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Dear Colleagues,

As of February 2026, we have completed the third year of our journal's publication life. We have published the thirteen issue of Journal of Pulmonology and Intensive Care (JoPIC) under the shield of Medihealth Academy. In addition to all researchers, referees and editorial board who contributed to the preparation of the journal; we would like to thank the printing team for their effort in preparing it for publication. This thirteen issue includes three original research, a case reports and a review. Periodicals are popular with their readers and researchers. In the upcoming period, with your support, our goal is for JoPIC to be indexed in nationally and internationally accepted scientific indexes. I would like to thank you in advance for your contribution.

Prof. Dr. Berna Akıncı Özyürek
Editor in Chief

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Nutritional approach outcomes in palliative care patients with malnutrition

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ABSTRACT

Aims: In this study, we aimed to investigate the effects of dietary patterns on activity and performance scores, symptom levels, laboratory parameters, anthropometric measurements and mortality in palliative care patients with high malnutrition risk score.

Methods: The effects of enteral and parenteral feeding methods, which are the predominant feeding methods, on admission-discharge laboratory parameters, performance scales, activity indices, anthropometric measurements, symptom scales, infection status, duration of antibiotic use and mortality were evaluated in 103 patients aged 18 years and older who were hospitalized in the palliative care service.

Results: When evaluated on the scales, it was seen that enteral fed patients had better initial scores than parenteral fed patients. There was no difference between the nutrition groups in the mean length of stay in the palliative care service and the frequency of infection, whereas the duration of antibiotic use was longer, transfer to the intensive care unit (74% vs. 12%, $p < 0.05$) and mortality rates (13% vs. 4%, $p < 0.05$) were significantly higher in the parenterally fed group.

Conclusion: The data from this study showed that in palliative care patients with malnutrition, patients with lower activity and performance scores required more parenteral nutrition and that the need for parenteral nutrition, edema and poor performance at baseline were independent predictors of mortality.

Keywords: Enteral nutrition, nutritional support, palliative care, parenteral nutrition

INTRODUCTION

'Palliative care' is a discipline that aims to improve the quality of life by providing physical, social, psychological, and spiritual support to patients, their relatives or caregivers at the end stage of diseases such as cancer with limited treatment options.¹ Scales showing the current status of palliative care and disease prognosis were used. Some of these include the Palliative Performance Score (PPS), Palliative Prognostic Score (PaP), Palliative Prognostic Index (PPI), Barthel Activity Index (BAI), and Karnofsky Performance Scale (KPS).

After nutritional status assessment in palliative care units, patients in need of nutritional support should be identified, appropriate nutritional treatment administered individually, and the results monitored.² In patients with a high malnutrition risk score or malnutrition, a decrease in the duration of hospitalization, a decrease in the complications of the current disease, and improvement in general well-being and activity scores are expected with appropriate nutritional therapy.

In this study, we aimed to investigate the effect of nutritional therapy on laboratory parameters, including inflammatory markers, anthropometric measurements, activity and performance status, and symptom levels determined using appropriate scales, as well as the effect of nutritional therapy on hospitalization duration and mortality in patients aged ≥ 18 years with high malnutrition risk scores who were followed up in a palliative care unit.

METHODS

This study was designed as a prospective, follow-up study. Ethical approval was obtained from the Non-interventional Clinical Researches Ethics Committee of Kırıkkale University (Date: 09.10.2019, Decision No: 2019.10.05). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study included 103 patients aged 18 years and older who were hospitalized for at least three days or more in the palliative care service of the department of internal medicine between

15.11.2019 and 15.03.2020 and who had a risk score of 3 or higher determined by Nutritional Risk Screening-2002 (NRS-2002) during hospitalization. The exclusion criteria were as follows: patients under 18 years of age, patients hospitalized for less than three days, patients with a risk score of less than 3 as determined by the NRS-2002 during hospitalization, and patients with limb amputation.

Background information, smoking history, diseases that caused hospitalization, comorbidities that were not the primary reason for hospitalization, diet, presence of infection, duration of antibiotic use, height, body weight, and BMI (body-mass index) were recorded for each patient. CBC (complete blood count) parameters including Hb (hemoglobin), Plt (platelet), LEU (leukocytes), NEU (neutrophils), LYM (lymphocytes), glucose, CRP (C-reactive protein), TC (total cholesterol), TGL (triglycerides), HDL (high density lipoprotein), LDL (low density protein), BUN (blood urea nitrogen), Cr (creatinine), Na (sodium), K (potassium), Alb (albumin), Ca (calcium) and P (phosphorus) were measured during hospitalization. CBC parameters, including Hb, Plt, LEU, NEU, LYM, glucose, BUN, Cr, Na, K, and Alb values, were recorded at discharge from the palliative care service. CRP/alb, Neu/Lym (NLR), and Plt/Lym (PLR) ratios were calculated at admission and discharge as markers of infection. At admission and before discharge from the palliative service, anthropometric measurements, including KPS, BAI, Edmonton Symptom Assessment Scale (ESAS), PPS, NRS-2002, Upper mid-arm circumference (UMAC), and calf circumference of all patients were determined and recorded. The ESAS, which evaluates the severity of the symptoms of pain, sadness, insomnia, fatigue, nausea, anorexia, anxiety, well-being, and shortness of breath with a score between 0 and 10 points, was administered by the researcher in accordance with the statements of patients and their relatives. The PPS, which included the patient's symptoms, ability to perform daily activities, dependency status, and medical care needs, and the PPS, which included the sub-headings of self-care, nutrition, mobility, activity/disease finding, and level of consciousness, were also completed and recorded by the researcher. The comorbidity status of patients was determined during hospitalization using the Charlson Comorbidity Score.³

