Severe pharyngeal pain vi. Interstitial pneumonitis	Recovery from milder disease generally began within eight to 10 days of onset, with lysis of fever and resolution of headache, sore throat, and chest pain
iv.	Experimental infection of Rhesus monkeys with Lassa virus and a closely related <i>Arenavirus</i> , <i>Mozambique virus</i> [16]	Experimental inoculation	Nine rhesus monkeys		i. Fever ii. Conjunctivitis iii. Reduction in the intake of food and water		Lungs	i. Interstitial pneumonia ii. Unique pulmonary arteritis	Death
v.	Acute abdominal pain in patients with Lassa fever: Radiological assessment and diagnostic challenges [17]	Review	–	i. Presence of abnormal bleeding from mouth, gum, nose, vagina, urinary tract (ii) Haemoptysis, bleeding from the ear; (iii) Swollen neck and face; (iv) Red eyes or conjunctivitis (often bilateral); (v) Spontaneous abortion; (vi) Deafness during illness; (vi) Shock or systolic blood pressure < 100 mmHg vii. Pleural effusion	Swollen lymph nodes	–	Eyes, lungs, abdomen, and internal tissues	i. Pulmonary edema ii. Pulmonary hemorrhage iii. Acute respiratory distress syndrome iv. Aspiration pneumonia v. Pleural effusion or ascites	i. Pericardial effusion with or without pericarditis' ii. Death

Table 1 (cont.). Summary of literature on the pulmonary involvement of Lassa fever

S/N	Title	Study design/ type	Sample size	Inclusion criteria	Signs/symptoms	Case Fatality Rate	Parts affected	Complications	Outcome
vi.	Lung uptake of Tc-99m-Tin colloid in a patient with Lassa fever (Nigeria) [18]	Case report	An 18-year-old Nigerian girl		Fever (38°C) Hemorrhage			Increased reticuloendothelial system activity, intravascular clumping and embolization	
vii.	A case of Lassa fever imported into Wiesbaden, Germany [19]	Case report	A 57-year old Nigerian man (Germany)	i. Disorientation ii. Marked stiffness of the neck	Fever, diarrhea, and general malaise	–	–	Seizure Pulmonary embolism	i. Cardiac and respiratory failure ii. Death
viii.	Clinical laboratory, virologic, and pathologic changes in hamsters experimentally infected with pirital virus (<i>Arenaviridae</i>): a rodent model of Lassa fever [20]	Experiment	Five hamsters		i. Viremia ii. In the lung sections, scattered neutrophils were seen in the interstitium	100%		Focal pulmonary hemorrhage	Death
ix.	Clinical presentations of Lassa fever in non-endemic parts of the world: a systematic review [21]	Review	22 primary cases of imported Lassa fever		i. Fever ii. Residence in or travel to Lassa fever endemic area	22.7%	Lungs and chest	Cough, pleuritic chest pain and shortness of breath. Pleural effusion was also reported, and pulmonary embolism	i. Acute respiratory distress ii. Death
x.	Infection of type I interferon receptor-deficient mice with various old world arenaviruses: a model for studying virulence and host species barriers [22]	Review (Experimental inoculation)	Type I Interferon receptor-deficient IFNAR ^{-/-} mice	Type I Interferon receptor deficiency	–	–	Lungs	Congestion and edema of the viscera, interstitial pneumonitis, presence of mononuclear cells in the focal interstitial compartments, especially in the capillaries	
xi.	The pathology of human Lassa fever [23]	Review	Seven Lassa fever cases		Fever		Lungs (Parenchyma and pleural space)	Pharyngitis, pleural effusion, pulmonary edema, and interstitial pneumonitis	Impairment of the immune system alongside continual replication of Lassa virus in affected tissues of the body

Table 1 (cont.). Summary of literature on the pulmonary involvement of Lassa fever

S/N	Title	Study design/ type	Sample size	Inclusion criteria	Signs/symptoms	Case Fatality Rate	Parts affected	Complications	Outcome
xii.	Endotheliopathy and platelet dysfunction as hallmarks of fatal Lassa fever [24]	Case studies	98 confirmed Lassa fever cases	–	Facial and pulmonary edema, pleural effusions, ascites, petechiae mucosal membrane bleeding, and cough	33–80%			
xiii.	Pathology and pathogenesis of Lassa fever: novel immunohistochemical findings in fatal cases and clinico-pathologic correlation [25]	Case reports of postmortem tissue samples	12 confirmed Lassa fever cases	–		100%	Lung alveoli	Intra-alveolar edema in lung	Death
xiv.	Pathogenesis of Lassa fever in cynomolgus macaques [26]	Experimentation	Comparison of tissues from three animals at an early- to mid-stage of Lassa infection with tissues from three animals collected at terminal stages of Lassa infection	–	–	–	Lung interstitial	Mild interstitial pneumonia	Death, among animals at the terminal stage of Lassa infection
xv.	Pathogenesis of recent Lassa virus isolates from lineages II and VII in cynomolgus monkeys [27]	Experimental study of unvaccinated cynomolgus monkeys	–	–			Lung	i. Viremia in the lungs ii. Thickening of the alveolar septum and advanced interstitial pneumonia iii. Widespread neutrophilic infiltration, and acute respiratory distress in fatal cases	Death
xvi.	Late diagnosis of Lassa fever outbreak in endemic areas lead to high mortality, Kenema District, Sierra Leone, February–March 2019 [28]	Case reports	Two people; an eight-year-old male, and a 15-year-old female	–	Fever, headache, and sore throat	100%	Lungs and orifices	Bleeding	Death

Table 1 (cont.). Summary of literature on the pulmonary involvement of Lassa fever

S/N	Title	Study design/ /type	Sample size	Inclusion criteria	Signs/symptoms	Case Fatality Rate	Parts affected	Complications	Outcome
xvii.	Beyond Lassa Fever: Systemic and structural barriers to disease detection and response in Sierra Leone [29]	Qualitative analysis of local policy and guidance documents, key informant interviews with policy and practice actors, and focus group discussions and in-depth interviews with health care workers and community health workers	Eight focus group discussions, and eight in-depth interviews	Previous history of handling ill individuals with one or more of the following: malaise, fever, headache, sore throat, cough, nausea, vomiting, diarrhea, myalgia, chest pain, hearing loss and a history of contact with excreta of rodents or with a case of Lassa fever	Abdominal pain, diarrhea, vomiting and fever	–	Lungs and orifices	Seizure and bleeding	Intra-uterine fetal demise; death of the pregnant woman
xviii.	Differential pathogenesis of closely related 2018 Nigerian outbreak clade III Lassa virus isolates [30]	Case reports	i. Five serum samples; samples were obtained during symptomatic illness ii. Ten female cynomolgus macaques	–	–	–	Lung interstitial	i. Weight loss, and increased respiration ii. Mild to marked interstitial pneumonia with edema	Death
xix.	Diagnostics for Lassa fever virus: a genetically diverse pathogen found in low-resource settings [31]	Narrative review	–	–	–	15–20% mortality rate among severe cases	Lungs	Presence of fluid in the lung cavity	Acute respiratory distress, shock, seizures, tremor, disorientation and coma, and death
xx.	Exotic viral hepatitis: A review on epidemiology, pathogenesis, and treatment [32]	Narrative review	–	–	Headache	–	Pleural surfaces	Shock and respiratory distress due to pleural effusion	Death

