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Review

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Anaphylaxis: A Life-Threatening Hypersensitivity Reaction

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ABSTRACT

Anaphylaxis is an acute, life-threatening systemic hypersensitivity reaction, primarily mediated by immunoglobulin E. Food allergy is the most common trigger, followed by medications. Patients with anaphylaxis typically present with cutaneous or mucosal symptoms, often accompanied by respiratory and gastrointestinal manifestations. Epinephrine remains the first-line treatment for anaphylaxis. It is crucial to educate patients and caregivers on recognizing anaphylactic symptoms and the proper use of epinephrine autoinjectors.

Keywords: Anaphylaxis, children, immunology and allergy

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INTRODUCTION

Anaphylaxis is a rapidly developing, life-threatening systemic hypersensitivity reaction of varying clinical presentation and severity, resulting from the sudden release of mediators from mast cells and basophils.[1] It is the most severe clinical manifestation of allergy and can be fatal if left untreated. Prompt diagnosis and effective treatment are crucial for patient survival, making it an essential emergency condition that every physician should recognize and manage effectively.

DEFINITION

Anaphylaxis was first described in 1902 by Richet and Portier during vaccination studies in dogs, and they defined it as symptoms occurring in response to immunity.[2] The earliest recorded case of anaphylaxis is believed to be the death of Egyptian Pharaoh Menes in 2640 BC due to a bee sting. According to modern terminology, anaphylaxis mediated by immunological mechanisms such as immunoglobulin E (IgE), immunoglobulin G, and the complement system is classified as allergic (immunologic) anaphylaxis. In contrast, anaphylaxis resulting from non-immunological mechanisms, previously termed anaphylactoid reactions, is now referred to as non-allergic anaphylaxis. Anaphylaxis occurring without identifiable triggers is classified as idiopathic anaphylaxis (IA).

ETIOLOGY AND EPIDEMIOLOGY

The incidence of anaphylaxis remains uncertain; however, the estimated lifetime prevalence in the general population ranges from 0.05% to 2%.[3] The prevalence is higher in children. One study reported an overall incidence of anaphylaxis across all age groups as 49.8/100,000 person-years, while in the 0–19 years of age group, the incidence was 70/100,000 person-years.[4] Recent studies indicate an increasing prevalence of anaphylaxis, particularly among young individuals.[5] There has been a noticeable rise in hospital admissions due to food-related anaphylaxis among children.[6] This increase is particularly significant among children under the age of 10. A study by Lin et al. found that hospital admissions in this age group quadrupled between 1990 and 2006.[7]

Food, medications, and insect stings are the most common triggers of anaphylaxis across all age groups.[7] The most frequently implicated foods include cow's milk, eggs, soy, peanuts, tree nuts, fish, and shellfish. The most common medications causing anaphylaxis are antibiotics and nonsteroidal anti-inflammatory drugs. Other rare causes include latex, aeroallergens, and vaccines.

Food allergy is the leading cause of anaphylaxis in children, followed by medications.[8] In a retrospective study conducted in Turkey, foods accounted for 38.4% of anaphylaxis cases, followed by venom (37.5%) and medications (21%).[9]

PATHOPHYSIOLOGY

Anaphylaxis is classically mediated by IgE, leading to mast cell and basophil degranulation and the subsequent release of mediators.[10] These mediators can be classified into two groups: Preformed mediators (histamine, heparin, tryptase, chymase, carboxypeptidase A3, tumor necrosis factor-alpha [TNF-α], and cathepsin G) and newly synthesized mediators (platelet-activating factor [PAF], prostaglandin D2, leukotriene C4, cytokines such as interleukin [IL]-5, IL-6, IL-8, IL-13, IL-33, TNF-α, and granulocyte-macrophage colony-stimulating factor, as well as chemokines including MIP-1α, MIP-1β, and MCP-1).

In some cases, mast cells and basophils can be immunologically activated without IgE mediation.[11] Anaphylaxis can also occur through non-immunological mechanisms. Physical factors such as exercise, cold, heat, ultraviolet radiation, and certain drugs such as ethanol and opioids can directly induce mast cell degranulation, leading to anaphylaxis.

IA refers to cases where no specific trigger can be identified.[11] The exact incidence and prevalence of IA remain unknown. Its clinical presentation is similar to other forms of anaphylaxis, with an acute onset that may worsen within minutes to hours. Although the pathophysiology of IA is not yet fully understood, it is hypothesized that an IgE-mediated pathway triggered by unknown factors may be the underlying mechanism.

CLINICAL PRESENTATION

Anaphylaxis most commonly affects five organ systems, including the skin, mucosa, respiratory, cardiovascular, gastrointestinal, and neurological systems.[1,2,12] Symptoms typically appear within 5–30 min following parenteral exposure, but they may take up to an hour or more to develop. After oral exposure, symptoms usually manifest within the first 2 h but can be delayed for several hours. The faster the onset of symptoms, the more severe the anaphylaxis is likely to be. Early-onset reactions carry a higher risk of fatality. Initial symptoms include a sense of unease, fear of death, dizziness, and syncope.

At the onset of an anaphylactic reaction, "prodromal symptoms" such as mild itching, a burning sensation in the palms, soles, or anogenital region, metallic taste, anxiety, headache, and disorientation may occur.[3] The clinical manifestations of anaphylaxis are summarized in Table 1.

DIAGNOSIS

The diagnosis of anaphylaxis is primarily clinical.[1,13] A detailed history should be obtained promptly in patients presenting with anaphylactic symptoms; however, treatment should not be delayed. The clinician should inquire whether the patient was exposed to potential anaphylactic triggers before symptom onset and whether any underlying conditions could mimic anaphylaxis. Anaphylaxis is diagnosed if any of the three criteria summarized in Table 2.

Key history elements include the timing of symptom onset after exposure, treatments received during the attack, and attack duration.[2,12,14] A detailed history of potential triggers is crucial. Questions should cover food and medication intake in the preceding 6 h, insect stings, physical activity, and exposure to temperature extremes. In female patients, the association with the menstrual cycle should be explored.

In 2006, the National Institute of Allergy and Infectious Diseases and the Food Allergy and Anaphylaxis Network developed a consensus definition of anaphylaxis, outlining diagnostic criteria.[15]

The most commonly affected systems in anaphylaxis are the skin, respiratory, and cardiovascular systems.[15] Although skin involvement is observed in 80%–90% of cases, anaphylaxis can occur without cutaneous manifestations, making diagnosis more challenging. Respiratory symptoms are more common in children, whereas cardiovascular symptoms predominate in adults.[16]

Table 1. Clinical manifestations of anaphylaxis

System	Symptoms
Skin and mucosa (80–90%)	• Urticaria, angioedema, morbilliform rash • Itching, tingling, hot flashes, flushing • Periorbital itching, swelling, erythema, conjunctival itching, tearing • Lip, tongue, uvula, and soft palate itching and swelling • Itching in the external ear canal, palms, soles, and genital area.
Respiratory system (40–70%)	• Nasal: Rhinorrhea, congestion, itching, sneezing • Laryngeal: Hoarseness, choking sensation, stridor, dysphonia, dysphagia • Pulmonary: Dyspnea, wheezing, bronchospasm, respiratory failure, cough, chest tightness • Cyanosis.
Cardiovascular system (10–45%)	• Hypotension • Tachycardia, bradycardia, arrhythmia • Chest pain, palpitations • Shock, syncope • Cardiac arrest.
Gastrointestinal system (30–45%)	• Nausea, vomiting • Abdominal pain, cramping • Diarrhea.
Neurological system (10–15%)	• Fear of death, restlessness • Altered consciousness, seizures • Confusion • Headache, blurred vision • Sudden behavioral changes • Irritability and clinging to caregivers (in infants and young children).
Other symptoms	• Sweating, incontinence • Metallic taste, dysphagia • Uterine contractions.

LABORATORY

Anaphylaxis is primarily diagnosed clinically.[1] However, in some cases, laboratory tests such as serum tryptase and histamine levels can be utilized. Elevated serum histamine levels measured between 15 min and 1 h after the onset of symptoms may aid diagnosis. A serum tryptase level >11.4 mcg/L or an increase above baseline (>2 ng/mL+1.2×[baseline tryptase level]) measured between 15 min and 3 h after symptom onset supports the diagnosis of anaphylaxis.[12] However, normal levels do not exclude anaphylaxis.[2]

Additional markers of mast cell activation, such as carboxypeptidase A3, chymase, PAF, and cytokines (urinary leukotriene E4 and 9α, 11β prostaglandin F2), may also be used in diagnosing anaphylaxis.[2] In addition, the basophil activation test has recently been introduced as a diagnostic tool for anaphylaxis.

DIFFERENTIAL DIAGNOSIS

The most common condition mistaken for anaphylaxis is a vasovagal syncope episode.[12] In vasovagal syncope, sudden hypotension occurs due to vagal stimulation, often accompanied by bradycardia, whereas anaphylaxis typically presents with tachycardia. Vasovagal syncope is also characterized by pallor and sweating without urticaria or respiratory symptoms. Other conditions in the differential diagnosis of anaphylaxis include asthma attacks, urticaria, panic attacks, hyperventilation syndrome, and various forms of shock.

Table 2. Diagnostic criteria of anaphylaxis

1. Acute onset (within minutes to hours) involving skin and/or mucosal tissue (e.g., generalized urticaria, itching or flushing, swelling of lips, tongue, or uvula), plus at least one of the following:
2. a) Respiratory symptoms (dyspnea, wheezing, bronchospasm, stridor, reduced PEF, hypoxemia)
    b) Hypotension or signs of end-organ dysfunction (hypotonia, collapse, syncope, incontinence)
3. Exposure to a likely allergen with onset of at least two of the following within minutes to hours:
    a) Skin and/or mucosal involvement (e.g., generalized urticaria, itching, flushing, or angioedema)
    b) Respiratory symptoms (dyspnea, wheezing, bronchospasm, stridor, reduced PEF, hypoxemia)
    c) Hypotension or associated symptoms (hypotonia, collapse, syncope, incontinence)
    d) Persistent gastrointes-tinal symptoms (cramping, abdominal pain, vomiting)
4. Hypotension occurring within minutes to hours after exposure to a known allergen:
    a) In infants and children: Systolic blood pressure below age-specific thresholds or a >30% decrease from baseline
    b) In adults: Systolic blood pressure <90 mmHg or a >30% decrease from baseline

Hypotension thresholds: <70 mmHg for infants (1 month–1 year), (70+[2×age in years]) mmHg for children (1–10 years), and <90 mmHg for adolescents (11–17 years). PEF: Peak expiratory flow.