Within the first three days of hospitalization, the nutritional regimen was determined by the Hospital Nutrition Team in accordance with the ESPEN (European Society for Clinical Nutrition and Metabolism guidelines). Enteral nutrition was the preferred method of nutrition in all patients, and a parenteral nutrition regimen was initiated in patients with chronic intestinal failure, failure in adequate enteral nutrition intake within 48 hours, and patients who did not accept or tolerate oral intake.⁴ A feeding route in which more than 60% of the patients' daily nutritional needs were met was considered the dominant feeding route. The manner in which patients left the palliative care service was recorded.

The effects of enteral and parenteral nutrition, which were the predominant feeding methods for all patients hospitalized in the palliative care service and included in the study, on laboratory parameters, performance scales, activity indices, anthropometric measurements, symptom scales, infection status, duration of antibiotic use, and mortality were evaluated.

Statistical Analysis

SPSS Statistics 21.0 (IBM SPSS Inc, Chicago) was used for statistical analysis. Descriptive statistics related to continuous data were expressed as mean±standard deviation. A value of p<0.05 was considered statistically significant. Whether the data were normally distributed was checked by Kolmogorov-Smirnov test and Shapiro-Wilk test. Bonferroni correction was applied for multiple comparisons.

RESULTS

A total of 103 patients were included in the study. During their hospitalization in the palliative care service, 73 patients received predominantly enteral nutrition (9 with nasogastric tube, 6 with percutaneous endoscopic gastrostomy (PEG), 58 with oral nutritional fluids) and 30 patients received predominantly parenteral nutrition (5 with central parenteral nutrition and 25 with peripheral parenteral nutrition). Demographic data and statistical results are given in **Table 1**. No significant difference was found between enteral and parenteral nutrition groups in admission UMAC and Calf circumference measurements.

Table 1. Demographic data of patients hospitalized in palliative care service with malnutrition according to dietary patterns

	Enterally feeding patients n=73	Parenterally feeding patients n=30	Total n=103	p
Age (years)	67.7±14.9	73.9±12.5	69.5±14.4	0.07
Gender (%)				
Female	32 (44)	10 (33)	42 (40)	0.44
Male	41 (56)	20 (67)	61 (60)	
Height (cm)	164.0±10.9	167.4±10.4	165.7±10.7	0.14
Body weight (kg)	59.0±11.7	60.5±12.5	62.2±12.1	0.89
Smoking (%)				
Yes	41 (56)	19 (63)	60 (58)	0.66
No	32 (44)	11 (37)	43 (41)	
BMI (kg/m ²)	22.0 ± 4.6	21.5±4.2	21.8±4.4	0.79
Reason for hospitalization (%)				
Malnutrition	17 (23)	5 (17)	22 (21)	0.32
Infection	35 (48)	19 (63)	54 (53)	0.34
Pain	16 (22)	3 (10)	19 (18)	0.08
General condition disorder	5 (7)	3 (10)	8 (8)	0.28

Data are presented as the mean±SD or number (percentage ratio). BMI: Body-mass index

The distribution of comorbid diseases of palliative care patients receiving enteral and parenteral nutrition is shown in **Table 2**. Hospitalization and discharge laboratory values of the patients are shown in **Table 3**.

better in enteral fed patients ($p < 0.01$) (**Table 4**). All symptoms of patients hospitalized in the palliative care service who received enteral nutrition therapy were significantly reduced at discharge (**Table 5**).

When the two feeding groups were compared, it was found that baseline PPS and KPS scores and BAI were significantly

No significant difference was found between the enteral and parenteral nutrition palliative care patient groups in terms of

Table 2. Distribution of comorbid diseases of palliative care patients receiving enteral and parenteral nutrition