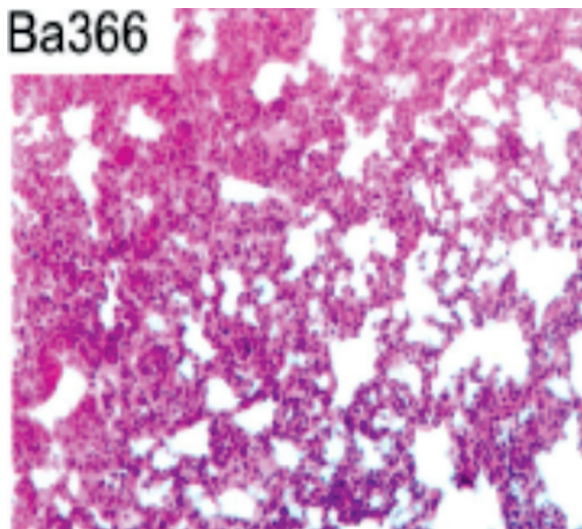


FIGURE 2. Lung tissue showing variable degrees of interstitial pneumonia in Lassa virus infected mice



FIGURE 3. Plain chest radiograph of a patient with Lassa fever showing massive bilateral consolidations due to acute respiratory distress syndrome

complications, and death was the only fatal outcome reported [16].

In a review article that reported acute abdominal pain in patients with LF, the inclusion criteria were abnormal bleeding from the orifices, conjunctivitis, deafness, spontaneous abortion (for pregnant females), and shock [17]. The resulting complication of LF on the pulmonary system included pulmonary edema, pulmonary hemorrhage, acute respiratory distress, pleural effusion, and aspiration pneumonia [17].

Findings from a case report of a febrile 18-year-old LF female patient reported complications such as pulmonary embolization, intravascular clumping, and increased reticuloendothelial system activity [18].

Another case report of a 57-year-old Nigerian LF case imported into Wiesbaden, Germany documented symptoms such as fever, diarrhea, and general malaise. Complications reported included seizure and pulmonary embolism, while cardiac and respiratory distress and death were the outcomes [19].

In an experimental study of clinical, laboratory, virologic, and pathologic changes in hamsters experimentally infected with the pirital virus (*Arenaviridae*) using five hamsters; viremia, and scattered neutrophils in the lung interstitium were observed. Focal hemorrhage was the only pulmonary manifestation of LF reported, and this culminated in the death of all the hamsters [20].

In a study that aimed to determine the clinical presentations of LF in non-endemic parts of the world, a CFR of 22.7% was reported among 22 primary cases of imported LF. Cough, pleuritic chest pain, shortness of breath, and pleural effusion were the reported complications, while acute respiratory distress and death were the documented outcomes [21].

In their review article, Rieger et al. [22] reported that the pathological manifestations of LF on the pulmonary system among seven LF cases included congestion and edema of the viscera. Interstitial pneumonitis was also present with mononuclear cells and megakaryocytes in two LF cases. In addition, mononuclear cells were also reported in the focal interstitial compartments, especially in the capillaries (Fig 3).

Also, reports from a review conducted by Winn et al. [23] concerning seven cases of LF documented pulmonary features such as pharyngitis, pleural effusion, pulmonary edema, and interstitial pneumonitis. LASV targets lung parenchyma and the pleural space. A consequence of the effect of LASV was thus impairment of the immune system alongside continual replication of LASV in affected tissues of the body. Pneumonia with or without pleural effusion, and acute respiratory distress syndrome are indicators of a severe case of LF. Acute respiratory distress is a major pulmonary complication of LF and is the frequent cause of death in LF.

A review of seven confirmed LF cases documented symptoms such as fever, pharyngitis, and

breathing difficulties. LF infection affected the lung parenchyma and pleural space, thereby resulting in pleural effusion, pulmonary edema, and interstitial pneumonitis [24].

The summary of other studies is as shown in Table 1 [12, 14–32].

DISCUSSION

Lassa fever (LF) is a multi-systemic disease. However pulmonary presentations are not the initial or primary manifestation. From this review, we found that the involvement of the pulmonary system is an indication of the severity of LF. About 20% of patients may later develop pleural or pericardial “rubs” (grating noises heard as the heart beats) and could ultimately progress to a pleural effusion [12, 13]. Other studies have similarly reported that the common presentation of pneumonia in LF includes cough and dyspnea with frequencies of 23.1 and 30.8% respectively [33, 34]. However, no diagnosis can be made as a result of a cough because the cough is a minor criterion for LF [35]. An LF diagnosis could be possibly made with persistent fever, although this is not a definitive diagnosis [36]. Definite diagnosis for LF is made through polymerase chain reaction (PCR) using throat washing and pleural fluid of the patient [37]. Patients may present with breathlessness and will need to require respiratory support which could be in the form of high-flow oxygen or mechanical ventilation, which is largely unavailable in most hospitals in West Africa [38, 39].

Bowen and colleagues reported inflammation and edema of the local cords which progresses to laryngospasm and eventually reduced air entry in the patients [38]. Patients could present with choky sensations and cyanosis. They also reported a case of pharyngitis, exudative tonsillitis, cervical adenopathy, and facial and neck swelling [38]. The patient was reported to have bled profusely from the site of the tracheostomy, because of prolonged clotting time.

This review revealed that LASV replicates in the lung parenchyma and pleural space, causing pathological changes which result in an impairment of the immune system. When the immune system becomes compromised, the body’s defense mechanism becomes weakened, and affected patients become vulnerable to other infections and systemic dysfunction as well [37–39]. The sequence of these events, therefore, explains the observed increase in case fa-

tality rate among LF patients whose pulmonary systems are involved. This occurrence, therefore, posits that primary prevention of LF is key to avoiding complications that are associated with the infection. Also, suspected cases of LF should promptly consult health personnel to avert complications associated with the delay in LF reporting and treatment.

Registration

This review was not registered on any public repository. The protocol for the study was prepared and can be accessed upon reasonable request from the corresponding author. No amendment was made to the protocol.

Limitations

The Scopus and Web of Science databases were not screened as relevant sources of studies and could have introduced some biases in this review. Quality assessment of included studies was not done. In addition, the differences in technologies used, and the lack of universally acceptable strategies for managing the pulmonary manifestations of LF make it impossible to compare and draw conclusions about the effectiveness of one strategy over others. It is therefore pertinent to identify the requirements for managing the pulmonary manifestations of LF for adoption by physicians to improve health outcomes among LF patients.

CONCLUSIONS

The pulmonary manifestations of LF range from pneumonia to pleural effusion, acute respiratory distress, visceral congestion and edema, and pneumonitis. Complications following the involvement of the pulmonary system could result in death. Therefore, clinicians should apply these pulmonary features of LF as a form of high index of suspicion in areas known with LF endemicity in making a presumptive diagnosis for LF. In addition, clinicians should use these features as a prompt to request for LF polymerase chain reaction to make a confirmatory diagnosis. Health workers at the community level in LF-endemic areas in West Africa should be educated on the pulmonary features of LF to improve early presentation in health facilities and prompt case management. It is also required that community members are educated on the pulmonary effects of LF to facilitate timely presentation and management, especially in LF-endemic communities.

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Conflict of interest

The authors declare no conflict of interests.