TREATMENT

The key to managing anaphylaxis is early recognition and rapid intervention.[17] At the onset of an anaphylactic episode, it is difficult to predict the severity, progression, or resolution, as the exact determinants of anaphylaxis remain unclear. Due to this uncertainty, early intramuscular (IM) epinephrine administration is crucial in preventing life-threatening symptoms. Epinephrine is the first-line medication and should never be delayed.

Epinephrine should be administered IM into the anterolateral thigh (vastus lateralis muscle).[18] The recommended dose is 0.01 mg/kg (0.01 mL/kg) of 1 mg/mL epinephrine, with a maximum dose of 0.3 mg (3 decigrams) in children and 0.5 mg (5 decigrams) in adults. The latest 2025 UpToDate guidelines recommend a uniform epinephrine dose of 0.01 mg/kg per injection, with a maximum dose of 0.5 mg, using a 1 mg/mL formulation and a 1 mL syringe. Epinephrine doses may be repeated every 5–10 min as necessary.[12] Treatment of anaphylaxis is summarized in Table 3.

Table 3. Treatment of anaphylaxis

Medication	Dose	Maximum dose	Route
Epinephrine (1 mg/mL)	0.01 mg/kg	0.3 mg	IM (lateral thigh)
Diphenhydramine	1 mg/kg	50 mg	IV
Ranitidine	1 mg/kg	50 mg	IV
Methylprednisolone	1–2 mg/kg	50 mg	IV
Salbutamol	2.5 mg	2.5 mg	Inhalation

IM: Intramuscular injection; IV: Intravenous injection.

Epinephrine should be administered at the first suspicion of anaphylaxis, as there are no absolute contraindications for its use.[2] Even in elderly patients and those with cardiovascular disease, the benefits of epinephrine outweigh the risks.[1] If an epinephrine auto-injector is used, a dose of 0.15 mg is recommended for children weighing 7.5–25 kg, while 0.3 mg is used for those over 25 kg.[19] The dose may be repeated every 5 min if necessary. In cases of refractory anaphylaxis requiring repeated doses, an epinephrine infusion should be initiated.[12]

Second-line treatments include removing the triggering factor, proper patient positioning, oxygen and fluid support, and inhaled beta-2 agonist therapy.[18] However, these are supportive measures and are not life-saving interventions.

Patients should be placed in a supine position with their legs elevated to enhance venous return.[3] Those experiencing hypotension should remain in this position until symptoms resolve, as sudden repositioning can lead to fatal “empty ventricle syndrome.”

High-flow oxygen (6–8 L/min) should be provided The latest 2025 UpToDate guidelines recommend administering oxygen at 15 L/min using a non-rebreather mask or high-flow oxygen masks capable of delivering at least 70–100% oxygen.[2]

For bronchospasm, 0.15 mg/kg salbutamol can be administered through inhalation every 15–20 min, up to a maximum of six doses.[12] If stridor due to laryngeal edema develops, nebulized epinephrine (2–5 mL, 1 mg/mL) may be administered in addition to IM epinephrine.

Intravenous (IV) access is essential in all anaphylaxis cases.[20] Due to increased vascular permeability, significant intravascular fluid loss can occur rapidly. Children should receive 20 mL/kg normal saline over 5–10 min, with repeat doses as needed. Up to 100 mL/kg may be required. If IV access is not feasible, intraosseous administration should be considered.

MONITORING AND DISCHARGE

Due to the risk of biphasic reactions, monitoring for at least 4–6 h is recommended.[20] Patients with respiratory symptoms should be observed for 6–8 h, while those with hypotension should be monitored for at least 12–24 h. Some authors recommend up to 24 h of observation, as reactions can occur within 72 h.[21]

Before discharge, risk factors should be evaluated, and patients should receive written action plans and prescriptions for epinephrine auto-injectors, along with proper usage instructions.[22] Referral to an allergy specialist for identifying triggers and preventive measures is essential.[23]

Indications for Epinephrine Auto-Injector Prescription[17]

1. Any patient with a history of anaphylaxis
2. Patients with a history of systemic allergic reactions
3. Patients with concurrent food allergies and asthma
4. Individuals allergic to peanuts, fish, or shellfish
5. Patients with IgE-mediated immediate food allergies should also be considered for an epinephrine auto-injector.

BIPHASIC REACTION

A biphasic reaction refers to the recurrence of anaphylactic symptoms after initial resolution without re-exposure to the allergen. It typically occurs within 12–72 h following the initial reaction.[20] Reported incidence rates vary from 1% to 20%.[17]

Severe initial anaphylaxis requiring multiple epinephrine doses may increase the risk of a biphasic reaction.[24] Although corticosteroids have been used to prevent prolonged anaphylaxis symptoms, a 2020 systematic review found no evidence supporting their efficacy in preventing biphasic reactions.

As anaphylaxis is unpredictable in its severity and course, early epinephrine administration is critical to prevent life-threatening complications.[25] A series of 164 fatal anaphylaxis cases found that the median time from symptom onset to respiratory or cardiac arrest was 5 min for iatrogenic anaphylaxis (e.g., anesthetics, IV drugs, and contrast agents), 15 min for insect stings, and 30 min for food-induced anaphylaxis.

Healthcare professionals must be well-trained in recognizing, managing, and preventing anaphylaxis.[26] Patients should be prescribed an epinephrine auto-injector, educated on its use, and referred to an allergist for further evaluation.

CONCLUSION

Many cases of anaphylaxis, and especially the potential for second-phase reaction, are underrecognized and undertreated, with potentially life-threatening consequences.[21] Immediate administration of epinephrine intramuscularly is often lifesaving, but repeated doses may be necessary in combination with other medications. Due to the risk of biphasic reactions, monitoring for at least 4–6 h is recommended. Patients with respiratory symptoms should be observed for 6–8 h, while those with hypotension should be monitored for at least 12–24 h.

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Developing an Evaluation Tool for the Urban Family Medicine Program of the Iranian Health System

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ABSTRACT

Objectives: This research aimed to develop an evaluation tool for the urban family medicine program of the Iranian health system.

Methods: This was a mixed-methods study. Following the literature review, a qualitative study was conducted through interviews with experts, executives, and presenters. Subsequently, the indicators derived from the literature review and qualitative study were merged, and the Delphi questionnaire (initial tool) was designed. The tool items were sent to 30 experts based on two criteria: Importance and executability. The evaluation tool was validated after two rounds of Delphi. In addition, index weights were calculated for the selected indicators, and index profiles were compiled.

Results: A total of 103 indicators were obtained from the literature review (23 structural, 57 process, and 23 output indicators). From the interview sessions, 17 indicators were derived (11 outcome indicators, 5 process indicators, and 1 structural index). The initial tool was created by merging the listed indicators from the literature review and qualitative sessions, followed by two rounds of Delphi with eight dimensions (service delivery, human resources, maternity and drug facilities, information systems, financial resources, community participation, and partnership) and 70 final indicators.

Conclusion: A precise and comprehensive evaluation of the family medicine program, based on the Donabedian model's three domains of structure, process, and outcomes, enabled the identification of strengths, problems, and systemic challenges. This paves the way for improving the service quality and customer satisfaction.

Keywords: Family practice, health status indicators, primary health care, program evaluation

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INTRODUCTION

The history of family medicine traces back to the period following World War II (World War II).[1] It was during this time that America recognized the board of family medicine in 1969, addressing the rise of various medical specialties and the marginalization of general medicine.

In Iran, the initial steps toward health system reforms included the establishment of health cooperatives in the latter half of 1999 in collaboration with the Ministry of Cooperation.[2] In addition, the comprehensive Tabriz network project was initiated in East Azerbaijan province in 2001. The project was validated by the Director-General of the World Health Organization (WHO) and senior experts from the Ministry of Health, Treatment, and Medical Education. By 2006, the family medicine program was implemented for villages and cities with populations under 20,000.

In 2011, urban family medicine commenced in two provinces, Mazandaran and Fars, under the title of Family Medicine version 02.[3] However, in East Azerbaijan province, urban family medicine began with the opening of health complexes in Tabriz in 2015, aiming for universal health coverage—complete population coverage, a comprehensive service package, and reduced out-of-pocket payments. A key feature of this program is the comprehensive management of health, regional health management by health complexes utilizing all capabilities (governmental and non-governmental), and shifting the focus of the University of Medical Sciences from providing services to ensuring the delivery of desirable services. This shift increases responsibility and responsiveness to the populace based on service packages and the continuous, comprehensive improvement of health service quality processes. The family medicine approach aims to enhance households' access to a defined service package at a reasonable cost through trained and motivated systems, ensuring high-quality, continuous, and comprehensive primary care for individuals and families of all ages and genders.[4-8] Given these factors, meticulous implementation of family medicine programs in urban areas is deemed essential for the health system. Identifying the shortcomings of the program requires a thorough examination of its dimensions and an evaluation of its execution. Undoubtedly, pinpointing challenges and issues is impossible without an appropriate tool.

This study aimed to develop an evaluation tool for an urban family medicine program in Iran's health system.

METHOD

This study employed a mixed methods approach. Initially, the evaluation method for the family medicine program (evaluation method, indicators used, evaluation timing, feedback provision, and potential problem correction) was determined in various countries using a narrative review method. The data from this stage were collected from diverse databases. English language databases, including PubMed, Scopus, Google Scholar, and Persian language databases, including IranDoc, IranMedex, SID, and Magliran. The initial search keywords were family medicine, family physician, family doctor, Family Practice, referral system, urban, city, metropolises, assessment, evaluation, monitoring, indicator, index, control, implementation, instrument, tool, checklist, dimensions, and their Persian equivalents on the domestic websites. Selecting and screening evidence from different sources is shown in Figure 1.

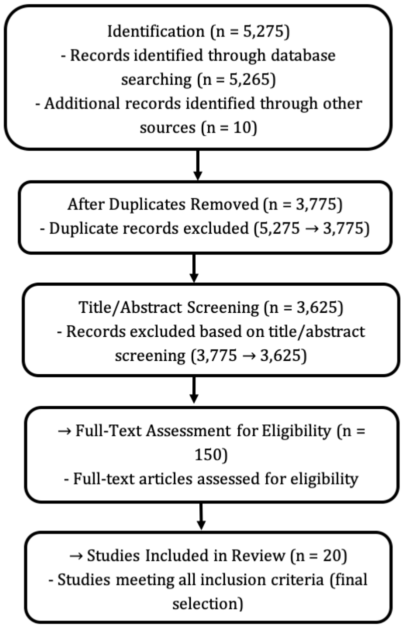
Identification (n = 5,275)
- Records identified through database searching (n = 5,265)
- Additional records identified through other sources (n = 10)
After Duplicates Removed (n = 3,775)
- Duplicate records excluded (5,275 → 3,775)
Title/Abstract Screening (n = 3,625)
- Records excluded based on title/abstract screening (3,775 → 3,625)
→ Full-Text Assessment for Eligibility (n = 150)
- Full-text articles assessed for eligibility
→ Studies Included in Review (n = 20)
- Studies meeting all inclusion criteria (final selection)

Figure 1. Selecting and screening evidence from different sources.