Comorbid disease	Enterally feeding patients n=73	Parenterally feeding patients n=30	Total n=103	p
Diabetes mellitus (%)	24 (32)	9 (30)	33 (32)	0.95
Hypertension (%)	49 (67)	21 (70)	70 (67)	0.95
Anemia (%)	58 (79)	27 (90)	85 (83)	0.32
Cerebrovascular accident (%)	11 (15)	5 (17)	16 (16)	0.84
Dementia (%)	16 (21)	10 (33)	26 (25)	0.33
Malignancy (%)	39 (53)	16 (53)	55 (53)	0.99
Coronary artery disease (%)	22 (30)	11 (37)	33 (32)	0.68
Heart failure (%)	14 (19)	10 (3)	17 (17)	0.23
Acute kidney injury (%)	16 (21)	6 (20)	22 (21)	0.99
Chronic kidney disease (%)	18 (24)	5 (17)	23 (22)	0.53
Pulmonary thromboembolism (%)	6 (8)	2 (7)	8 (8)	0.78
COPD (%)	24 (32)	11 (37)	35 (34)	0.88
Pressure sore (%)	16 (21)	17 (57)	33 (32)	<0.01
Infection (%)	58 (79)	27 (90)	85 (83)	0.32
Edema (%)	26 (36)	20 (67)	46 (45)	<0.01
Charlson Comorbidity Score*	8.1±0.4	9.3±0.6	8.4±3.1	0.75
Duration of antibiotic use (days)*	13±1	19±3	15±12	0.02

Data are presented as numbers (percentage ratios) or mean±SD. COPD: Chronic obstructive pulmonary disease

Table 3. Comparison of hospitalization and discharge laboratory parameters in patients receiving enteral and parenteral nutrition therapy in palliative care service

Laboratory parameters	Enterally feeding patients n=73			Parenterally feeding patients n=30			P*
	Hospitalization	Discharge	p	Hospitalization	Discharge	p	
Hemoglobin g/dl	11.1±2.1	11.0±1.7	0.51	11.2±0.4	10.2±0.3	0.03	0.03
Leukocytes x10 ³ /mm ³	10.8±10.5	9.1±4.5	0.11	10.7±2.8	10.8±1.3	0.26	0.07
Neutrophils x10 ³ /mm ³	7.2±5.2	6.5±3.6	0.22	6.5±0.6	9.5±1.2	0.44	0.02
Lymphocytes x10 ³ /mm ³	1.3±0.8	1.6±0.8	<0.01	1.2±0.1	1.0±0.1	0.22	<0.01
Neutrophils/ lymphocytes	8.1±1.0	5.1±0.5	<0.01	8.1±1.6	17.1±4.7	<0.01	<0.01
Platelets x10 ³ /mm ³	284±147	282±134	0.42	258±16	191±21	0.50	0.02
Platelet/lymphocyte	498±241	197±12	<0.01	325±62	257±41	0.15	0.61
Creatinine mg/dl	1.2±0.4	1.2±0.5	0.21	1.3±0.7	1.2±0.6	0.29	0.15
Urea mg/dl	33±10	27±12	0.12	31±9	32±6	0.18	0.54
Glucose mg/dl	113±23	110±30	0.33	108±25	106±24	0.27	0.19
Sodium mmol/L	135±4	138±3	0.18	134±5	133±4	0.12	0.14
Potassium mmol/L	4.0±0.5	3.9±0.8	0.22	3.9±0.6	4.1±0.3	0.35	0.18
Phosphorus mmol/L	2.5±1.0	2.7±0.8	0.30	2.4±0.8	2.3±1.0	0.28	0.32
Calcium mmol/L	7.7±0.9	7.9±0.8	0.21	7.6±0.7	7.7±0.8	0.22	0.24
CRP mg/L	70.9±66.1	52.7±58.1	0.01	67.8±8.6	87.5±9.8	0.15	0.01
Albumin g/dl	3.1±0.6	3.0±0.6	0.01	3.1±0.6	2.5±0.6	<0.01	0.01
CRP/albumin	24.6±2.8	19.0±2.7	0.03	23.3±3.2	39.2±5.2	<0.01	<0.01
Total cholesterol mg/dl	178±9	-	-	158±10	-	-	0.19
Triglycerides mg/dl	144±8	-	-	116±10	-	-	0.38
HDL mg/dl	40±2	-	-	43±3	-	-	0.42
LDL mg/dl	105±8	-	-	90±8	-	-	0.29

Data are presented as mean±SD. *Statistical significance level of the comparison of the difference in hospitalization-discharge in parenterally fed patients and the difference in hospitalization-discharge in enteral fed patients. CRP: C-reactive protein, HDL: High density lipoprotein, LDL: Low density protein

Table 4. Comparison of hospitalization and discharge performance scores in palliative care patients receiving enteral and parenteral nutrition therapy

Performance scales	Enterally feeding patients n=73			Parenterally feeding patients n=30			p*
	Hospitalization	Discharge	p	Hospitalization	Discharge	p	
Barthel Activity Index	40±3	41±3	0.06	30±3	15±3	<0.01	<0.01
Palliative Performance Score	42±2	44±3	0.17	20±2	7±3	<0.01	<0.01
Karnofsky Performance Score	42±2	44±2	0.23	29±2	15±3	<0.01	<0.01

Data are presented as mean±SD. *Statistical significance level for the comparison of the difference between hospitalization and discharge in patients receiving parenteral nutrition and the difference between hospitalization and discharge in patients receiving enteral nutrition

Table 5. Comparison of hospitalization and discharge symptoms in enteral and parenteral fed palliative care patients with the Edmonton Symptom Assessment Scale