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SUPPLEMENTARY DOCUMENT				Checklist item	Location where item is reported
Section and Topic	Item				
TITLE					
Title	1	Identify the report as a review			Page 1
ABSTRACT					
Abstract	2	See the PRISMA 2020 for the Abstracts checklist			Page 2
INTRODUCTION					
Rationale	3	Describe the rationale for the review in the context of existing knowledge			Pages 3 and 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses			Page 4
METHODS					
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses			Page 5
Information sources	6	Specify all databases, registers, websites, organizations, reference lists, and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted			Page 5
Search strategy	7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used			Page 5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process			Page 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process			Page 5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect			Page 5–6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information			Page 5–6
Study risk of bias assessment	11	Specify the methods used to assess the risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process			Page 5
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results			Not applicable
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis [e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)]			Page 7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling missing summary statistics, or data conversions			Not applicable
	13c	Describe any methods used to tabulate or visually display the results of individual studies and syntheses			Page 7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used			Not applicable
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression)			Not applicable
Reporting bias assessment	13f	Describe any sensitivity analyses conducted to assess the robustness of the synthesized results			Not applicable
	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases)			Not applicable

SUPPLEMENTARY DOCUMENT (cont.).			
Section and Topic	Item	Checklist item	Location where item is reported
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome	Not applicable
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram	Page 5
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded	Pages 5 and 6
Study characteristics	17	Cite each included study and present its characteristics	Page 7–9
Risk of bias in studies	18	Present assessments of risk of bias for each included study	Not applicable
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots	Not applicable
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies	Pages 7–9
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect	Not applicable
	20c	Present results of all investigations of possible causes of heterogeneity among study results	Not applicable
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed	Not applicable
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed	Not applicable
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence	10
	23b	Discuss any limitations of the evidence included in the review	10
	23c	Discuss any limitations of the review processes used	
	23d	Discuss the implications of the results for practice, policy, and future research	12
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including the register name and registration number, or state that the review was not registered	6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared	6
	24c	Describe and explain any amendments to the information provided at registration or in the protocol	6
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review	12
Competing interests	26	Declare any competing interests of review authors	12
Availability of data, code, and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review	Not applicable

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71; For more information, visit: <http://www.prisma-statement.org/>

DEVELOPMENT AND VALIDATION OF HEAT WAVE HAZARD ADAPTATION TOOL: A STUDY PROTOCOL

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ABSTRACT

INTRODUCTION: Global warming, climate change, temperature fluctuations, and increasing concern about their possible impacts on health have drawn the attention of scholars and academia around the world. Previous studies suggested heat waves can increase mortality and diseases, the demand for ambulances, hospitalization rates, and severe consequences, especially in vulnerable groups. The most effective measures can be taken by effective planning and providing practical solutions in the mitigation and preparedness stage to prevent and mitigate the effects of disasters. Given the absence of a tool to determine the level of adaptation in the world, this study aimed to identify the strategies to adapt to heat waves and develop a tool to measure the level of adaptation to heat waves.

MATERIAL AND METHODS: This exploratory sequential mixed methods (qualitative-quantitative) study was conducted in three phases. In the first phase, a qualitative study was carried out by conducting interviews with people affected by heat waves. The interview data were used to identify the themes related to adaptation to heat waves and the strategies to adapt to heat waves. In the second phase, a systematic review study was conducted to identify the strategies to adapt to heat waves in the world. Afterward, the data from the qualitative phase and systematic review were used to develop the items in the heatwave adaptation tool. Finally, in the third phase (the quantitative study), the psychometric properties of the developed tool were assessed using face validity, content validity, construct validity, and reliability indexes.

CONCLUSIONS: The developed tool can measure the level of adaptation behaviors of people against heat waves in different communities. Thus, an awareness of less adaptable and more vulnerable communities can contribute to conducting some mitigation and preparedness interventions in these communities.

KEY WORDS: climate change; heat waves; adaptation; tools

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INTRODUCTION

Disasters pose severe threats to the life, development, and evolution of human society and disaster risk management requires a systematic process, including executive, and organizational decisions, other capacities to perform policies, strategies, and social capacity to reduce the negative effects and consequences of risks [1–3]. Unexpected incidents and disasters and the resulting damage are increasing due to environmental changes, economic, social, and political factors [3–6]. The excessive use of fossil fuels followed by the expansion of industrial activities has caused an increase in temperature and consequently global warming leading to visible climatic changes in different parts of the world [7]. According to the reports of the International Conference on Climate Change (IPCC), climate fluctuations have increased more than before and have caused phenomena such as unpredictable climate changes, including heat waves [8]. Thus, during the last 100 years, the average temperature on the planet has increased by 0.74 degrees Celsius. Projections show that compared to the period from 1850 to 1900, the average global temperature level until 2081–2100 is likely to increase by 1.0 and 1.8 degrees Celsius in the very low greenhouse gas emission scenario, 2.1 and 3.5 degrees Celsius in the medium greenhouse gas emission scenario, and 3.3 and 5.7 degrees Celsius under the high greenhouse gas emission scenario [9]. In addition, the frequency of extremely hot days will increase and the frequency of extremely cold days will decrease [9].

Global warming currently has significant and costly effects on societies, individual and public health, and the environment [10, 11]. According to previous studies, heat waves lead to an increase in deaths, heatstroke-related diseases, exacerbation of chronic diseases including cardiorespiratory diseases, and an increase in the need for emergency and ambulance services [7–9, 12–15]. Examining the effects of heat waves in the workplace also shows that many outdoor workers are at high risk of adverse health outcomes. In 2018, it was reported that 45 billion working hours were lost compared to the year 2000 due to the effects of the heat wave [16]. Exposure to daily heat during the hot season is a particular issue, especially for working people who cannot use air conditioning or other technical cooling methods [13, 17, 18].

These effects vary in various spatial and temporal patterns depending on the environmental, social,

and economic situation of countries [19, 20]. While the frequency or magnitude of extreme weather events such as heat waves have increased, the population and assets at risk have also increased, and they are more vulnerable to these climatic changes. Therefore, the management of risks caused by climate-related disasters should be developed at any local and international scale, and disaster mitigation and preparedness strategies should be identified and offered [12, 21–23]. Adaptation to heat waves is one of these strategies used to reduce the consequences of heat waves [24].

Adaptive behaviors can reduce adverse effects on health and various dimensions of individual and social life. However, adaptation strategies may include autonomous and planned adaptation [25]. Autonomous adaptation occurs without coordinated planning at the individual or social levels, and planned adaptation refers to deliberate policy actions with conscious interventions. Planned adaptation strategies should become a requirement to mitigate the adverse health effects and other consequences of extreme heat events. Heatwave adaptation assessments can address significant gaps in vulnerability and management of heat wave effects [26–29].

Research on disaster management shows that adaptation measures are closely related to risk reduction [30–33]. Adaptive measures are needed to reduce harm from heat waves at all levels and for all groups. To this end, some information is required about the current level of knowledge of the affected community and their adaptation methods against the heat wave. This information can be used as a guide for the necessity or non-necessity of interventions as well as the design of interventions [34]. In fact, when establishing adaptation policies for society, policymakers need to be aware of adaptive behaviors [35].

Although many research efforts have been taken in different parts of the world, none of the studies had used a standard tool to determine the level of adaptation of societies against heat waves, and there is no such tool, and sometimes the level of adaptation has been measured through questionnaires that were not psychometrically evaluated [36–39]. These restrictions make it difficult to draw a complete picture of current public adaptive behaviors [39, 40].