The primary research question was, "What are the evaluation indicators of the family medicine program in various countries?" A manual search of journals, selected articles, organizational reports, published government documents, websites, and other accessible sources of information was conducted. The inclusion criteria for articles and reports were the presence of evidence based on evaluation indicators, as well as monitoring and oversight of the family medicine program. Articles in languages other than Persian and English were excluded. Following the search, the selected articles were thoroughly reviewed, and pertinent information was extracted in the extensive review section using a specially designed data extraction form. Subsequently, a qualitative study was conducted to fulfill the first objective. At this juncture, data were gathered from experts and stakeholders who met the criteria for participation in the study. These individuals, with a minimum of 5 years of experience, included managers, deputies, and faculty members from Tabriz University of Medical Sciences, as well as experts from the family medicine program in cities across the East Azerbaijan Province where the program was implemented. A purposive sampling method was employed, whereby the researcher selected participants who could best address the study questions and contribute to achieving the research objectives based on the utility of the samples. The interview sessions were conducted by selecting the participants. At the end of each session, data were analyzed using both manual and in-content analysis approaches. To develop an evaluation tool for the family medicine program, indicators derived from a review of texts from various countries and a qualitative study within the province were consolidated. Duplicate cases were removed and similar instances were categorized under the titles most frequently referenced in the evidence gathered. Subsequently, the Delphi questionnaire was formulated.

The questionnaire was distributed to 30 stakeholders meeting the study's entry criteria (university faculty members, health managers, and deputies with a minimum of 5 years of experience in university health and treatment networks, and family medicine program experts from implementing cities), based on two criteria: Importance and executability.

The response process entailed evaluating each index on a 9-point scale for "importance" and "executability." It was imperative for the expert to assign a score from 1 to 9 for each indicator. "Importance" referred to the necessity of including each item in the final tool, while "executability" denoted the feasibility of implementing and measuring the item under the current conditions of our country. The final acceptance of each index required a minimum score of seven in both dimensions. In addition, a section titled "place for recording opinions" was included at the end of the questionnaire for experts to note any additional insights. In the first Delphi round, out of the 80 indicators synthesized from the first and second objectives, five were immediately discarded due to low scores, and 14 were reassessed in the second round, resulting in the elimination of another five indicators scoring below 7. Ultimately, 70 indicators were selected, each scoring above seven in both rounds. An index identity card was created for all indicators obtained. For the analysis of the data obtained from the expert evaluations, descriptive statistics methods were used. Specifically, the mean, median, standard deviation, and range were calculated for each index in both dimensions (importance and executability) to summarize the distribution of expert ratings. These measures were used to provide an overview of how experts rated each indicator.

RESULTS

Evaluation indicators identified in the literature review were systematically classified into three domains – structural, process, and outcome indicators – to ensure comprehensive assessment. Structural/process indicators and results obtained from the literature review are summarized in Table 1.

To gather expert opinions on the evaluation of the urban family medicine program, interview sessions were conducted with the target group. The age of participants was normally distributed, with a mean of 46.0±5.2 years, while work experience in primary health care showed a non-normal distribution, reported as a median of 20.0 (5.0–30.0) years. All participants held postgraduate degrees in medical sciences, including medicine, health, and healthcare services management.

The study participants identified evaluation indicators for the program across three domains: Input, process, and output. The output indicators were further categorized into three subdomains: Quality, equity, and performance indicators. The main topics and subtopics of the dimensions and evaluation indicators of the urban family medicine program are summarized in Table 2.

By integrating appropriate dimensions and indicators, and after two rounds of Delphi, the final indicators were selected. The weight of each index was calculated based on the opinions of experts and an index certificate was prepared for each selected indicator. Indicators obtained from the Delphi study are summarized in Table 3.

DISCUSSION

According to the WHO, the Donabedian model is recognized as a suitable framework for evaluating healthcare services.[9] This model emphasizes three core areas: Structure, process, and outcome. The structure encompasses resources, such as equipment and human resources utilized in service production and delivery. This process involves actions that lead to the successful utilization of resources to produce effective services. Outcomes included anticipated results, such as patient satisfaction, treatment, and disease management.

This study categorizes program evaluation indicators into three fields: Input, process, and output. Input indicators pertain to the health team members' level of knowledge and skills, while process indicators cover the volume of necessary referrals, reverse referrals from Level 2, family doctors' retention, swift and easy access to services during waiting periods, and specialists' collaboration in care. Output indicators focus on quality, encompassing the satisfaction level of the population served, acceptance of family doctors among the populace, and in terms of equity, the extent of families' exposure to crippling costs, direct out-of-pocket payments, and in the functional domain, life expectancy indicators, birth rates, under-five mortality rates, maternal mortality index, actual service coverage, service utilization rates, and quality-adjusted life expectancy.[10]

The WHO's 2014 report, titled "Conceptual and Strategic Approach to the Family Medicine Program" states that individuals should recognize the benefits of timely healthcare services via the family medicine approach.[11] This includes high-quality care without extensive wait times, referral and follow-up mechanisms, access to necessary service packages and medications without financial burdens at the point of service, and comprehensive, effective care accessible to the entire population. Healthcare services should fulfill the

Table 1. Structural/process indicators and results obtained from literature review

No	Indicators	
1.	Structural	Percentage of PHC centers with evidence of cooperation with other sectors (holding meetings, joint projects, etc.)
	Processes	Percentage of the population under coverage registered in the health center
	Output	The ratio of reported patients to PHC each month who are managed due to mental health conditions
2.	Structural	Percentage of essential CVD and diabetes mellitus drugs without inventory in the past 3 months
	Processes	Percentage of health center employees who have been vaccinated against Hepatitis B process (3 doses)
	Output	The percentage of patients with high blood pressure with initial laboratory examinations
3.	Structural	Percentage of PHC centers with a standard list of essential drugs available
	Processes	Percentage of prescriptions that include antibiotics in outpatient clinics
	Output	The percentage of registered patients with a 10-year cardiovascular risk in the past year
4.	Structural	Percentage of PHC centers with a shortage of any items of essential drugs for the past 3 months
	Processes	Percentage of correct referrals (upward) in the past 6 months (under special conditions)
	Output	The percentage of 5-year-old children screened for anemia
5.	Structural	Percentage of PHC centers with clear and written instructions/strategy for payment costs
	Processes	Percentage of healthy injections in the health care center
	Output	The level of staff satisfaction
6.	Structural	Percentage of PHC centers with easy access to essential basic technology and equipment
	Processes	Percentage of employees who have attended continuous training on quality, safety, and patient health in the past year.
	Output	The number of adverse events reported (vaccination/drug prescription)
7.	Structural	Percentage of PHC centers with minimum personnel standards (at least one standard model is followed in PHC centers)
	Processes	Percentage of registered patients with a blood pressure higher than 149 mmHg in the past 2 follow-up visits
	Output	The percentage of children under 24 months vaccinated according to the national protocol
8.	Structural	Job descriptions are updated periodically and are accessible to all health team personnel.
	Processes	Average waiting time in outpatient clinics
	Output	The percentage of pregnant women who have been fully vaccinated against tetanus (lockjaw)
9.	Structural	Percentage of personnel in PHC centers who have received their updated job descriptions
	Processes	Percentage of registered diabetic patients with controlled fasting blood sugar in the past 2 status visits
	Output	The level of patient satisfaction
10.	Structural	Number of in-service training programs organized for employees in the past 6 months per job category (general practitioner, nurse, and others)
	Processes	Percentage of injections that were performed with new sterilized standard healthy syringes
	Output	The percentage of patients aware of patient rights and responsibilities
11.	Structural	Availability of updated clinical guidelines and their access to all employees at the PHC level
	Processes	Compliance with HH guidelines
	Output	The percentage of diabetic patients with HbA1C (Hemoglobin A1C) <7%
12.	Structural	Percentage of prescriptions and laboratory investigations that are in line with national clinical guidelines
	Processes	Percentage of patients with high blood pressure registered in the past visit
	Output	The percentage of hospital feedback received in referred cases
13.	Structural	Percentage of PHC centers with tools, equipment, and guidelines to support referrals
	Processes	Percentage of pregnant women's first visit in the first trimester of pregnancy
	Output	The percentage of referred patients who were satisfied with the referral (availability of essential services, staff behavior, and low cost)
14.	Structural	Percentage of PHC centers with trained health volunteers as active partners in service delivery
	Processes	Percentage of smokers present in smoking cessation counseling
	Output	The percentage of children aged 1–2 years who have received full vaccination
15.	Structural	Percentage of PHC centers actively working with youth or women's groups
	Processes	Percentage of patients with Type 2 Diabetes Mellitus who have had a fundus eye examination in the past 12 months

Table 1. Structural/process indicators and results obtained from literature review (Cont.)

No	Indicators	
	Output	The percentage of individual coverage of the self-care program
16.	Structural	Percentage of PHC centers that have established a "community-based committee" that helps to manage the PHC center
	Processes	Percentage of pregnant women receiving at least 4times ANC visits
	Output	The number of side effects reported (immunization/drug)
17.	Structural	Percentage of PHC centers that cooperate with non-governmental organizations (NGOs) or other local representatives
	Processes	Percentage of pregnant women who have seen health education (nutritional care, symptoms of anemia, observance of health principles, and symptoms of high-risk pregnancy)
	Output	The percentage of children under 23 months immunized according to the national protocol
18.	Structural	Number of days of drug shortage per year for 2 essential drugs defined in the health center
	Processes	Percentage of children under 5 years old who have had their weight and height measured in the past year
	Output	The percentage of diabetic individuals with HbA1C <7%
19.	Structural	Percentage of PHC centers with clear laws, regulations, and instructions for service costs
	Processes	Defined and completed population under coverage and family / individual file
	Output	The percentage of pregnant women who received at least 6 times ANC
20.	Structural	Percentage of visitors who receive PHC services without financial hardship
	Processes	Average percentage of registered families in PHC centers
	Output	The percentage of children under 5 years whose weight and height have been measured in the past year
21.	Structural	Percentage of PHC centers contracted with agencies/health insurance companies
	Processes	Average percentage of current family / individual files available in PHC centers
	Output	The percentage of newborns who are exclusively breastfed in the first 6 months
22.	Structural	Percentage of the covered population who have had at least one basic visit
	Processes	Percentage of visitors to the PHC center who are outside the defined list of doctors
	Output	The level of employee satisfaction
23.	Structural	Percentage of 13 essential drugs for non-communicable diseases without stock in the past 3 months (heart and vascular, diabetes, high blood pressure, and COPD)
	Processes	Average number of people under the visit list for each of the doctors
	Output	The percentage of appropriate referrals (upward) in the past 6 months (with specific conditions) with appropriate feedback
24.	Processes	Percentage of referrals from each PHC center out of total daily visits in each center
25.	Processes	Percentage of places and PHC centers with integrated emergency readiness and response intervention
26.	Processes	Percentage of employees at the PHC level who have been trained to provide EHSP services with defined responsibilities and duties
27.	Processes	Percentage of PHC centers that store, register, and report drugs safely and securely on a monthly basis
28.	Processes	Percentage of visitors who comply with family medical regulations and regulations
29.	Processes	Percentage of PHC centers that collect, match, and report health information on a monthly basis
30.	Processes	Percentage of PHC centers that use health information is analyzed for better and informed decision-making
31.	Processes	Percentage of mothers who have given birth in the past 6 months and have received at least 4 prenatal care
32.	Processes	Percentage of registered patients with diabetes who have full research and examinations in their files
33.	Processes	Percentage of patients with mental disorders who have had a follow-up visit according to a specific time according to the national protocol
34.	Processes	Percentage of pregnant women with the first visit in the first trimester
35.	Processes	Percentage of the population, aged 30–59, with overweight and obesity who have received counseling services for behavior change
36.	Processes	Percentage of smokers, 18 years and older, who receive smoking cessation counseling
37.	Processes	Percentage of students aged 6–14 who have been treated with fluoride
38.	Processes	Percentage of people with COPD who have had a follow-up visit and treatment in the past year
39.	Processes	Percentage of health center employees who have been immunized for Hepatitis B (3 doses)