Symptom	Enterally feeding patients n=73			Parenterally feeding patients n=30			p*
	Hospitalization	Discharge	p	Hospitalization	Discharge	p	
Pain	5±2	2±1	<0.01	6±1	3±1	<0.01	0.88
Fatigue	6±1	4±2	<0.01	6±1	5±2	<0.01	<0.01
Nausea	5±2	2±1	<0.01	6±1	3±1	<0.01	0.46
Sadness	5±2	2±1	<0.01	7±1	6±1	0.07	<0.01
Concern	6±2	4±1	<0.01	7±1	7±2	0.16	<0.01
Insomnia	4±2	2±1	<0.01	5±2	4±2	0.02	<0.01
Feeling bad	6±2	4±2	<0.01	7±1	7±2	0.02	<0.01
Loss of appetite	5±2	3±2	<0.01	7±1	6±2	0.03	<0.01
Shortness of breath	4±1	2±1	<0.01	5±2	5±2	0.88	<0.01
Skin/nail changes	4±1	2±1	<0.01	4±1	4±1	0.10	<0.01
Mouth sores	4±1	2±1	<0.01	4±2	4±2	0.09	0.16
Numbness in the hands	3±1	2±1	<0.01	3±1	3±1	0.20	0.18

Data are presented as mean±SD. *Statistical significance level for the comparison of the difference between hospitalization and discharge in patients receiving parenteral nutrition and the difference between hospitalization and discharge in patients receiving enteral nutrition

mean length of stay in the ward. While most of the enterally fed patients were discharged (84%), the majority of patients requiring parenteral nutrition were admitted to the intensive care unit (73%). The mortality rate during hospitalisation was significantly higher in patients receiving parenteral nutrition (13% versus 4%, p<0.01).

When the two groups were compared in terms of baseline BAI, KPS, PPS scores, all baseline activity index and performance scores were significantly higher in the surviving group. While enteral nutrition was the predominant mode of nutrition in surviving patients, parenteral nutrition was the predominant mode of nutrition in deceased patients.

The effect of categorical variables such as type of nutrition, presence of pressure sores and presence of edema on mortality was tested by logistic regression analysis. It was found that the mortality rate was 22.8 times higher in parenteral fed patients compared to enteral fed patients and the need for parenteral nutrition had a significant effect on the increase in mortality (p<0.01). Mortality rate was 3.6 times higher in patients with edema compared to patients without edema and the presence of edema had a significant effect on mortality (p=0.02). On the other hand, although the presence of pressure sores was significantly higher in the deceased patient group, it did not lead to a statistically significant increase in mortality.

When the baseline activity index, performance scores and length of hospital stay were included in the regression analysis, in addition to the need for parenteral nutrition and edema, patients' baseline low KPS score emerged as

a variable affecting mortality. Although the presence of comorbidities and comorbidity scores did not differ between those who survived and those who died, edema continued to be an independent determinant of mortality when acute kidney injury, chronic kidney disease and congestive heart failure, which may be related to edema, were included in the regression analysis.

In the comparison between surviving (n=4) and deceased (n=26) parenteral fed patients, anemia and edema increased mortality (p=0.019 for anemia and p=0.001 for edema). In the enterally fed patient group, high leukocyte count (p=0.033), infection (p=0.013) and pulmonary embolism (p=0.044) were found to increase mortality in the comparison between survivors (n=61) and deaths (n=12). The most common causes of death were multi-organ failure and sepsis, followed by respiratory failure and myocardial infarction.

DISCUSSION

The study included 103 patients aged 18 years and older who were hospitalized for at least three days or more in the palliative care service of the department of internal medicine. 73 patients received predominantly enteral nutrition and 30 patients received predominantly parenteral nutrition. The patients included in the study were heterogeneous in terms of underlying diagnoses and disease severity. When comparing enteral and parenteral nutrition groups, no significant difference was observed in serum biomarkers and inflammatory parameters during hospitalisation; however, the initial performance scores of patients who could not

tolerate enteral nutrition and required parenteral nutrition were significantly worse. In this group of patients with impaired baseline performance scores who subsequently required parenteral nutrition, an increase in intensive care requirements and in-hospital mortality rates was observed. The need for parenteral nutrition was associated with higher mortality rates and intensive care requirements.

Palliative care aims to reduce symptoms and improve the quality of life of patients and their relatives.⁵ Early detection of malnutrition and implementation of effective nutritional treatments are important for hospitalized patients, especially in palliative care services. The current disease status is decisive in the choice of diet. Orrevall et al.⁶ showed that nausea, vomiting, and gastrointestinal obstruction are the most common reasons for parenteral nutrition in palliative care patients.

In a study of 384 patients, elevated CRP, NEU, NLR, and PLR decreased mean survival, but only neutrophil count was an independent predictor of mean survival in multivariate analyses.⁷ In our study, no significant effect of inflammatory markers, including baseline Leu, Neu, CRP, CRP/albumin, PLR, and NLR, on mortality was observed in malnourished patients hospitalized in palliative care.