Besides, there have been severe heat waves in recent years in some parts of the world including Iran, especially in areas with a hot climate, such as

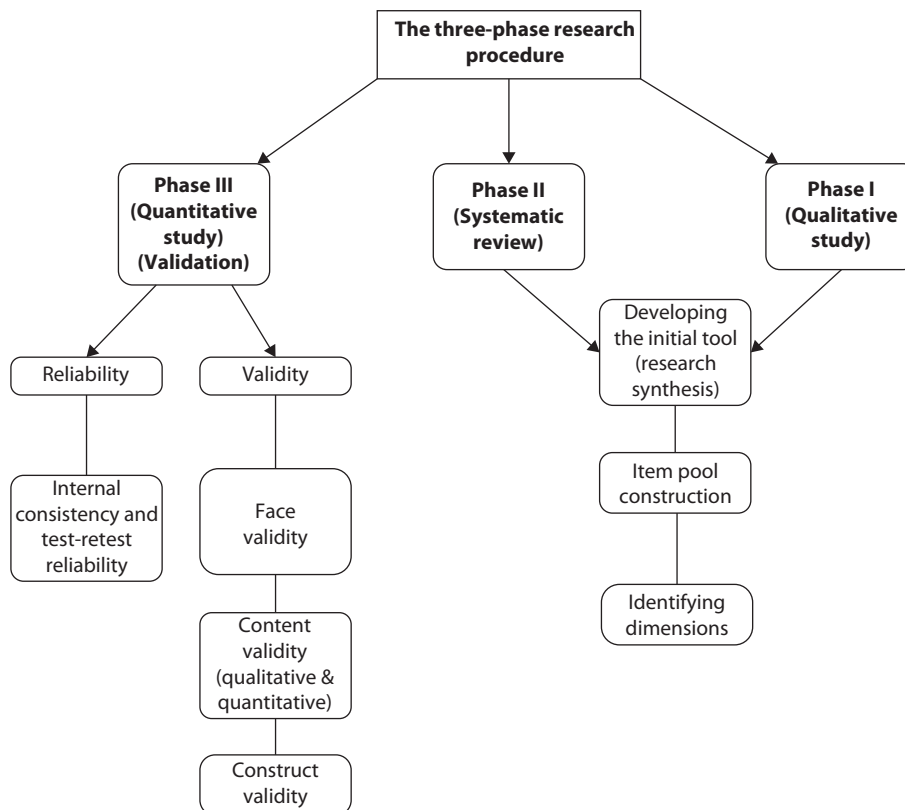


FIGURE 1. The steps taken to conduct the study

Khuzestan Province. Thus, from a scientific point of view, natural hazards, including heat waves, which are currently increasing in intensity and rapidly fluctuating due to human actions, need to be managed following a disaster mitigation and preparedness approach. To this end, a tool is needed to measure the level of adaptation of the affected communities. Then, the resulting data can be used to formulate hazard mitigation and preparedness programs for less adaptive areas. Accordingly, one of the top priorities for managing the effects of natural hazards, including heat waves, is to determine the level of adaptation. Such information can help determine resources, facilities, and planning needed to improve adaptation. Moreover, the resulting information can be used to identify adaptation solutions in societies with a higher level of adaptability.

MATERIAL AND METHODS

Research design

This mixed methods (qualitative-quantitative) study was conducted in three consecutive phases (Fig. 1).

Phase 1: Identifying experiences of adaptation against heat waves (the qualitative study)

- **Objective:** This phase followed two objectives: Identifying adaptation strategies against heat waves and defining the concept of adaptation to heat waves (The phase was completed in 2020).
- **Research population:** The research population consisted of residents in Dezful and Ahvaz, who were selected from different age groups, occupations, and related offices and departments including the Department of Meteorology, Department of Agriculture Jihad, Department of Environment, Resources and Forestry, Municipality, and the universities of medical sciences in Dezful and Ahvaz.
- **Sampling:** The respondents were selected using purposive and convenience sampling with maximum dispersion. To achieve this goal, interviews were conducted with people from different occupations and different age groups, and the sampling process continued until the data saturation point.

- **Inclusion criteria:** Being a resident of Dezful or Ahvaz to have experience with heat waves, being 18 years old and above, the willingness to participate in research, and having the time to take the interview.
- **Exclusion criteria:** The unwillingness to participate in the study.
- **Ethical considerations:** The protocol for this study was approved by the Ethics Committee of Kerman University of Medical Sciences (1401.084. IR.KMU.REC).
- **Data collection instrument:** An interview guide form was used to collect data.
- **Data collection method:** The data were collected through semi-structured interviews.
- **Data analysis method:** MAXQDA 18 software was used to codify and analyze data. Colaizzi's seven-step method was used to analyze the data: First, each respondent's statements were recorded, transcribed, and read several times. Significant statements were underlined in the second step. In the third step, a general theme was extracted from each significant statement. In the fourth step, the extracted themes were categorized based on their similarities. In the fifth step, the identified categories were merged into a thorough description of the phenomenon in question, and more general categories were formed. In the last step, the findings were returned to the respondents and they reviewed and validated the findings [41].
- **Data validation (through supplementary interviews):** To ensure that the findings reflect the respondents' real experiences, the four criteria of credibility, dependability, confirmability, and transferability proposed by Lincoln and Guba were used [41].

Phase 2: Identifying solutions to adapt to heat waves in the world (A systematic review)

- **Objective:** The second phase of the study presented a systematic review of studies addressing adaptation to heat waves to discover and identify behaviors and strategies to adapt to heat waves in urban areas (This phase was completed in 2021).
- **Research population:** All English databases or reliable and accessible international databases including MBIS, Web of Science, PubMed, and Scopus, as well as Persian databases, including Iranian Research Institute for Information Science and Technology (IranDoc), Islamic World Science Citation Database (ISC), Iran Publications Database, and the Scientific Information Database (SID) were searched. The search strategy focused on three groups of keywords related to "adaptation" (adaptation, resilience, compatibility, damage reduction, resilient behavior, risk mitigation behaviors), "heat waves" (extremely hot weather and high temperatures), and "global warming and climate change".
- **Research sample:** The research sample included international documents, records, and articles focusing on adaptation measures against heat waves in Persian and English.
- **Inclusion criteria:** All articles whose full text was available, the articles that used suitable methods and data and proposed strategies for adapting to heat waves, the articles in which heat waves were specifically addressed as a fundamental problem, and the articles on climate change that specifically addressed heat waves were included in this study.
- **Exclusion criteria:** Review articles, letters to editors, proceedings, specialized articles on adaptation to heat waves in animal husbandry, studies on cultivation of special plants and laboratory studies, genetics, and strategies for adaptation to urban heat islands excluding the effects of heat waves were excluded.
- **Research setting:** The articles were collected from libraries, universities, the Internet, and the national intranet.
- **Data collection instrument:** A data extraction form was used to collect data including the research methodology, title, first author, year of publication, research type, research procedure, sampling method, sample size, research setting, data collection instruments, results, and information related to heat wave adaptation solutions.
- **Data collection method:** A systematic review was conducted using the PRISMA 2020 Checklist. Endnote was used to store and organize the articles. After entering all the articles into the software, duplicate articles were identified and removed. Then, two researchers removed irrelevant titles by studying the titles and abstracts of the articles. Finally, after reviewing the full text of the articles, 58 articles were selected from a total of 1529 articles. The remaining 58 articles were individually screened based on the

inclusion and exclusion criteria. After removing irrelevant articles, the full text of the remaining articles was searched. Then, the quality of each article was assessed based on a standard format separately by two researchers. In cases of disagreement between the researchers, a third researcher helped to select the most relevant cases. Afterward, the adaptation components and solutions were extracted from the articles using the data extraction form (first author, year of publication, country, results, etc.). After reviewing the results and extracting adaptation strategies, the extracted and classified adaptation strategies were validated through an individual survey of subject-matter experts and a panel of emergency health experts and professionals.