Table 1. Structural/process indicators and results obtained from literature review (Cont.)

No	Indicators	
40.	Processes	Percentage of safe injections in health and treatment centers
41.	Processes	Percentage of employees who have seen continuous training on patient quality and safety during the past year.
42.	Processes	Percentage of compliance with hand hygiene guidelines
43.	Processes	Percentage of patients with high blood pressure with initial laboratory examinations
44.	Processes	Percentage of patients with high blood pressure registered with BP <140/90 in the past 2 follow-up visits
45.	Processes	Percentage of registered diabetic patients with fasting blood sugar controlled in 2 follow-up visits
46.	Processes	Percentage of registered NCD patients aged 30 and over with a 10-year cardiovascular risk recorded in the past year
47.	Processes	Percentage of children aged 6–9 months who are tested for anemia
48.	Processes	Percentage of women who have had at least one postpartum care in the first 6 weeks
49.	Processes	Percentage of people who work in a workshop under 20 years old and have been basic visits and occupational care in the past years
50.	Processes	Percentage of the population aged 30 and over, with diabetes who have performed the following examinations: Hemoglobin A1c (HbA1c)/Examination: Eye examination / Foot examination / Blood pressure measurement
51.	Processes	Percentage of the population aged 20 years and older with depression who have undergone the following assessments: • Active follow-up • Risk assessment for non-communicable diseases • Evaluation of drug side effects
52.	Processes	Percentage of pregnant women who have seen health education about: Nutritional care/Anemia/Health service/ High-risk pregnancy symptoms
53.	Processes	Performing TB screening in high-risk groups
54.	Processes	Women aged 30–59 who have had at least 1 Pap test in the past 5 years
55.	Processes	Percentage of risk factors for AIDS in the population under coverage
56.	Processes	Percentage of microbial water sampling according to the standard
57.	Processes	Percentage of registered patients in NCD with blood pressure recorded twice in the past follow-up visit

ANC: Antenatal care; COPD: Choronic obstructive pulmonari disease; CVD: Cardiovascular disease; EHSP: Essential health services package; NCD: Non communicable disease; PHC: Primary health care; TB: Tuberculosis.

Table 2. The main topics and subtopics of the dimensions and evaluation indicators of the urban family medicine program

Dimensions and evaluation indicators	Input	The level of knowledge and skill of health team members
	Process	The amount of necessary referrals
		Rate of reverse referrals from level 2 to level 1
		The retention rate of family doctors
		Ease and speed of access to services (waiting time perspective)
		The level of cooperation of specialists in care
	Output	Quality:
		The level of satisfaction of the covered population
		The level of acceptance of family doctors among the population.
		Justice:
		The extent to which families are exposed to catastrophic payment
		The amount of direct out-of-pocket payments
		Performance:
		Life expectancy
		Birth rate
		Death rate under 5 years
		Maternal mortality rate
		Actual coverage of services, rate of people using services
		Life expectancy adjusted by quality

Table 3. Indicators obtained from the Delphi study

Area	Indicator	Weight of Indicator
Health care status	Death rate of children under 1 year old	0.72
	Birth rate	0.63
	Mortality rate of children under 5 years old	0.63
	Percentage of mothers with ≥4 antenatal care visits during pregnancy (past 6 months)	0.72
	Percentage of children aged 12–23 months with full immunization	0.72
Service delivery	The percentage of implementation of EHSP components (essential health services package)	0.63
	The percentage of executive centers that have implemented the last revision of the service package	0.63
	Percentage of implementing centers that have the latest revision of the service package	0.63
	Percentage of hospital feedback received in referred cases	0.63
	Average waiting time in outpatient clinics	0.63
	Percentage of correct referrals (upward) during the past 6 months (under certain conditions)	0.63
	The percentage of referred patients who were satisfied with the referral (availability of essential services, staff behavior, and low cost)	0.72
	Percentage of centers with tools, equipment, and guidelines to support referrals	0.72
	Percentage of injections performed with new sterilized standard healthy syringes	0.72
	The average number of people under the visit list of each doctor to implement the EHSP plan	0.63
	The percentage of guideline/treatment protocol based on standardized disease definitions	0.63
	Percentage of implementing centers that have access to treatment guidelines/protocols based on standardized diagnostic definitions	0.63
	The percentage of implementing centers that implemented standardized treatment guidelines/protocols based on diagnostic definitions	0.63
	Availability of updated clinical guidelines and its accessibility to all staff at the urban family physician level	0.63
	The percentage of executive centers where population and household division is done	0.63
	The percentage of executive centers with a map of the region	0.72
	The percentage of centers where the prevalence of diseases and deaths have been determined	0.72
	Percentage of PHC facilities where the population covered is defined	0.72
	The average percentage of families registered in PHC centers	0.63
	Percentage of program implementation centers with the quality assessment system	0.63
	Percentage compliance with HH guidelines	0.63
	The percentage of employees who participated in continuous training about quality, safety, and patient health during the past year	0.72
	The percentage of safe injections in the health care center	0.63
	Percentage of health center employees who were vaccinated against hepatitis B (3 doses)	0.72
	The percentage of prescriptions and laboratory investigations that are in line with national clinical guidelines	0.63
Human resources	Percentage of executive centers with minimum personnel standards (at least one standard model is followed in executive centers)	0.72
	Percentage of PHC-level staff trained to provide EHSP services with assigned responsibilities and duties	0.72
	The number of in-service training programs for employees organized during the past 6 months per job category (general practitioner, nurse, and others)	0.63
	The percentage of employees determined based on the covered population	0.72
	The percentage of employees who are determined based on the EHSP	0.72
	The percentage of personnel in executive centers who have received their updated job descriptions	0.63
	The percentage of centers where job descriptions are periodically updated and accessible to all executive-level personnel	0.63

Table 3. Indicators obtained from the Delphi study (Cont.)

Area	Indicator	Weight of Indicator
Facilities, equipment, and medicine	Percentage of implementing centers with the available standard list of essential drugs	0.63
	The percentage of primary health care facilities and centers managed by a family physician specialist	0.72
	The percentage of primary health care facilities and centers that have been visited at least twice in the past 6 months	0.63
	Percentage of primary health care facilities where service delivery is based on a family medicine approach	0.63
	The percentage of family medical infrastructure centers	0.63
	Percentage of centers with a standard list of equipment	0.72
	Percentage of centers with the standard list based on EHSP	0.63
	The percentage of centers that have equipment is based on the standard list of equipment	0.63
	The percentage of supply of essential drugs based on the essential service package	0.63
	Percentage of centers with essential drugs	0.63
	Percentage of centers with a list of essential drugs	0.63
	Percentage of PHC facilities and centers with integrated emergency preparedness and response intervention	0.63
	Percentage of essential CVD drugs and diabetes mellitus without inventory in the past 3 months	0.63
	Number of drug shortage days per year for 2 essential drugs defined in the health center	0.72
	Percentage of executive centers with shortages of each item of essential drugs for the past 3 months	0.72
	The percentage of implementing centers that store, register, and report medicines safely and regularly on a monthly basis	0.72
Information system	Percentages of centers that collect, reconcile, and report health information on a monthly basis	0.63
	The average percentage of current cases of families/individuals in PHC centers	0.72
	Percentage of centers that use analyzed health information to make better and informed decisions	0.63
	Percentage of centers with information feedback	0.63
	The percentage of registered patients of neurological and mental patients who have complete investigations and tests in their files	0.72
	The percentage of registered patients with high blood pressure who have complete investigations and tests in their files	0.63
	The percentage of registered patients with diabetes who have complete investigations and tests in their records	0.72
Financial resources	Percentage of PHC centers with clear rules and regulations and guidelines for service charges	0.63
	Percentage of clients who receive PHC services without financial hardship	0.63
	The percentage of centers that have been allocated credit for the family medicine program	0.63
	The percentage of centers where resources have been allocated for equipment maintenance	0.63
	Percentage of PHC centers with contracts with health insurance agents/companies	0.72
	Percentage of implementing centers with clear, written guidelines/strategy for payment fees	0.63
Community participation	Percentage of centers with trained health volunteers as active partners in service delivery	0.63
	Percentage of centers with active work in connection with youth groups or women	0.63
	The percentage of clients who follow family medicine rules and regulations	0.63
Partnership	Percentage of centers that cooperate with NGOs or other local representatives	0.63
	Percentage of PHC centers with evidence of cooperation with other sectors of society (holding meetings, joint projects, etc.)	0.63

CVD: Cardiovascular disease; EHSP: Essential health services package; HH: Hand hygiene; NGO: Non-governmental organization; PHC: Primary health care.

criteria of accessibility, financial feasibility, collectability, comprehensive quality, effectiveness, non-discrimination, and age appropriateness. The indicators identified in this tool align with many global health indicators.

Eskandarizadeh and Dehnavieh's study, by the title of "Assessment of Primary Healthcare System in Areas Covered by Family Physician Project in Southeastern Iran," assessed the program across access, care comprehensiveness, coordination, and continuity.[12] Many of these aspects are also mentioned in our study's evaluation tool.