One study showed that KPS scores were worse in the group requiring parenteral nutrition at discharge from the palliative care service than in enteral-fed patients.⁸ In our study, no significant improvement was observed in BAI, PSS or KPS scores in patients who were able to receive enteral nutrition upon discharge and who had better performance scores at baseline. In patients who could not tolerate enteral nutrition during hospitalisation, had lower performance scores and required parenteral nutrition, deterioration in performance scores and overall health status was observed.

In a study of 446 patients, it was found that the amount of edema decreased significantly in patients who responded to nutritional therapy and gained weight gain.⁹ In another study, 21% of participants received less than 50% of the calculated daily energy requirement, and the rate of edema development was six times higher in these patients, although the amount of weight lost at discharge was slightly higher than that in other patients.¹⁰ Although we found diet and edema to be independent determinants of mortality, we did not evaluate the relationship between malnutrition or daily caloric intake and edema.

In a study of 2099 patients, the prevalence of pressure sores was 12.9%.¹¹ The nutritional status of 27% of patients was inadequate, and a significant difference was found between the nutritional status of patients with and without pressure sores.¹¹ The fact that pressure sores were observed more frequently in patients receiving parenteral nutrition therapy in our study may be related to their poor nutritional status, activity, and performance scores. When all patients included in the study were evaluated, although the proportion of patients with pressure sores and edema was significantly higher in the deceased patient group than in the surviving patient group, the effect of pressure sores on mortality was not significant in contrast to the presence of edema.

Elke et al.¹² reported that enteral and parenteral nutrition had no effect on mortality in patients hospitalized in intensive care units. In a meta-analysis, mortality and complication rates, except for infection, were found to be similar in enteral-fed and parenteral-fed patients.¹³ In a study conducted in Japan with 3750 non-cancer patients, mortality rates were significantly lower in the enteral-fed patient group.¹⁴ In our study, in the multiple regression analysis evaluating the factors affecting mortality in palliative care patients receiving nutritional therapy due to malnutrition, it was found that the need for parenteral nutrition had an independent effect on the increase in mortality ($p < 0.01$) and that the mortality rates in the parenterally fed patient group were 22.8 times higher than in the enterally fed patients. The rates of transfer to the intensive care unit and in-hospital mortality were found to be higher in patients with low performance scores who could not tolerate enteral feeding during admission. Although the enteral and parenterally fed patient groups did not differ in terms of infection frequency, the duration of antibiotic use was significantly shorter, and discharge rates were higher in the enterally fed patient group. In addition, high leukocyte count and the presence of infection were found to be significant determinants of mortality in enterally fed patients.

Limitations

The heterogeneous nature of the patients included in the study in terms of underlying diagnoses and disease severity makes it difficult to attribute the data to a specific disease group. Although our study associates the need for parenteral nutrition with low performance scores, there is a limitation in that this situation may stem from the initial clinical severity of the patients rather than a cause-and-effect relationship.

CONCLUSION

The results of this study on palliative care patients with malnutrition support studies reporting that mortality is significantly lower in patients who can be fed enterally than in those who require parenteral nutrition. In conclusion, the data obtained from this study showed that patients with malnutrition and low activity and performance scores in palliative care require more parenteral nutrition. In our study, an increase in mortality rates was observed in patients with low performance scores who required parenteral nutrition. The need for parenteral nutrition was associated with higher mortality rates and intensive care requirements.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval was obtained from the Non-interventional Clinical Researches Ethics Committee of Kırıkkale University (Date: 09.10.2019, Decision No: 2019.10.05).

Informed Consent

Written informed consent was obtained from all individual participants prior to their inclusion in the study. Participants were fully informed about the study's aims, procedures, potential risks and benefits, and their rights—including the right to withdraw at any time without consequence. All participants voluntarily signed a written informed consent form.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Concept: H.K., İ.K.; Design: M.T., H.K.; Supervision: H.K.; Resources: M.T., H.K.; Materials: M.T., H.K.; Data Collection and/or Processing: M.T., İ.K.; Analysis and/or Interpretation: H.K., İ.K.; Literature Search: H.K., İ.K.; Writing: M.T.; Critical Review: H.K., İ.K.

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The relationship between troponin levels in pneumonia and the severity of pneumonia and the oxidant-antioxidant balance

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ABSTRACT

Aims: This study aimed to determine the association between serum troponin levels and pneumonia severity, and to evaluate the oxidant-antioxidant balance in patients with community-acquired pneumonia.

Methods: A total of 100 patients diagnosed with community-acquired pneumonia and 100 healthy volunteers were enrolled in this prospective, case-control study conducted at Ankara City Hospital between October and December 2019. Troponin, native thiol, total thiol, disulphide, ischemia-modified albumin, C-reactive protein, and procalcitonin levels were analyzed and compared between groups. Pneumonia severity was determined using the Pneumonia Severity Index.

Results: Troponin levels were significantly higher in the pneumonia group than in the control group ($p < 0.05$), with a mean troponin of 48.03 ng/L in pneumonia patients and 3.15 ng/L in controls. Troponin levels correlated positively with c-reactive protein and procalcitonin values ($p < 0.05$) and were significantly higher in patients with abnormal echocardiography and electrocardiogram findings. Native thiol and total thiol levels were significantly lower in pneumonia patients, while the disulphide/native thiol and disulphide/total thiol ratios were higher ($p < 0.05$). Ischemia-modified albumin, levels were also higher in the pneumonia group ($p < 0.05$). Troponin and ischemia-modified albumin levels increased significantly with pneumonia severity index stage.