- **Data analysis strategy:** The results of qualitative and quantitative studies extracted through the systematic review were organized and reported in a table.
- **Developing the primary tool (research synthesis):** The heat wave adaptation tool was developed based on the findings of the qualitative phase and systematic review. In this phase, the primary codes extracted from the qualitative phase and the systematic review were categorized based on “adaptation solutions against heat waves”. Then, the items were individually re-examined, and the related categories were carefully identified. Similar items were merged and their relevance was assessed by experts and professors. Furthermore, after removing irrelevant items, an item bank was developed for further validation.

Phase 3: The validation of the heat wave adaptation tool:

- **Objective:** Validating the heat wave adaptation tool.
- **Research population:** People living in Dezful and Ahvaz.
- **Sampling:** The respondents were selected using cluster sampling from the residents in different districts of two cities of Dezful and Ahwar in proportion to their population. The population of Ahvaz was about three times that of Dezful. Ahvaz had eight districts and Dezful had four districts.
- **Inclusion criteria:** Being over 18 years old, resident, and the willingness to participate in the study.

- **Exclusion criteria:** Unwillingness to participate in the study.
- **Research setting:** Dezful and Ahvaz.
- **Data collection instrument:** A structured questionnaire was developed with items scored on a five-point Likert scale to assess the components of adaptation to heat waves.
- **Data collection method:** The respondents were selected using cluster sampling from both cities in proportion to their population. The number of respondents selected from Ahvaz was three times that of Dezful. Dezful had 4 districts. Thus, the number of respondents selected from this city was divided by 4 to determine the number of respondents in each district. The similar procedure was repeated for Ahvaz with 8 districts. To this end, the number of respondents selected from this city was divided by 8 to determine the number of respondents in each district. The questionnaires were completed through street evaluations. For example, in a district with 3 streets, the questionnaires were divided by 3 and a questionnaire was completed for every three houses or shops in each street.

DATA ANALYSIS

Quantitative face validity assessment

At this phase, after explaining the objectives of the study, 10 respondents were asked to express their opinion regarding the comprehensibility of each item based on a five-point Likert scale (5 — totally comprehensible, 4 — somewhat comprehensible, 3 — moderately comprehensible, 2 — slightly comprehensible, and 1 — very incomprehensible). Afterward, the impact score of each item was calculated using the following formula:

$$\text{Impact Score} = \text{Frequency [\%]} \times \text{Importance}$$

Where frequency (percentage) refers to the number of people who gave a score of 4 or 5 to an item and importance is the average score of importance on the above Likert scale. If the impact score exceeds 1.5, the item will be considered suitable for further analysis [42]. However, the items with a score of less than 1.5 had a high level of difficulty and ambiguity.

Qualitative face validity assessment

Qualitative interviews were conducted with the same respondents who rated the items in the previous

Table 1. Estimating CVR based on Lawshe's table [43]

Number of raters	Minimum acceptable CVR
5	0.99
6	0.99
7	0.99
8	0.75
9	0.78
10	0.62
11	0.59
12	0.56
13	0.54
14	0.51
15	0.49
20	0.42
25	0.37
30	0.33
35	0.31
40	0.29

stage. They were asked to specify the reason(s) for the incomprehensibility of any item with a score of less than 1.5. Thus, using the feedback from the respondents, the problematic items were revised to make them more comprehensible.

Qualitative content validity assessment

Ten disaster and emergency experts qualitatively assessed the content validity of the checklist. They rated the items in terms of grammar, wording, clarity, classification and scoring, order and importance, and relevance. Afterward, the items were revised based on their feedback. However, no item was removed at this stage.

Quantitative content validity assessment

The content validity of the instrument was assessed quantitatively using the content validity ratio (CVR) and the content validity index (CVI):

A. Estimating the content validity ratio (CVR)

To calculate the CVR, the items were assessed by 10 experts using Lawshe's method (Tab. 1). The experts were asked to determine whether each item operationally measured a theoretical construct or not. To this end, each item was rated on a 3-point scale (3 — necessary, 2 — useful but not necessary, and 1 — not necessary) [57].

The experts were different from the respondents surveyed in the qualitative content validity stage. The items with a minimum CVR of 0.62 were considered acceptable.

B. Estimating the content validity index (CVI)

Ten raters assessed the items to find out the extent to which they measured the intended construct. The raters scored the relevance of each item on a four-point Likert scale (1 — not relevant, 2 — somewhat relevant, 3 — relevant, and 4 — very relevant). The CVI value was calculated as the percentage of the acceptable score for each item scored 3 or 4 using the following formula [44]:

$$CVI = \frac{\text{The number of raters giving a score of 3 or 4}}{\text{The total number of raters}}$$

The items with a CVI score higher than 0.79 were considered relevant. The items with a CVI score of 0.79 to 0.70 were considered controversial and needed revision. Finally, the items with a CVI score of less than 0.70 were irrelevant and removed. Moreover, the item-level content validity index (I-CVI) was used to assess the quantitative content validity of each item. The scale-level content validity index (S-CVI) was also used to assess the content validity of the whole scale. I-CVI is a raw score. For example, a completely relevant item, which is scored 4 by 7 out of 10 raters has an I-CVI score of 0.7 [45]. S-CVI/average is called the average of I-CVI scores and was reported in the reviewed articles.

S-CVI/universal is a ratio of items of an instrument that were scored 3 and 4 by all raters in terms of relevance. It is a proportion of the items of a tool that are scored 3 or 4 in terms of the content by the raters [45]. Instrument developers often consider a value of 0.80 as the lowest acceptable requirement for S-CVI/average, but they propose an S-CVI score of 0.90 and above and an I-CVI score of 0.78. Furthermore, to increase the response accuracy, the probability of chance agreement (CP) in the responses to the items was first checked to reduce the probability that the respondents had reached an agreement about the instrument items by chance. To this end, the modified Cohen's kappa coefficient (K^*) was calculated using the following formula as an indicator of the evaluators' agreement about the relevance or non-relevance of the item [46]:

$$K^* = \frac{I-CVI - p_c}{1 - p_c} \quad p_c = \left[\frac{N!}{A!(N-A)!} \right] \cdot 5^N$$

Table 2. Estimating I-CVI and K values

Number of raters	Items scored 3 or 4	I-CVI	K
3	3	1.00	1.00
3	2	0.67	0.47
4	4	1.00	1.00
4	3	0.75	0.67
5	5	1.00	1.00
5	4	0.80	0.76
6	6	1.00	1.00
6	5	0.83	0.81
6	4	0.67	0.57
7	7	1.00	1.00
7	6	0.86	0.85
7	5	0.71	0.65
8	8	1.00	1.00
8	7	0.88	0.88
8	6	0.75	0.72
9	9	1.00	1.00
9	8	0.89	0.89
9	7	0.78	0.76

$$k = \frac{\text{Proportion}_{\text{Agreement}} - \text{Proportion}_{\text{Chance agreement}}}{1 - \text{Proportion}_{\text{Chance agreement}}}$$

Where N is the number of raters and A is the number of agreements in terms of relevance.