The study by Jahromi et al. utilized the urban family doctor program, employing primary care tools that prioritize providing care as the main feature.[13] Secondary features included access to services, continuity of care, coordination of care, and comprehensiveness of care. Assessment dimensions encompass geographical, cultural, and organizational access; financial access; continuity of information; longitudinal continuity; interpersonal continuity; and cooperation between different levels of care. Additional evaluation indicators such as medical equipment, service delivery, patient visits, activity hours, holiday and after-hours activities, non-therapeutic home visits, service payments, distance to provider centers, cultural characteristics, computer and software usage, medical information storage, information utilization and analysis, annual visits, duration of patient-provider relationship, referral system, disease management, treatment procedures, and technical skills for consultation and communication with specialists were selected and evaluated. It appears that the indicators and areas mentioned in this study overlap with those of the present study.

A review of studies in this field indicates that before the current study, the primary care evaluation questionnaire designed by the WHO and the Netherlands Institute for Health Services Research was used to assess the urban family doctor program.[14-18] This tool, which is less comprehensive than the one designed in this study, measures only four areas: Access to services, continuity of care, coordination of care, and comprehensiveness of care. The newly designed tool encompasses eight areas: Healthcare status, service delivery, facilities and medicine, information system, financial resources, community participation, partnership, and indicators related to each area. It can be asserted that this tool is inspired by the primary framework of health care governance and possesses sufficient sensitivity to reflect the actual state of the urban family doctor program's implementation. Donabedian's model for assessing quality in health care.[19] Its breadth allows for a more nuanced evaluation compared to existing tools, which often focus narrowly on service delivery and overlook governance, community engagement, or resource adequacy.[20,21] Given the multidimensional nature of primary health care in urban settings – especially in contexts, such as Iran, where rapid urbanization and health transitions are ongoing – such a holistic evaluation framework is essential for guiding policy adjustments and strengthening health system responsiveness.[22] Thus, the current tool offers a promising foundation for continuous monitoring and quality improvement within the urban family medicine program.

CONCLUSION

Effective implementation of the urban family medicine program will enhance societal health levels, achievable through accurate assessment across various domains. Evaluating the urban family medicine program is essential, necessitating indicators related to healthcare status, service delivery, human resources, facilities, equipment, medicine, information systems, financial resources, community participation, and partnership. The significance and feasibility of the index underscores the importance of all pertinent fields and indicators.

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First Level Healthcare Providers not Preferred? Reasons for Preferring the Third Level

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ABSTRACT

Objectives: This study aimed to investigate the reasons why patients prefer tertiary pediatric outpatient clinics instead of primary healthcare services.

Methods: The research was conducted with patients who visited the pediatric outpatient clinic at Kafkas University Faculty of Medicine Hospital in 2023. Data were collected through face-to-face interviews with patient relatives.

Results: A total of 378 patients were included in the study. When the reasons for referral to tertiary healthcare services were analyzed, 168 (44.4%) were patient-related, 97 (25.7%) were physician-related and 113 (29.9%) were health system-related. The family doctor being considered insufficient was the most common with 71 (42.3%) patient-related reasons. Among physician-related reasons, a Family doctor's referral to a pediatric specialist was 97 (25.7%). Moreover, distance from the family doctor with 63 (55.8%) of the reasons related to the health system.

Conclusion: The study revealed that none of the cases required tertiary-level intervention, indicating that the present system encourages unnecessary specialist visits and diagnostic testing.

Keywords: Referral and consultation, primary care, pediatrics

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INTRODUCTION

As is well known, in 2003, the Ministry of Health launched the Health Transformation Program.[1] The previously region-based healthcare delivery model was transformed into a population-based model. This change; however, brought along several challenges. One of the main problems was the de facto elimination of the referral chain, despite its continued existence "at the legal level."[2]

Before the Health Transformation Program, healthcare users were required to first consult a first-level healthcare provider (health centers).[3] When an individual visited a first-level healthcare provider, they would either receive an outpatient diagnosis and treatment or, if necessary, be referred to second-level healthcare institutions for further examination and treatment. Upon visiting a second-level healthcare institution, the patient would be evaluated by a second-level healthcare physician. If hospitalization was required, the patient would be admitted; if outpatient treatment was appropriate, treatment would be planned, and recommendations would be sent to the first-level physician. After the implementation of the Health Transformation Program, this referral chain was effectively abolished, allowing patients to directly access second and third-level healthcare institutions at any time. However, this caused disruptions in communication between physicians across different levels and provided a basis for the arbitrary behaviors of healthcare users.[4]

This study aimed to determine the reasons why patients apply to tertiary pediatric outpatient clinics instead of primary health care services.

METHOD

The population of the descriptive study was calculated by including patients who applied to the pediatric outpatient clinic of Kafkas University Faculty of Medicine Hospital in 2023. Considering that approximately the same number of patients would apply in 2024, after removing duplicate applications, the study population was determined as 7,233 patients. Accordingly, the sample size of the study was calculated as 365 patients with a 50% prevalence, 95% confidence interval, and 5% margin of error.

The variables of the study include sociodemographic characteristics related to the family, mother, and child, as well as reasons for not visiting first-level healthcare providers. The data collection form, which includes variables such as age, gender, and maternal education level, was prepared based on the Türkiye Demographic and Health Survey.[5] In addition, the mothers of the patients were requested why they applied to tertiary health services instead of primary health services. The data for the study were collected through face-to-face interviews with the relatives of patients.

In statistical analysis, the SPSS v20.0 (IBM SPSS Statistics for Windows, Version 20.0; Armonk, NY, USA) package program was used, and descriptive measures such as percentage and frequency were applied.

RESULTS

A total of 378 patients were included in the study. The sociodemographic characteristics of the patients and their parents are summarized in Table 1.

When the reasons for referral to tertiary healthcare services were analyzed, 168 (44.4%) were patient-related, 97 (25.7%) were physician-related and 113 (29.9%) were health system-related. The reasons for patients' referral to tertiary healthcare services are summarized in Table 2.

Table 1. The sociodemographic characteristics of the patients and their parents

	n (%)
Gender	
Male	195 (51.6)
Female	183 (48.4)
Age groups	
Newborn	14 (3.7)
1–24 months	66 (17.5)
2–5 years	81 (21.4)
6–17 years	217 (57.4)
Mother's education	
Uneducated	44 (11.6)
≤12 years	252 (66.7)
12–16 years	82 (21.7)
Mother's occupation	
Employed	120 (31.8)
Unemployed	258 (68.2)
Residence	
Urban	265 (70.1)
Rural	113 (29.9)

Table 2. The reasons for patients' referral to tertiary healthcare services

Reasons	**n (%)**
Patient-relative reasons	71 (42.3)
Family doctor being considered insufficient	27 (16.1)
Belief that further tests are needed	22 (13.1)
Birth occurred in the hospital where the research was conducted	20 (11.9)
Belief that university services are better	15 (8.9)
"Since I'm here, let's get checked"	13 (7.7)
"I didn't think of going to the family doctor"	
Physician-related reasons	97 (25.7)
Family doctor's referral to a pediatric specialist	
Health system-related reasons	
Distance from the family doctor	63 (55.8)
Being a guest	20 (17.7)
Out-of-office hours visit	18 (15.9)
Unable to get an appointment at the second level	12 (10.6)

DISCUSSION

The discussion will be examined under three main headings: first, patient/patient relative-related reasons; second, physician-related reasons; and third, system-related reasons.

When all reasons are considered as a whole, it is found that 44 out of every 100 visits are due to reasons related to the patient's relatives. The most significant reason for visiting the third level appears to be patient relative-related reasons. Among these, the belief that the family doctor is insufficient ranks first. Family doctors track and monitor children's weight, height, and development from the newborn period, as well as childhood vaccinations. The monitoring of healthy children, which is an important part of child health, by family doctors, along with sometimes prescribing treatments used regularly for chronic illnesses of parents, might have led families to perceive family doctors as inadequate in understanding their child's illnesses. The second most common reason related to patient relatives is that 16.1% of parents stated that they visited the third-level hospital because they thought their child's symptoms required further tests. When the patients' medical history was investigated in more detail, it was found that families, after searching for information about their child's complaints on the internet, feared that it could be a serious illness and requested further investigation.

In terms of healthcare services, as individuals become more familiar, they are more likely to trust well-known healthcare professionals or hospitals.[6] Another study has shown that familiarity with hospital staff or satisfaction from a previous visit influences hospital choice.[7] In a study conducted with patients over the age of 65 who applied to tertiary care, it was observed that those who did not know their family physician did not use tertiary care effectively.[8] Due to the trust-building mentioned here, 13.1% of patient relatives may have preferred to continue their children's follow-up visits at the hospital where the birth took place. In a study conducted by Boscarino and Steiber, it was shown that the presence of specialist doctors, the quality of facilities, and the size of the hospital are among the criteria considered when choosing a hospital.[7] In our study, 11.9% of families stated that they visited the third-level healthcare institution because they believed the university hospital was better. The selective admission of patients has allowed for longer examination times and more qualified healthcare services for fewer patients compared to the second-level, leading to the perception that there is more attention given to patients and their conditions. It is also a fact that the ease of access to academicians in different departments at the third-level hospital has contributed to this perception. Perhaps for this reason, patient relatives have been seen to bring a different family member for examination, and thus, they also enter the pediatric outpatient clinic. In addition to being an example of cases that could have been diagnosed and treated at the first level due to the failure of the referral chain, this situation demonstrates that healthcare services are being sought solely from a service-focused perspective.

Physician-related reasons account for 26 out of every 100 visits. When these reasons are examined, the most common is the family doctor's referral to a pediatrician after their examination. With the absence of a referral system and the increasingly stimulated demand for healthcare, every patient tends to seek examination/consultation from a specialist doctor. Whether necessary or not, this request from patient relatives often results in the suggestion, "If the complaint doesn't go away, see a specialist." Especially for pediatric patients, such suggestions have become routine and are gradually making access to specialists increasingly impossible. In second place are cases where "the family doctor is afraid of treating pediatric patients." The family doctor, when faced with patient relatives seeking help for their child's complaints, primarily offers preventive and health-promoting services as a first-level physician. According to a frequently encountered scenario, when the complaint persists the next day, the family may return to the family doctor with increased anxiety, and the physician may face questioning or accusatory behavior regarding their diagnosis and treatment suggestions. Unfortunately, due to the increasing incidents of violence against physicians in our country, family doctors may more frequently refer pediatric patients to specialist doctors. The family of a child patient visiting the third-level pediatric outpatient clinic expressed that the family doctor does not treat pediatric patients. In third place is the situation where the family doctor's treatment does not lead to improvement. This issue actually has two aspects: First, there are situations where the family doctor's knowledge and skills may be inadequate. Second, it is when the treatment or recommendations given by the doctor do not meet the expectations of the family and are either not used or used inadequately (e.g., for an insufficient amount of time). For example, post-infectious coughs that can last up to 4 weeks after an Upper Respiratory Tract Infection diagnosis are one of the most common complaints encountered in studies like this one. 30 out of every 100 visits are due to system-related issues. Among system-related reasons, the most common is the distance from the family doctor and the difficulty in reaching them. Due to the geographical location of Kars, especially in winter, roads in some villages are closed due to snowfall, which prevents patients from reaching their family doctor. In addition, the fact that mobile family health services in some villages are only provided once or twice a week leads patients to visit urban centers or healthcare institutions with better facilities for their complaints. A study by Gesler and Meade also showed that the distance factor is a significant determinant in access to and use of healthcare services.[9] Similarly, a study in a rural province of China, investigating the preferences of hypertensive patients for first-level healthcare institutions, found that participants whose residences were closer to first-level healthcare facilities were about 10 times more likely to prefer them over those whose residences were closer to district hospitals or higher-level hospitals.[10] The second most common reason is when families visiting from other cities cannot be examined by their family doctor due to the family doctor being in a different city. The third most common reason is out-of-office hour visits. Family medicine working hours are from

8:00 am to 5:00 pm, except on official holidays. Outside of these hours, when patients have complaints, they often visit the emergency department without waiting, as there are no obstacles. In addition, after visits to the emergency department on weekends or after long official holidays, child patients are often referred to specialists, leading to an increase in the number of patients visiting our clinic. It was also found that of patients visited our clinic because they could not get an appointment with a specialist at the second level.