Conclusion: Elevated serum troponin and ischemia-modified albumin levels, along with altered thiol-disulphide balance, may reflect increased oxidative stress and disease severity in pneumonia. These biomarkers may contribute to clinical assessment and prognosis in pneumonia cases.

Keywords: Pneumonia, cardiac troponin, thiol, disulfide, ischemia-modified albumin

INTRODUCTION

Pneumonia accounts for a significant proportion of physician visits, treatment costs, work and school days lost, and deaths worldwide.¹ It is the most common cause of death from infection.^{2,3} Several inflammatory biomarkers are used to predict disease severity and monitor treatment in pneumonia cases.⁴ At the same time, some objective criteria have been defined to assist physicians in deciding whether to hospitalise patients. The most commonly used index in this regard is the Pneumonia Severity Index (PSI). The selection of the appropriate empirical antibiotic and the severity of the patient's condition in pneumonia patients are determined according to the PSI.

Cardiac troponins (cTn) are highly sensitive and specific markers of myocardial damage. In acute coronary syndrome, elevated cTn levels are important for both prognosis and treatment guidance. However, elevated cTn levels may also be seen in conditions other than acute coronary syndrome,

such as heart failure (acute and chronic), aortic dissection, aortic valve disease or hypertrophic cardiomyopathy, cardiac contusion, cardioversion, ablation, pacing, inflammatory diseases such as myocarditis and pericarditis, pulmonary embolism or severe pulmonary disease, hypothyroidism, and renal dysfunction.⁵ There is no comprehensive study on the relationship between elevated troponin levels and the severity of pneumonia in children, except for one study conducted in children.

Antioxidant defence systems are responsible for preventing damage caused by reactive oxygen species in the body. Thiols are organic compounds containing a sulphhydryl (-SH) group that play a critical role in preventing the formation of any oxidative stress conditions in cells. They play important roles in stabilising protein structures, regulating protein functions, regulating enzyme functions, and in receptors, carriers, Na-K channels, and transcription.⁶



There is considerable evidence indicating that abnormal thiol disulphide homeostasis plays a role in the pathogenesis of various diseases. In respiratory system diseases such as asthma, chronic obstructive pulmonary disease (COPD), and asthma-COPD overlap syndrome, community-acquired pneumonia and pulmonary thromboembolism.⁷⁻⁹

Ischemia-modified albumin (IMA) is a test that has received food and drug administration (FDA) approval among newly investigated cardiac markers.¹⁰ The principle of the test is based on the reduction in albumin's cobalt-binding capacity due to chemical changes in albumin caused by oxidative free radicals formed during ischaemia, hypoxia and acidosis. This new albumin molecule is also called ischaemia-modified albumin. The formation of this new albumin molecule, which has lost its cobalt-binding ability, is one of the earliest markers of ischaemia.¹¹ Recent studies show that IMA, which has come to the fore as a cardiac ischaemia marker, may also increase in different pathologies.^{12,13} In today's conditions, where we are constantly exposed to oxidative stress, there are insufficient studies evaluating the relationship between pneumonia and oxidative stress. This study aimed to investigate the relationship between troponin levels in pneumonia and the severity of pneumonia, and to assess the oxidant-antioxidant balance, thereby exploring its potential use as a biomarker for pneumonia and for grading the severity of pneumonia. Although individual associations between pneumonia and cardiac troponin, thiol-disulphide homeostasis, or ischemia-modified albumin have been previously reported, there is limited evidence regarding the co-assessment of these biomarkers in adult patients with community-acquired pneumonia, particularly in relation to disease severity. Co-assessment of these biomarkers could potentially improve the assessment of pneumonia severity by providing a more comprehensive perspective on the interaction between myocardial damage, oxidative stress, and inflammatory load in pneumonia. In our study, we showed that serum troponin and ischemia-modified albumin levels were increased in patients diagnosed with pneumonia and that, as assessed by the PSI, they changed in parallel with pneumonia severity. We share our study to contribute to the literature.

METHODS

This study was conducted at the Ankara City Hospital Chest Diseases Clinic between October and December 2019. Ethical approval for this prospective, case-control study was obtained from the Clinical Researches Ethics Committee of Yıldırım Beyazıt University Faculty of Medicine (Date: 09.10.2019, Decision No: 102). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study population included outpatients and inpatients who presented to the Chest Diseases Clinic of Ankara City Hospital with a diagnosis of community-acquired pneumonia during the study period. Patients were classified according to the PSI as follows: outpatients with PSI I and II, inpatients with PSI III, IV, and V, and patients admitted to intensive care based on intensive care admission criteria.