Then, the Cohen's kappa coefficient was estimated with the number of agreements on relevance (1-CVI) and the probability of chance agreement. Cohen's kappa coefficient is interpreted as follows:

1. Cohen's kappa coefficient of 0.40 to 0.59 shows a poor agreement.
2. Cohen's kappa coefficient of 0.60 to 0.74 shows a good agreement.
3. Cohen's kappa coefficient of greater than 0.74 shows perfect agreement.

The items that met the third requirement ($K^* > 0.74$) were kept and the other items were removed [42, 45]. In the present study, all I-CVI, PC, and K^* values were calculated (Tab. 2).

Construct validity

Exploratory factor analysis was run to assess the construct validity of the instrument. In exploratory factor analysis, the researcher does not have any pre-suppositions about the number or nature of the

variables, and as the name suggests, it is exploratory. Thus, this analysis allows the researcher to discover the main constructs needed to generate a theory or model from a relatively large set of latent constructs in a set of questions. In exploratory factor analysis, the researcher does not have any presumptions about the factors or constructs in the instrument. However, the goal is to find out what the constructs in the instrument are like and under which factor or group each item is placed [47].

Prerequisites for running exploratory factor analysis

- **Sample size:** Comrey and Lee's scale was used to estimate the sample size in this study. Comrey and Lee proposed a graded scale of sample size for scale development: 100 — poor, 200 — fair, 300 — good, 500 — very good, and 1000 — excellent [39]. Therefore, in the present study, the estimated number of respondents required for factor analysis was 403 people.
- **The communality of the variables:** The communality of the variables explains the percentage of variance that a variable has in all factors. Thus, it can be considered a reliable indicator. A high communality of the variables shows that the sample size is adequate. In the communality of the variables table, items with a communality value of less than 0.2 are removed by exploratory factor analysis [48]. In this table, there was no communality of less than 0.2.
- **Overdetermination:** The minimum required number of variables for each extracted factor was 3 variables. The factors with less than 3 variables are considered weak and unstable [49].
- **Factor loading:** In this study, the minimum acceptable factor loading for the presence of an item in a factor was 0.3, which was calculated using the following equation [50]:

$$CV = 5.152 \div \sqrt{(n - 2)}$$
 Where CV is the number of extractable factors and n is the sample size [50].
- **Normality:** Factor analysis is more powerful for the data that have a normal distribution. The assumption of normality was checked by univariate distribution based on skewness of ± 3 and kurtosis of ± 7 [51]. The determinant value was estimated as 0.58 using multivariate distribution.
- **Correlation:** Another prerequisite was the existence of a correlation between variables [49].

Following a strict approach, the minimum required correlation is 0.3 [45]. However, based on a moderate view, regardless of the r value, only the items whose correlation value was above 0.05 were removed [42, 49]. In the present study, p -value was used as a measure of correlation which was significant for all items.

- **Missing values:** If some respondents did not answer some items, the missing data should be taken into account so that they do not affect the desired estimates [42].
- **Sampling adequacy:** The size of sampling adequacy is shown in the anti-image diameter of the correlation matrix. Here, the variables with a measurement accuracy of less than 0.5 were removed (FLD, 2000). In the SPSS output, two Bartlett's and Kaiser-Meyer-Olkin (KMO) values are estimated as the indicators of sampling adequacy. The KMO value should be above 0.5 for each item. Besides, the result of Bartlett's test should be significant [52, 53]. In the present study, both the KMO and KMO values were estimated for each item. Bartlett's values were found to be significant.

Data extraction

In SPSS software, there are seven data extraction models [50]. In this study, exploratory factor analysis was performed using the maximum likelihood method.

Determining the number of factors

In this study, two criteria, i.e. scree plot (Cattel, 1996) and Kaiser's (1960) criteria were used to determine the number of factors.

- **Scree plot:** A scree plot is used to replace the variance of each component in the data and also to determine the effective number of factors that can be extracted. In this plot, the eigenvalues are drawn on the horizontal axis and the number of factors on the vertical axis. The factors in this plot are selected visually and wherever the plot fails, the factors that are placed before it, are known as suitable factors [42]. In this study, the scree plot was used as the main criterion, which obtained three factors.
- **Eigenvalue:** If there are several variables and a composite variable is created by adding them, this variable will have a dispersion that is directly related to the dispersion of the responses given to each variable. Since variables with a larger

variance have a greater effect on the composite variance, it is necessary to standardize the variables before summing them, or in other words, calculate the Z score. In factor analysis, this value is called the eigenvalue. Only factors with an eigenvalue of 1 or greater are considered for significance, and factors with eigenvalues of less than one are discarded [54]. Keyser's values estimated through the eigenvalues for three extracted factors were 3.09, 2.78, and 2.04, respectively. Thus, the eigenvalues for all three extracted factors were obtained above 1.

The rotation of the extracted factors

Through rotation, the variables that are placed on more than one factor are mainly assigned to one factor [55]. The common rotation techniques are direct oblimin and promax. Direct oblimin tries to simplify the mathematic structure and output, while promax is useful on larger datasets due to its speed. Promax ultimately leads to a higher correlation between factors and achieving a simple construct (Gorsuch, 1983) [42]. In this study, Promax rotation was used. Then, after substituting the items in three extracted factors, the factors were named and their reliability was checked.

Reliability analysis

Reliability refers to the degree of stability and internal consistency of the results produced by a tool in repeated and multiple measurements. Thus, it is associated with the credibility and repeatability of a tool. There are several methods to assess the reliability of an instrument, specifically the test-retest method and internal consistency [56]. In this study, the reliability of the instrument was assessed using the test-retest method and internal consistency. Internal consistency was evaluated using Cronbach's alpha and average inter-item correlation (AIC). The values greater than 0.7 were acceptable. An AIC of 0.2 to 0.4 was considered to indicate good internal consistency. Then, the instrument was re-administered to check its consistency [57]. The ICC values were interpreted as follows: Less than 0.4 (poor reliability), 0.4–0.6 (moderate reliability), 0.6–0.8 (good reliability) and 0.8–1 (perfect reliability) [58]. The final instrument was administered to 30 persons. It was re-administered after 14 days to the same persons with the same conditions. Then, the scores obtained in these two stages were compared using the correlation coefficients.

DISCUSSION

Although many research efforts have been taken in different parts of the world, none of the studies had used a standard tool to determine the level of adaptation of societies against heat waves, and there is no such tool, and sometimes the level of adaptation has been measured through questionnaires that were not psychometrically evaluated [36–39]. Most studies have highlighted the increased frequency and length of heat waves and their harmful effects on health [7, 8, 59–65]. Thus, governments and related officials should pay more attention to heat waves and seek effective solutions for greater adaptation and damage mitigation measures. These measures can reduce the human and financial consequences of heat waves. Accordingly, the tool developed in the study focused on adaptation solutions. Thus, the tool can measure the adaptation level against heat waves in different regions. The outcomes can be used to formulate effective adaptation interventions and solutions.

Using the findings from the qualitative phase of the study and the data from the interviews, the themes related to adaptation and adaptation solutions and strategies were extracted. Overall, two themes of “adaptive paradigm” and “adaptive strategies” were extracted. Each theme was divided into two main categories and several subcategories. For example, the main category of “governance measures” was divided into four subcategories, including managerial and research subcategories. In the systematic review, eleven strategies for adaptation to heat waves including education and awareness raising, green infrastructure, and critical infrastructure were identified. The items in the instrument were formed by merging the obtained codes. Afterward, the psychometric properties of the tool were assessed. The items were placed into three factors that play a significant role in adaptation to heat waves.