This study has several limitations. First, it was conducted at a single tertiary care center, which limits the generalizability of the findings to other regions or healthcare settings with different demographic or structural characteristics. Second, data collection relied on face-to-face interviews with patient relatives, making the results susceptible to recall and reporting bias. Participants may have misremembered events or provided socially desirable responses. Third, the study did not include the perspectives of healthcare providers, such as family physicians or pediatricians, which could have enriched the analysis by offering a more balanced view of the referral dynamics. In addition, the cross-sectional nature of the research captures only a specific time frame and does not account for seasonal or temporal changes in healthcare-seeking behavior. While health literacy was highlighted as an influencing factor, it was not directly measured or assessed, limiting the ability to determine its precise role. Finally, potential confounding variables such as socioeconomic status, cultural beliefs, and previous healthcare experiences were not fully explored or controlled, which may have influenced patients' preferences for tertiary care services.

CONCLUSION

This study shows that none of the patients visiting the tertiary pediatric outpatient clinic required tertiary-level care, highlighting a misuse of services due to the breakdown of the referral system. Factors, such as lack of trust in primary care, perceived need for specialist attention, and systemic access issues contributed to this trend. These patterns lead to unnecessary diagnostic testing, increased costs, and inefficiencies across the healthcare system. Strengthening the referral chain and improving public health literacy – particularly about when to seek primary versus specialist care – are key to ensuring more effective use of healthcare resources.

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Smoking and Sleep Quality Among Turkish Adults: A Cross-Sectional Study

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ABSTRACT

Objectives: This study aims to investigate whether there is a relationship between smoking status, sleep quality, and self-efficacy perception.

Methods: A cross-sectional study was conducted among adults who visited the family medicine clinic of a tertiary hospital between May and July 2023. A 20-item questionnaire prepared by the researchers, the Pittsburgh Sleep Quality Index (PSQI), the Fagerström Test for Nicotine Dependence (FTND), and the General Self-Efficacy Scale were used.

Results: In the study, 440 participants were included. The median PSQI, General Self-Efficacy Scale, and FTND scores were 12.0 (6.0–21.0), 64.5 (42.0–85.0), and 3.0 (0.0–10.0), respectively. Smokers had significantly higher PSQI scores compared to non-smokers and former smokers (12.0 [6.0–21.0] vs. 11.0 [6.0–18.0] vs. 11.0 [8.0–17.0], respectively, $p<0.001$). However, Self-efficacy scores did not differ significantly among the groups ($p=0.431$). While a significant positive correlation was found between FTND scores and PSQI scores, no significant correlation was found between self-efficacy ($r=0.140$, $p=0.036$, and $p=0.689$, respectively).

Conclusion: There was a significant association was observed between smoking and poorer sleep quality. However, no significant relationship was found between smoking status and self-efficacy perception.

Keywords: Self efficacy, sleep disorders, smoking, tobacco use disorder

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INTRODUCTION

Smoking remains one of the most critical public health challenges of the 21st century, claiming 8.7 million lives globally each year, with 80% of these deaths occurring in low- and middle-income countries.[1,2] In Türkiye, around 16 million people smoke, resulting in 100,000 deaths annually attributed to smoking-related issues.[1] While the physical health risks of smoking are well-documented, its psychological and behavioral impacts – particularly on sleep quality and self-efficacy – are less comprehensively studied, especially in non-Western contexts like Türkiye. This gap limits the development of culturally relevant, evidence-based interventions that are crucial in primary care settings, where physicians play a pivotal role in smoking cessation efforts.

Sleep quality, a critical determinant of physical and mental health, is frequently compromised among smokers due to nicotine's stimulant effects that disrupt circadian rhythms and reduce sleep efficiency.[3,4] However, the literature presents conflicting findings: Meta-analyses have linked smoking to poor sleep outcomes, such as prolonged sleep latency and reduced REM sleep.[5] In addition, longitudinal studies suggest a bidirectional relationship, where poor sleep may also exacerbate nicotine dependence.[6] Confounding factors, including comorbid mental health conditions and socioeconomic stressors, are often unaddressed, further complicating interpretations.[7] Clarifying this relationship is essential, as sleep disturbances impair occupational performance, increase psychological distress, and may hinder smoking cessation efforts.[8]

Similarly, the relationship between smoking and self-efficacy is complex. The connection between smoking habits and self-belief is intricate involving psychological and behavioral aspects.[9] Studies generally suggest that low self-confidence can make it easier to start and continue smoking while high self-confidence is linked with efforts to quit smoking.[9-11] However, personal differences and environmental factors also play a role in shaping individual's beliefs about their capabilities. This discrepancy suggests that cultural context may influence how self-efficacy shapes smoking behaviors. Despite potential synergies, sleep quality and self-efficacy are rarely examined together in smoking research. Poor sleep may erode self-efficacy by impairing emotional regulation and decision-making, thereby reinforcing smoking habits. Conversely, high self-efficacy could mitigate sleep disturbances by fostering healthier routines. Most existing studies, however, isolate these variables, and the majority of evidence comes from Western populations, limiting generalizability to countries like Türkiye. Importantly, this study provides practical insights for primary care settings, where family physicians are the first point of contact in healthcare. Understanding how sleep quality and self-efficacy intersect in the context of smoking can inform holistic, culturally sensitive intervention strategies. For instance, if sleep quality mediates the smoking–self-efficacy relationship, incorporating sleep hygiene education into cessation programs could enhance their effectiveness. Given Türkiye's high smoking prevalence, limited behavioral health resources, and the central role of primary care providers in smoking cessation counseling, these insights are crucial for developing effective interventions to reduce tobacco-related morbidity and mortality.

Therefore, the present study aimed to investigate the relationship between smoking status, sleep quality, and self-efficacy perception among Turkish adults.

METHOD

This cross-sectional study was conducted between May and July 2023 at the Family Medicine Clinic of a tertiary care hospital in Erzincan, Türkiye, a setting that provides comprehensive services and serves as a primary point of contact for a diverse patient population, making it suitable for assessing smoking-related health behaviors. The study population consisted of voluntary individuals aged 18 years and older who visited the clinic for any reason and were proficient in Turkish, with individuals diagnosed with sleep disorders or using sleep-related medications excluded to eliminate confounding factors affecting sleep quality. The sample size was calculated based on the recommendations of MacCallum et al. for factor analysis, which suggests interviewing at least 20 participants per survey question; given the 20 questions in the survey, the initial target was 400 participants, with the final number increased to 440 to account for a potential 10% data loss.[12] The dependent variables in this study were sleep quality and self-efficacy perception, while the independent variables included smoking status and nicotine dependence level. In addition, demographic characteristics such as age, gender, marital status, educational level, and family history of smoking were considered as control variables to account for potential confounding effects.

Participants were administered a 20-item questionnaire prepared by the researchers through a literature review, which inquired about their demographic data, smoking, alcohol, tea, and coffee consumption status. In addition, the Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality, the Fagerstrom Test for Nicotine Dependence (FTND) was used to measure the level of nicotine addiction among smokers, and the General Self-Efficacy Scale was used to assess self-efficacy perception.

The PSQI is a scale developed by Buysse et al. in 1989 and adapted into Turkish by Ağargün et al.[13,14] It is used to measure sleep quality. The PSQI consists of 7 components: Subjective sleep quality, latency, duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. Each item is evaluated on a 0–3 point scale, and the sum of the scores of the seven components yields the total PSQI score. The total score ranges from 0 to 21, with higher scores indicating poorer sleep quality.[14] The reliability of the Turkish version of the PSQI has been reported with a Cronbach's α of 0.69, indicating acceptable internal consistency.

FTND is a test developed by Heatherton et al. and adapted into Turkish by Uysal et al. in Türkiye to measure nicotine dependence among smokers.[15,16] The Turkish version of the FTND has been found to have moderate reliability, with a Cronbach's alpha of 0.56. The FTND, consisting of six questions, categorizes nicotine addiction severity as follows: Scores of 0–2 indicate very low dependence, 3–4 indicate low dependence, 5 indicate moderate dependence, 6–7 indicate high dependence, and 8–10 indicate very high dependence.

General self-efficacy scale is a scale developed by Sherer and Adams, consisting of 17 items in a five-point Likert format.[17] Turkish validity and reliability study was conducted in 2010.[18] Each item on the scale is rated on a 1-5 scale. Items 2, 4, 5, 6, 7, 10, 11, 12, 14, 16, and 17 are reverse scored. The total score on the scale can range from 17 to 85; an increase in score indicates an increase in self-efficacy belief.[18] The Cronbach's alpha coefficient for the entire scale was found to be 0.80, indicating high reliability.

Data were analyzed using IBM Statistical Package for the Social Sciences (SPSS) Statistics 23 (SPSS, Chicago, IL). The Kolmogorov–Smirnov test assessed data normality. Since the data were not normally distributed, results were presented as median (min–max) for continuous variables and frequency and percentage for categorical variables. The Mann–Whitney U test was used to compare two independent groups, while the Kruskal–Wallis test was applied for comparisons involving more than two independent groups. Spearman correlation analysis was conducted to evaluate relationships between numerical variables. In addition, the Chi-square test was used to examine associations between categorical variables. The statistical significance level was set at $p<0.05$.

RESULTS

In the study, 440 participants were involved and the sociodemographic characteristics and smoking habits of the participants are summarized in Table 1.

Of the 225 participants who smoked, 192 (85.3%) had relatives who smoked, compared to 144 (75.4%) of the 191 non-smokers ($p=0.037$).