In our study, 100 patients diagnosed with pneumonia and 100 healthy volunteers were compared based on troponin, native thiol, total thiol, disulphide, IMA, haemogram, biochemistry,

postero-anterior (PA) chest X-ray, echocardiography (ECHO), electrocardiography (ECG), and chest computed tomography (CT) when necessary. The medical history, comorbidities, and physical examination findings of the pneumonia patients were recorded. Pneumonia patients were grouped according to whether they received outpatient treatment or inpatient treatment in the ward or intensive care unit. Patients were also assessed according to the PSI.

In pneumonia patients, a hemogram, biochemistry, arterial blood gas analysis, and PA chest X-ray were routinely performed to determine the severity of the disease. Chest CT was performed when necessary. The medical history, comorbidities, and physical examination findings of pneumonia patients and control group patients were recorded. Cardiovascular assessment of pneumonia patients was performed by a cardiologist using ECG and ECHO with cardiology consultation.

CRP levels were measured using a BNII Nephelometer Analyser (Siemens, Munich, Germany) with the CardioPhase hsCRP kit (Siemens Healthcare Diagnostics Products, Marburg, Germany) by turbidimetry. PMNLs were counted using the Sysmex XE-2100 automated haematology system (Sysmex, Kobe, Hyogo, Japan). Troponin T levels were measured using the cobas e411 device with the elecsys troponin T hs kit. IMA measurement was performed using a rapid, colorimetric method developed by Bar-Or et al. to determine cobalt reduced to albumin-binding capacity (IMA level). Briefly, 200 µL of patient serum was transferred to glass tubes and 50 µL of 0.1% CoCl₂ x 6H₂O (Sigma Aldrich Lot: S38901-248; Sigma Aldrich, St. Louis, MO, USA) was added. After gentle shaking, the mixture was incubated for 10 minutes to ensure sufficient cobalt albumin binding. Next, 50 µL of 1.5 mg/ml dithiothreitol (DTT) (Sigma-Aldrich Lot: D5545-1G; Sigma-Aldrich) was added as a decolourising agent. After 2 minutes, 1 ml of 0.9% NaCl was added to stop the cobalt-albumin binding. A blank was prepared for each sample. At the DTT addition step, 50 µL of distilled water was used instead of 50 µL of 1.5 mg/ml DTT to obtain a DTT-free blank. Absorbances were recorded at 470 nm using a spectrophotometer. Colour formation in DTT-containing samples was compared to colour formation in blank tubes, and results were expressed in absorbance units (ABSU) (Bar-Or D L. E., 2000).

The thiol disulphide balance measurement was performed using the automated spectrophotometric method described by Erel & Neselioglu.⁶ In this method, disulphide bonds were reduced with sodium borohydride to form free functional thiol groups. Unused reducing sodium borohydride was removed by consumption with formaldehyde to prevent the reduction of 5,5'-dithiobis-(2-nitrobenzoic) acid (DTNB). All thiol groups, including reduced and native thiol groups, were determined after reaction with DTNB. The amount of dynamic disulphide was obtained as half the difference between total thiols and native thiols. After determining native and total thiols, disulphide amounts were calculated. The disulphide/native thiol, disulphide/total thiol, and native thiol/total thiol ratios were then calculated as percentages.

The inclusion criteria for the study group were: agreeing to participate in the study, signing the consent form and being

a volunteer, having a diagnosis of pneumonia in accordance with the American Thoracic Society (ATS) criteria, and being over 18 years of age. Those with respiratory complaints who were found to have no disease following examination and testing, those with a history of lung disease, radiological sequelae control, screening examinations, etc., having agreed to participate in the study, having signed the consent form, being a volunteer, and being over 18 years of age were determined as the criteria for inclusion in the control group. Patients under 18 years of age, pregnant women, those who did not sign a written document indicating their acceptance of the study, those with mental disabilities, those with acute coronary syndrome, those with renal failure, those with a history of trauma, those with pulmonary thromboembolism, and those with a recent history of coronary intervention were not included in the study.

RESULTS

The mean age of the 100 patients diagnosed with pneumonia was 65.8±15.1, while the mean age of the control group was 59.0±16.0. Thirty-eight per cent (n=38) of the pneumonia group were female and 62 per cent (n=62) were male, while 54 per cent (n=54) of the control group were female and 46 per cent (n=46) were male (p values, respectively; p=0.071, p=0.102) (Table 1).

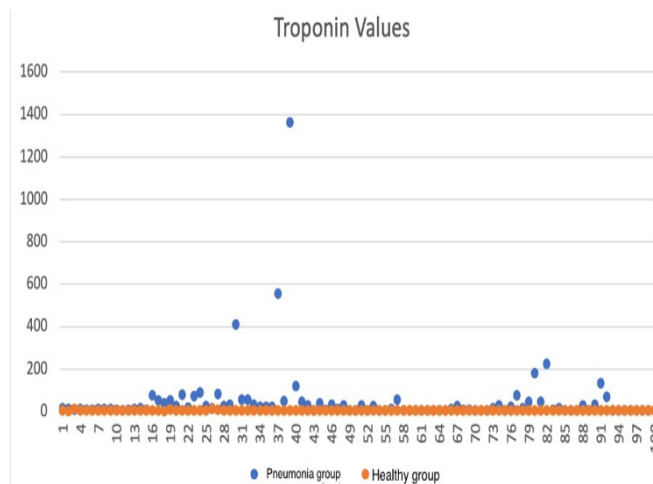


Figure 1. Pneumonia-distribution of troponin values in the control group

According to the parametric test results, the mean troponin level in the pneumonia group was 48.03 ng/L, while the mean in the control group was 3.15 ng/L; troponin levels were statistically higher in the pneumonia group. In the pneumonia group, troponin levels were statistically higher in those with pathological ECHO and ECG results compared to those without pathology (p<0.05). The troponin levels of pneumonia patients with normal ECHO were within normal limits when compared to the control group (Table 3).