Most of the studies on adaptation to heat waves have tried to discover individual behaviors, including effective adaptive behaviors against heat waves such as adequate hydration, paying attention to daily weather forecasts, modifying lifestyle, using air conditioners and fans, frequent showering, reducing the duration of outdoor activities, paying attention to health protection guidelines, reducing and changing the level of physical activity, paying attention to the type of clothing, doing things in the early hours of the day, going to parks, canopies, and

swimming pools, and using balconies in the cool hours of the day [30, 39, 66–70].

In addition to individual adaptive behaviors, organizing national programs to cope with the effects of heat waves is very important and improves the level of societal adaptation [71]. Moreover, managers and policymakers need to have a good perception of the dangers of heat waves [72]. Concerning individual planning, people must improve their knowledge by receiving information to protect themselves to formulate individual plans for adaptive behaviors. The heat wave adaptation tool was developed based on heat wave adaptation strategies used both in the affected society and around the world.

Limitations

Lack of face-to-face access to all study participants due to time interference with the COVID-19 pandemic was one of the main limitations in the qualitative phase of the research, so other communication methods were used, including phone conversations. Another limitation of the qualitative study was the bias in the analysis and interpretation of the results, which was maximized by adopting strategies such as examining qualitative data in different stages of analysis with some participants and research colleagues. One of the limitations in the implementation of the quantitative study parts of the research was the non-cooperation of some participants due to not having enough time to participate in the study, which was attempted by sending the questionnaire at a time determined by themselves and setting a longer response deadline and explaining the value of the participants' opinions. In the process of building the tool, we improved the process of participation in this study. Another limitation was the use of all dimensions of the society; because the qualitative study in the present research was conducted on the people of the society, the resulting tool was designed based on the individual dimension of people's adaptive behaviors.

CONCLUSIONS

The tool developed in this can direct the attention of senior health managers to preparedness against heat waves. Thus, they can identify the areas with less adaptation to heat waves, meet their needs by implementing damage mitigation programs, and help them avoid the economic, social, physi-

cal, and psychological effects of heat waves. The main contribution of the present study was that it addressed the concept of adaptation to heat waves using a combination of inductive and analogical methods. Besides, this is the first study in Iran to develop and validate a tool for assessing adaptation to heat waves. The developed tool can help planners in the Ministry of Health and researchers to evaluate the level of adaptation in different regions and formulate plans of action to reduce the consequences of heat waves.

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Conflict of interest

The authors declared no conflict of interest.

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BIOMARKERS LEVELS INDICATE COVID-19 SEVERITY AND FATALITY

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KEY WORDS: D-dimer; biomarker; COVID-19; SARS-CoV-2; severity; outcome

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To the Editor,

we read with great interest the article by Kilic and Dalkilinc Hokenek concerning to association between D-dimer levels and COVID-19 patients' mortality [1]. Since December 2019, a new coronavirus known as SARS-CoV-2 has produced a global outbreak of respiratory sickness known as coronavirus disease 2019 (COVID-19), which is still spreading rapidly. By the end of January 2023, there will have been over 668.8 million verified COVID-19 patients globally.

Understanding the fluctuation and profile of various biomarkers as a function of different COVID-19 outcomes would assist in the creation of a risk-stratified strategy for the management of individuals with this condition [2, 3]. One area of scientific interest is the thrombosis reported with this rare viral pneumonia. Unlike patients with community-acquired pneumonia, the COVID-19 patient appears to have an increased thrombotic reaction to the virus. The presence and severity of microthrombosis in these individuals have been linked to worse outcomes [4, 5]. D-dimer, a fibrin breakdown product, is well established as an indirect measure of thrombotic activity in venous thromboembolism (VTE) population risk assessment. Furthermore, D-dimer has been demonstrated to be raised in various hypercoagulable situations such as cancer, sepsis, pregnancy, and the postoperative period. D-dimer has been recognized as a helpful prognostic marker in this patient group, with the suspicion of thrombo-

sis in COVID-19 patients adding to disease severity and as a driving element of the respiratory illnesses observed in this disease process.

Elevated D-dimer levels have been found to be one of the most prevalent test results in COVID-19 patients requiring hospitalization. Kilic and Dalkilinc Hokenek indicate that patients with high D-dimer levels had higher in-hospital mortality rates. It is worth emphasizing here that [1] Zhang et al. [6] showed that D-dimer levels larger than 2.0 g/mL on admission (a fourfold rise) might successfully predict in-hospital mortality in COVID-19 patients, indicating that D-dimer could be an early and useful marker to enhance COVID-19 patient care.

With the global increase in COVID-19 cases due to its highly infectious nature, various research has reported on also other predictors of illness severity in COVID-19 patients.

According to studies, severe or fatal cases of COVID-19 disease are linked to an increased white cell count, creatinine, interleukin-6 (IL-6), C reactive protein (CRP), lactate dehydrogenase, blood urea nitrogen, markers of liver and kidney function as well as albumin levels, when compared to milder cases where survival is the outcome [7–10]. These studies provided an early insight into the impact of SARS-CoV-2 infection, although the conclusions cannot be generalized in many situations due to geographical limits, single-center experience, and small cohorts.

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In view of the above, it was critical to establish a worldwide database on the clinical parameters of COVID-19 patients, from which multivariate data analyses could be done.

Conflict of interest

The authors declared no conflict of interest.

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C-REACTIVE PROTEIN IN COVID-19 PATIENTS

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KEY WORDS: COVID-19; C-reactive protein (CRP); inflammation; biomarker; pneumonia

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To the Editor,

we were interested in the article by Ansari-Moghaddam et al. referring to the role of complete blood cell counts and C-reactive protein (CRP) in COVID-19 patients [1]. We fully agree that the search for early predictive markers in both COVID-19 and other diseases is extremely important, as it allows for the detection of the disease at an early stage and the early implementation of appropriate therapy [2]. Therefore, the analysis of the importance of CRP and other markers in COVID-19 is of key importance [3, 4].

C-reactive protein (CRP) is a biomarker commonly used to measure inflammation in the body. Elevated levels of CRP have been observed in patients with COVID-19, and it is thought to play a role in the severity of the disease. C-reactive protein (CRP) is produced by the liver in response to inflammation. It is considered to be a non-specific marker, meaning that it can be elevated in a wide range of conditions, including infections, autoimmune diseases, and cancer. However, in the case of COVID-19, CRP levels have been found to be particularly high, even in patients with mild symptoms.

Stringer et al. evaluated the role of CRP as a prognostic marker among 1,564 COVID-19 patients and showed that a threshold cut-off of CRP ≥ 40 mg/L performed well to predict mortality [5]. In another study by Smilowitz et al. CRP concentrations above 108 mg/L were associated with VTE, acute kidney injury, critical illness, and mortality, compared with CRP below this level [6].

The reason for the high CRP levels in COVID-19 patients is not entirely clear, but it is thought to be related to the severe inflammation that occurs in the lungs of patients with the disease. COVID-19 is a viral infection that causes severe damage to the respiratory system, and it is thought that the immune response to the virus leads to a significant amount of inflammation in the lungs [7]. This inflammation can cause the release of cytokines, which are chemicals that promote inflammation, and this in turn can lead to the production of CRP.

Another study that tried to correlate the CRP levels with the oxygen saturation level in COVID-19 patients found that patients with high CRP levels had a significantly higher risk of requiring oxygen therapy and intensive care [8]. The study also showed that CRP levels were an independent predictor of the need for oxygen therapy.