Correlation analysis revealed a significant positive correlation between FTND scores and PSQI scores and a significant negative correlation between self-efficacy and PSQI scores ($r=0.140$, $p=0.036$ and $r=-0.143$, $p=0.003$, respectively). No significant correlation was found between FTND scores and self-efficacy ($p=0.689$).

Of the 249 participants who were current smokers or had quit, 152 (61.0%) thought that smoking affected their sleep, 78 (31.3%) disagreed and 19 (7.6%) were unsure. The PSQI scores of those who thought smoking affected their sleep were 13.0 (6.0-21.0), those who thought it did not affect their sleep were 11.0 (7.0-17.0), and those who were not sure were 11.0 (8.0-14.0) ($p<0.001$).

Table 1. Sociodemographic characteristics and smoking habits of the participants

	n (%)
Gender	
Female	165 (37.5)
Male	275 (62.5)
Education	
Illiterate/literate	7 (1.6)
Primary/secondary school	38 (8.6)
High school	66 (15.0)
University	329 (74.8)
Marital status	
Married	199 (45.2)
Single	228 (51.8)
Widowed	13 (3.0)
Profession	
Non-operating	27 (6.1)
Student	79 (18.0)
Civil servant	181 (41.1)
Worker	84 (19.1)
Other	69 (15.7)
Smoking	
Yes	225 (51.1)
No	191 (43.4)
Quit smoking	24 (5.5)
Duration of smoking	
0–6 months	5 (2.0)
6 months–1 year	14 (5.6)
1–5 years	51 (20.5)
Over 5 years	179 (71.9)
A relative of a smoker	355 (80.7)
Yes	85 (19.3)
No	
Thinking about quitting smoking	
Yes	134 (59.8)
No	90 (40.2)
	Median (min–max)
Age (years)	29.5 (19.0–58.0)
FTND score	3.0 (0.0–10.0)
PSQI score	12.0 (6.0–21.0)
General self-efficacy scale score	64.5 (42.0–85.0)

FTND: Fagerstrom test for nicotine dependence; PSQI: Pittsburgh sleep quality index.

Regarding self-efficacy related to smoking opinions varied, 55 (22.1%) believed that it increased self-efficacy while most 175 (70.3%) disagreed and others remained undecided 19 (7.6%) ($p=0.155$).

Smokers had significantly higher PSQI scores compared to non-smokers and former smokers (12.0 [6.0–21.0] vs. 11.0 [6.0–18.0] vs. 11.0 [8.0–17.0], respectively, p<0.001). However, self-efficacy scores did not differ significantly among the groups (p=0.431).

DISCUSSION

This study investigated the relationship between smoking status, sleep quality, and self-efficacy perception among Turkish adults. The key results revealed that smokers had significantly poorer sleep quality compared to non-smokers, with those perceiving smoking as affecting their sleep showing higher PSQI scores. However, no significant association was observed between smoking status and self-efficacy perception. In addition, a strong familial influence was noted, as smokers were more likely to have relatives who smoked. The results of this study align with existing literature, where smokers commonly report impaired sleep quality. Nicotine's stimulant effect disrupts sleep by shortening sleep duration, increasing sleep latency, and reducing sleep efficiency.[19] Consistent with previous studies conducted in Türkiye, the results of this study emphasize that quitting smoking plays a crucial role in improving sleep quality.[20,21] Considering the negative effect of smoking on sleep, one can assume that quitting or reducing smoking is essential for sleep health.

In this study, a statistically significant but weak positive correlation was found between nicotine dependence and sleep quality scores, suggesting that higher nicotine dependence is associated with poorer sleep quality. Although the correlation coefficient indicates a weak association, its statistical significance underlines a consistent pattern in the data. This result implies that individuals with higher levels of nicotine dependence may require more targeted interventions that address both addiction and sleep disturbances as part of smoking cessation strategies.

Familial influence emerged as another significant factor. Smokers in this study were more likely to have relatives who smoked, suggesting that family behaviors may normalize smoking and reduce motivation to quit. This result is consistent with literature indicating that family and peer smoking behaviors increase smoking risk, particularly among adolescents.[22] There is a strong need to support people who want to stop smoking and motivate family members to do so.

Self-efficacy refers to an individual's belief in their ability to accomplish tasks and handle challenges. People with higher self-efficacy tend to persist in achieving goals, while those with lower self-efficacy may give up early due to fear of failure.[23] The mean General Self-Efficacy Scale score indicated that participants generally felt confident, though context-specific differences, such as in smoking behavior, may exist.

The link between smoking and self-efficacy remains unclear in the literature. Some studies suggest that non-smokers or former smokers have higher self-confidence, while others find no significant association.[24,25] Self-efficacy also appears to influence smoking initiation and cessation, with higher levels linked to better cessation outcomes.[26] In this study, although smokers had slightly higher self-efficacy scores than non-smokers, this difference was not significant. This may be due to smokers' beliefs that smoking reduces stress and enhances concentration and social acceptance, potentially creating barriers to quitting. Targeted interventions addressing these misconceptions may improve self-efficacy and support cessation efforts.

Although the difference between the groups was not significant, smokers who believed that smoking enhanced self-efficacy had lower self-efficacy scores than those who thought otherwise. This suggests that individuals with lower self-efficacy may continue smoking, assuming it boosts their confidence. Such beliefs could serve as psychological barriers to quitting. Therefore, addressing these misconceptions and promoting healthier ways to enhance self-efficacy are essential for effective smoking cessation.

One of the major limitations of this study is that it had a cross-sectional design that hinders the generalization of its results to a large part of the population. Larger-scale studies from various geographical locations could provide more generalizable results. The study data collection tools were based on self-reports: Hence, the data collection is subject to social desirability bias and recall bias. Furthermore, the stress, depression, anxiety, physical activity, malignancies, chronic diseases, and dietary habits of the participants were not controlled, and these are potential factors that could influence the quality of sleep and self-efficacy scores.

CONCLUSION

Based on the results of this study, it can be stated that smoking is associated with poorer sleep quality; however, no significant relationship was observed between smoking status and self-efficacy perception. Since smokers showed poorer sleep quality in this study, family physicians could consider screening for sleep disturbances when providing smoking cessation support. However, interventional studies are needed to determine whether improving sleep hygiene can directly enhance cessation outcomes.

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Short Communication

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Using the Framework of Entrustable Professional Activities to Assess Readiness among Master in Public Health Students

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ABSTRACT

Entrustable professional activities (EPAs) play a pivotal role in the delivery of competency-based education, as they enable the operationalization of complex competencies into measurable activities that are relevant to real-world practice. Entrustable Professional Activities (EPAs) developed for the Master of Public Health (MPH) program play a critical role in determining students' readiness for independent practice. The integration of EPAs into the MPH curriculum necessitates systematic planning and implementation to ensure alignment with the program's overarching goals and competencies. It is important to acknowledge the distinctive nature of EPAs in MPH programs, which differ significantly from those associated with clinical disciplines. In conclusion, EPAs play a defining role in preparing MPH students for effective and independent practice in public health. There is an immense need to adopt a systematic approach to integrate EPA into the program curriculum and thereby equip MPH students with the desired competencies to make meaningful contributions.

Keywords: Competency-based education, curriculum, education, health

INTRODUCTION

Entrustable professional activities (EPAs) play a pivotal role in the delivery of competency-based education, as they enable the operationalization of complex competencies into measurable activities that are relevant to real-world practice.[1] In other words, EPAs refer to specific activities that can be entrusted to students once they have acquired the desired knowledge and skills.[2] This approach advocates the delivery of student-centered education, wherein students take responsibility for their learning and make conscious efforts to attain the set competencies within the pre-defined timeframe.[3] In fact, as students are assessed for their performance on framed EPAs, teachers get an opportunity to provide constructive feedback, monitor their progress, and thereby make a decision regarding their ability to perform the task independently (entrustment).[1-3]

EPAS ASSESSING THE READINESS FOR INDEPENDENT PRACTICE

Master in Public Health (MPH) is an academic program designed to prepare students for their careers in the domain of public health, research, policy-making, and leadership.[4] EPAs framed for the MPH program become crucial to take a call regarding the readiness of students to in-

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dependently practice. This readiness can be ascertained by measuring the ability of students to effectively contribute to public health practice. The decision to allow MPH graduates to independently practice will depend on a number of indicators, such as the ability to deliver quality-assured public health services to positively influence health indicators of the general population, being accountable and responsible for their actions, and ensuring patient safety and welfare by implementing evidence-driven public health measures.[4-6] In addition, the students must also demonstrate problem-solving and critical decision-making skills, which happens to be crucial for effective public health practice.[6]

The framed EPAs give the opportunity to equip students with the leadership skills required to initiate and lead a wide range of public health interventions independently.[7] In continuation, students must develop the competency to effectively and efficiently collaborate with various stakeholders (namely, health professionals from different streams, communities, program managers, policymakers, etc.).[4] As students will be exposed to a number of real-world scenarios, they will be assessed for their adaptability to change and make ethical decisions in different contexts.[1] As EPAs have to be periodically assessed, the students are assessed for their readiness continuously, and it also enables a positive learning environment and professional development.[1,2] Moreover, EPAs can also assess the readiness of students to create a positive impact on the communities through effective public health interventions.[4]

INTEGRATING EPAS IN THE MPH CURRICULUM

The act of integrating EPAs into the MPH curriculum essentially requires systematic planning and implementation to ensure alignment with the overall goals and competencies of the program.[8-11] The process begins with the identification of key public health competencies and skills related to program planning, epidemiology, health promotion, etc.[4,8] This should be followed by the development of EPAs that are in alignment with the identified competencies and should be developed by involving different stakeholders.[9] Along similar lines, teachers can also incorporate EPAs that require the need for students to collaborate with other health professionals to promote teamwork and interdisciplinary practice.[10] The next step will be to align EPAs with the curriculum and learning objectives in such a way that the entire curriculum is covered.[4] Teachers must look to develop case studies and simulation exercises depending on the framed EPAs with the ultimate intention of providing exposure to authentic learning experiences, which enables the application of public health skills.[3,4] For each of the framed EPAs, specific workplace-based assessment tools are used to assess the progress of students.[11] There is always a possibility to include portfolio-based assessments to compile evidence about their performance.[12] Moreover, there is always a possibility to use technology-enabled platforms and simulation tools to mimic public health scenarios and assess the performance of students. There is an indispensable need for each of the performances by students to be followed up with the provision of constructive feedback to help them identify their strengths and areas that need more attention.[11] Further, MPH students should also be encouraged to record their reflections on their experiences, which enables lifelong learning and professional growth.[13] Finally, there has to be a mechanism to track the performance of students toward the attainment of EPAs throughout the duration of the program.[4]

ASSESSMENT OF EPAS IN THE MPH PROGRAM

Considering the variable nature of EPAs in MPH programs which are quite different as compared to the clinical subjects-related EPAs.[13,14] These assessment tools could be either workplace-based assessment tools that are employed in real-world settings (such as direct observation and case-based discussions) or tools that can be used in simulated settings (such as standardized patient encounters and objective structured clinical examinations).[13] In addition, tools such as portfolio-based assessments, peer assessment, and multisource feedback can also be employed to assess a wide range of competencies among MPH students.[4,13] These assessment methods can be either used in isolation or in combination to holistically assess the accomplishment of intended competencies by the MPH students, thereby making a decision regarding the readiness for independent practice.[13,14]

CONCLUSION

EPAs play a defining role in preparing Master of Public Health students for effective and independent practice in public health. There is an immense need to adopt a systematic approach to integrate EPA into the program curriculum and thereby equip MPH students with the desired competencies to make meaningful contributions.

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Case Report

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A COVID-19 Report of a Hypotensive Young Woman with Unique High C-Reactive Protein and Unexplained Increase in Ferritin and Lactate Dehydrogenase Serum Levels

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ABSTRACT

This case report aims to document the unusual presentation of low blood pressure in a coronavirus disease-19 (COVID-19) patient. A 22-year-old woman with a history of chronic allergic bronchitis, managed with montelukast 10 mg daily, presented to the emergency department with unique low blood pressure (averaging 90/56 mmHg) during and a month after recovering from COVID-19. The patient initially suffered from fever and cough, treated with paracetamol 500 mg as needed, Vitamin C 1000 mg daily, zinc 25 mg daily, and azithromycin 250 mg twice daily. Symptoms of the patient worsened after a week, leading to a chest X-ray that revealed pneumonia. Subsequent laboratory tests showed high C-reactive protein (CRP) levels and increased ferritin. The patient exhibited persistent low blood pressure, averaging 90/56 mmHg during her COVID-19 infection and for a month post-recovery. Laboratory findings included high CRP levels and elevated ferritin. Chest X-ray confirmed pneumonia.

Keywords: Coronavirus disease-19, hypotension, inflammation

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INTRODUCTION

The first patients during the Wuhan city outbreak who had coronavirus disease-19 (COVID-19) found that 30% of all patients, in addition to 37% of those with critical disease conditions, had hypertension.[1] Since then, many studies have confirmed the association between the severity of COVID-19 infection and the presence of hypertension.[2,3] However, recent reports confirmed that there is no association between hypertension and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or its severity. Hypertension is extremely prevalent in adults and those who are experiencing severe clinical manifestations and complications of COVID-19.[4] Recent reports showed that respiratory decompensated patients had increased blood pressure, possibly due to the viral effect on the renin-angiotensin-aldosterone system by COVID-19 infection.[5]

CASE REPORT

A 22-year-old female was suffering from fever and cough. The patient showed up in the emergency department with a unique low blood pressure during infection, which lasted for a month after recovery (blood pressure was average 90/56mmHg) and unique labs (abnormal lactate dehydrogenase [LDH] and ferritin levels). Ambulatory blood pressure monitoring was used. Previous baseline blood pressure was an average of 115/70 mmHg. Measured on several occasions before the infection.

The patient has a past medical history of chronic allergic bronchitis - she is on montelukast 10 mg once a day as a prophylactic treatment from the month of November till April each year. The patient also takes a Symbicort® inhaler once daily when she has a cough. The patient was not a smoker, nor did she drink alcohol.

The patient started experiencing a cough for 2 days, which she thought was her allergic bronchitis. Then, on the 3rd day, the patient started experiencing a fever above 38°C. Afterward, a Polymerase Chain Reaction test was done, and it was determined that the patient was COVID-19 positive with oxygen saturation 97%. At the beginning of March 2021, the 1st week of COVID-19 infections, the patient was taking paracetamol 500 mg whenever needed, Vitamin C 1,000 mg once a day, zinc 25 mg once a day, and azithromycin 250 mg twice a day. One week later, symptoms became worse, and a chest X-ray was done and showed pneumonia in the lungs, high C-reactive protein (CRP) levels, and an unexplained increase in serum ferritin level in the 2nd week of the course of infection. The laboratory test results of the patient are summarized in Table 1. Computed tomography scan from the 1st week of infection revealed no diagnostic indicators of COVID-19, presenting a seemingly unremarkable medical image that underscores the initial challenges in identifying the viral infection. Thorax computed tomography scan image of the patient is shown in Figure 1. However, the chest X-ray from the 2nd week dramatically illustrates the rapid progression of the disease, displaying evident radiographic changes consistent with COVID-19-related pneumonia. Chest X-ray of the patient is shown in Figure 2. This visual progression highlights the critical transition from an apparently asymptomatic state to a severe inflammatory response, demonstrating the complex and unpredictable nature of COVID-19's clinical manifestation. The dramatic difference between the two imaging studies emphasizes the importance of serial imaging and careful clinical monitoring, particularly in cases where initial diagnostic findings may be non-specific or inconclusive.

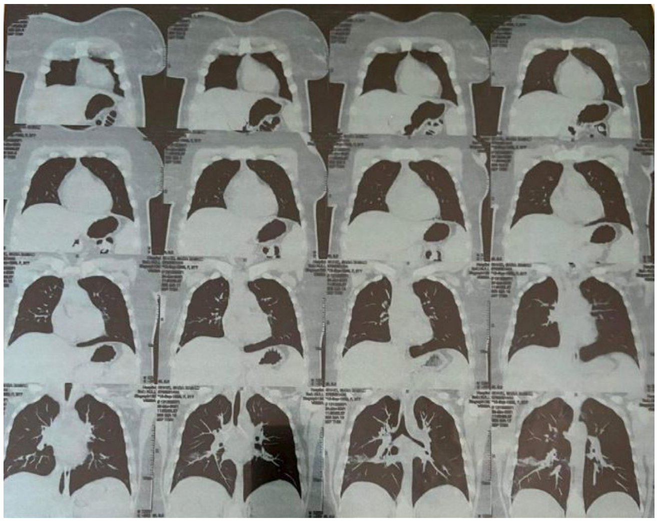

Figure 1. Thorax computed tomography scan image of the patient.

Table 1. The laboratory test results of the patient

	Conventional units	Normal range	International system units	Normal range
ALT (GPT)	34.90 U/L	<31.00 U/L	0.59 µkat/L	<0.53 µkat/L
AST (GOT)	29.00 U/L	<31.00 U/L	0.49 µkat/L	<0.53 µkat/L
GGT	40.00 U/L	9.00–54.00 U/L	0.68 µkat/L	0.15–0.92 µkat/L
ALP	56.10 U/L	35.00–104.00 U/L	0.95 µkat/L	0.60–1.77 µkat/L
LDH	502.00 U/L	<480.00 U/L	8.53 µkat/L	8.16 µkat/L
Total bilirubin	0.40 mg/dL	<1.20 mg/dL	6.84 µmol/L	<20.52 µmol/L
Direct bilirubin	0.23 mg/dL	<0.30 mg/dL	3.93 µmol/L	<5.13 µmol/L
Ferritin	463.00 ng/mL	15.00–150.00 ng/mL	463.00 µg/L	15.00–150.00 µg/L
D-Dimer	0.13 µg/mL	<0.50 µg/mL	130.00 ng/mL	<500.00 ng/mL
CRP	79.20 mg/L	<5.00 mg/L	7.92 mg/L	<5.00 mg/L

ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CRP: C-reactive proteins; LDH: Lactate dehydrogenase.

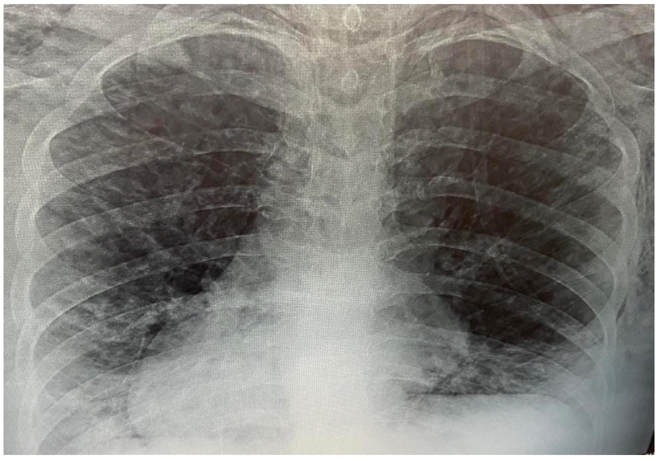

Figure 2. Chest X-ray of the patient.

The patient was hospitalized and suffered from low blood pressure (average 90/56 mmHg) for a month after recovery.

DISCUSSION

This case study aims to show that some cases of COVID-19 may experience hypotension. Angiotensin-converting enzyme 2, the primary gene involved in the etiology of hypertension, the primary binding receptor facilitating SARS-CoV-2 cell entrance in the organism, is usually upregulated, according to preclinical research employing these medication classes proven by Gallo et al. 2022.[6] Recent months have seen a number of papers demonstrating the potential link between hypertension and both the development of a worse prognosis for COVID-19 and the likelihood of SARS-CoV-2 infection.[7-10] The case involved a 22-year-old female who initially presented with bronchitis as well as a cough, quickly developing into a severe symptom of COVID-19 along with a hypotensive state that required hospitalization. Laboratory test results for our COVID-19 patient showed high CRP and an unexplained increase in Ferritin serum level in the 2nd week of the course of infection. LDH >500 U/L normal <450 U/L (represents organ damage), increased ferritin >450 ng/mL, CRP nearly 80 mg/L, hemoglobin level was 11.5 mg/dL.

Many studies confirmed the association between the severity of COVID-19 infection and the presence of hypertension.[2,3] However, recent reports confirmed that there is no association between hypertension and SARS-CoV-2 or its severity. Hypertension is extremely prevalent in adults, and they appear to be at particular risk of being infected with COVID-19 infection and those who are experiencing severe clinical manifestations and complications of COVID-19.[4] Recent reports showed that respiratory decompensated patients had increased blood pressure, possibly due to the viral effect on the renin-angiotensin-aldosterone system by COVID-19 infection.[5] Previous reports showed involvement of the autonomic nervous system, particularly in sympathetic skin reaction due to COVID-19 infection.[11] The present patient had low blood pressure during the infection, which lasted for a month after recovery (blood pressure was an average of 90/56 most of the time).

CONCLUSION

COVID-19 infection may potentially cause a hypotensive state for some unique features patients during the course of infection and may last for several weeks after recovery.[12] Autonomic response especially hypertension is an important aspect in the context of COVID-19 prevention and treatment.

Disclosures

Informed Consent: A written informed consent was obtained from the patient herself.

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