CRP levels are also thought to be associated with the risk of developing complications in COVID-19 patients. A study that looked at CRP levels in patients with COVID-19 found that those with high CRP levels were at a higher risk of developing pneumonia and acute respiratory distress syndrome (ARDS), which is a severe complication of COVID-19 that can lead to death [9].

In conclusion, C-reactive protein (CRP) is a biomarker that has been found to be elevated in COVID-19 patients. Elevated levels of CRP are thought to be associated with the severity of the disease, as well as the risk of complications such as pneumonia and

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ARDS. CRP levels have also been found to be an independent predictor of the need for oxygen therapy in COVID-19 patients. As such, CRP can be useful as a biomarker for monitoring the progression of the disease and for identifying patients who are at a higher risk of developing complications. It should be noted that CRP is not a specific marker for COVID-19 and high CRP levels can be caused by other conditions [10]. However, in the context of COVID-19, it can provide valuable information for clinical management and prognosis.

Conflict of interest

The authors declared no conflict of interest.

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WHY MITIGATION MEASURES ARE LESS CONSIDERED IN DISASTER MANAGEMENT IN LOW-INCOME COUNTRIES?

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ABSTRACT

After the earthquake in Indonesia and Japan, the governments gathered in Kobe and pledged to prioritize the following measures in their countries: Ensuring that disaster risk reduction is a national and a local priority with a strong institutional basis for implementation. Identifying, assessing and monitoring disaster risks and enhancing early warning. Using knowledge, innovation, and education to build a culture of safety and resilience at all levels. Reducing the underlying risk factors. Strengthening disaster preparedness for effective response at all levels. Also, in the Sendai Framework, they committed that the risk perception should be the priority of governments and should be considered in all civil structures. In this letter, there are reasons that can reduce mitigation measures of governments in earthquake-prone countries.

KEY WORDS: earthquake; mitigation measures; disaster management

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Dear Editor,
countries that are located on earthquake faults, according to the Hugo document, should consider proper management of the resilience of building structures so that the loss of life and property after an earthquake is as low as possible. Also, the first and most important action in the Sendai framework is the commitment of governments to risk perception against all possible hazards and strengthen the governance of risk management. But looking at different countries, we see differences in the implementation of these commitments [1–4].

A country like Japan has strengthened the resiliency of the structures against earthquakes of eight to eight and a half magnitude by fortifying the building structures, so that this intensity of the earthquake brings the

least financial and life losses for the residents of this country. And finally, an eight-magnitude earthquake is not considered a disaster for this country [5–7].

The most important lessons learned from the actions of the Japanese government for other earthquake-prone countries are:

1. Having a holistic preparedness (Scenario, Exercise, Exercise evaluation) to disaster reduction management.
2. Investing in the mitigation phase is important (structural and non-structural measures), but is not a substitute for preparedness
3. Extensive cooperation of all governmental and non-governmental sectors

But why do low-income countries in the Middle East try less to mitigation measures to reduce earth-

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quake impact? Because the results of mitigation measures are not obvious in the short term, so governments in these countries are more eager to do things that have an immediate answer. For this reason, most government measures in these countries are in the response and recovery phases. On the other hand, the weak and one-dimensional economy of these governments has also weakened investment in the resilience of building structures.

The recent earthquake in Turkey, caused a disaster and catastrophe status and requested international aid from the government of this country, if it happened in Japan, it would have been managed by the local and national governments.

It is very painful to hear about the death of more than 50,000 people in Turkey and Syria at a time when all governments should adhere to the Hyogo and Sendai framework. Appreciating all measures taken in the response and recovery phase, the need to invest in the resilience of structures in these countries is quite clear. Therefore, international organizations and high-income countries should help the governments in these countries to fulfill their commitment to the Sendai document. And the governments of these countries should be forced to implement their obligations in the field of mitigation and structural resilience.

Conflict of interest

All authors declare no conflict of interest.

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VIDEOLARYNGOSCOPY: THE RELEVANCE IN PATIENTS WITH COVID-19

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KEY WORDS: videolaryngoscope; direct laryngoscope; endotracheal intubation; SARS-CoV-2; COVID-19

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To the Editor,

The COVID-19 pandemic has placed a significant burden on healthcare systems worldwide, with critical care teams having to adapt rapidly to new challenges [1, 2]. Among these challenges is the management of the airways of patients with COVID-19, which poses a significant risk to healthcare workers due to the high viral load in the upper respiratory tract [3]. Videolaryngoscopy has emerged as a relevant tool for airway management in COVID-19 patients, offering a safer and more efficient alternative to traditional techniques.

Traditional airway management procedures, such as direct laryngoscopy, have been associated with an increased risk of aerosol-generating procedures (AGP) and transmission of SARS-CoV-2 to healthcare workers. AGP is a term used to describe medical procedures that can generate aerosols, such as coughing, sneezing, or speaking, which can contain infectious particles. AGP has been linked to an increased risk of transmission of COVID-19 to healthcare workers. Therefore, it is essential to reduce the use of AGP in the airway management of COVID-19 patients to minimize the risk of transmission.

Videolaryngoscopy has various advantages over conventional airway management treatments. For starters, it eliminates the need for a stethoscope since the camera offers a direct vision of the

vocal chords. Second, it cuts down on the amount of time spent on airway management treatments, which is especially significant in critically sick patients. Finally, it increases intubation success rates, lowering the risk of problems associated with several attempts at intubation.

Numerous studies have found that videolaryngoscopy improves airway management in COVID-19 patients [4–6]. A meta-analysis of 20 trials suggests that PPE reduces the effectiveness of endotracheal intubation [7]. The researchers also discovered that the use of direct laryngoscopy for intubating patients with suspected or confirmed COVID-19 by an incubator wearing level C PPE is associated with an overall reduction in intubation time and an increase in intubation success rates compared with video laryngoscopes.

In another study with 219 COVID-19 patients, videolaryngoscopy was reported to have a 97% success rate with a minimal incidence of problems [8]. In addition, videolaryngoscopy reduced the requirement for AGP by 50% when compared to direct laryngoscopy.

The use of personal protective equipment (PPE) is essential to reduce the risk of transmission of COVID-19 to healthcare workers during airway management procedures. However, the use of PPE can also reduce the efficiency of the procedures per-

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formed, as it can limit the field of vision and make it more difficult to perform certain tasks [9, 10]. Videolaryngoscopy can help overcome some of these challenges by reducing the need for direct visualization and improving the field of vision.

Several studies have reported on the efficacy of videolaryngoscopy in the airway management of COVID-19 patients while wearing PPE [5, 7]. A study involving 88 COVID-19 patients found that videolaryngoscopy had a success rate of 95% while wearing full PPE. The study also reported that the time spent on airway management procedures was reduced compared to direct laryngoscopy, despite the additional time required for donning and doffing of PPE.

Another study involving 106 COVID-19 patients found that videolaryngoscopy had a success rate of 96% while wearing full PPE. The study also reported that videolaryngoscopy reduced the need for AGP and decreased the time spent on airway management procedures.

Summarizing, the use of videolaryngoscopy represents an important advance in airway management for COVID-19 patients. It offers a safer and more efficient alternative to traditional techniques, which can help reduce the risk of transmission of COVID-19 to healthcare workers and improve patient outcomes.

Conflict of interest

All authors declare no conflict of interest.

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