	Pneumonia group		Control group	
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)
Age (years) (mean±SD)	65.8±15.1	66 (19 -92)	59.0±16.0	59 (19 -86)
	Pneumonia group	Control group	p-value	
	n	n		
Gender				
Female	38	54	p<0.05	
Male	62	46	p<0.05	
Total	100	100		
Smoking history				
Smoker	16	18	p>0.05	
Ex-smoker	50	31	p<0.05	
Non-smoker	34	51	p<0.05	
Total	100	100		

SD: Standard deviation, Min: Minimum, Max: Maximum

Average troponin value	Normal/median (min-max)	Pathological/median (min-max)
ECHO	3 ng/L (3-75.03)	32.9 ng/L (3,13-1360)
ECG	5.56 ng/L (3-409.2)	42.95 ng/L (19-66)

Min: Minimum, Max: Maximum, ECHO: Echocardiography, ECG: Electrocardiography

When troponin levels were assessed in pneumonia, troponin values were found to be significantly higher in the pneumonia group compared to the control group (p<0.05) (Table 2, Figure 1).

Troponin	n	Rank average	Sum of the series	U	Z	p
Pneumonia group	100	135.58	13558	1492	-9.584	.000
Control group	100	65.42	6542			

When examining the relationship between C-reactive protein (CRP) and procalcitonin (PCT), which are useful in the diagnosis and follow-up of pneumonia, and troponin, a moderate, significant positive correlation was found between troponin and CRP values in the pneumonia group (p<0.05). A high and significant positive correlation was found between troponin and PCT values in the pneumonia group (p<0.05).

When examining whether there was a significant difference in troponin values between the pneumonia groups according to the PSI stage, a statistically significant difference was observed between troponin values in at least two stages (p<0.05). A significant difference was observed between stage 1 and stages 3, 4, 5, and between stage 2 and stages 3, 4, 5 (Table 4, Figure 2).

When evaluating thiol disulphide levels in the pneumonia group, native thiol and total thiol levels were found to be significantly lower compared to the control group (p<0.05). There was no statistical difference between the disulphide values of the pneumonia group and the control group (p>0.05). The disulphide/native thiol ratio and the disulphide/total thiol ratio in the pneumonia group were statistically higher than in the control group (p<0.05). The native thiol/

Table 4. Troponin values according to the PSI stage in the pneumonia group

Groups	n	Rank average	Degree of liberty	P	Significant difference
PSI 1	18	16.06	4	.000	PSI 1-PSI 3 PSI 1-PSI 4 PSI 1-PSI 5 PSI 2-PSI 3 PSI 2-PSI 4 PSI 2-PSI 5
PSI 2	15	21.47			
PSI 3	14	57.07			
PSI 4	39	68.00			
PSI 5	14	70.57			

n: Number of patients, PSI: Pneumonia Severity Index

Table 6. Relationship between native thiol, total thiol, disulfide values and PSI phases

Rank average				
Groups	Native thiol	Native thiol	Total thiol	Disulfide
PSI1	18	69.72	67.89	51.8
PSI2	15	67.47	67.80	48.7
PSI3	14	43.21	45.79	50.9
PSI4	39	43.32	40.94	52.5
PSI5	14	34.89	40.96	47.07

PSI: Pneumonia Severity Index

Changes in troponin and CRP values according to PSI stages

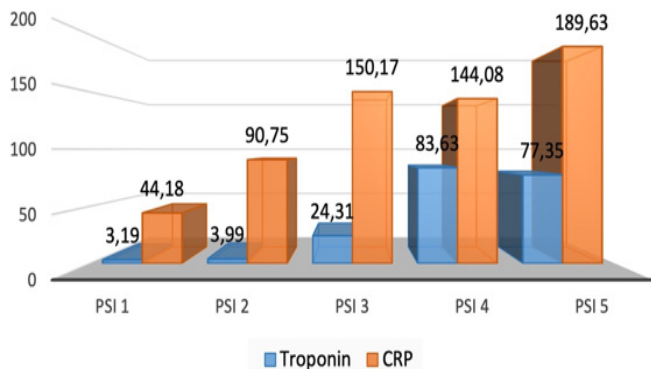


Figure 2. Change in troponin and CRP values according to PSI stages
CRP: C-reactive protein, PSI: Pneumonia Severity Index

Average IMA values according to PSI stages

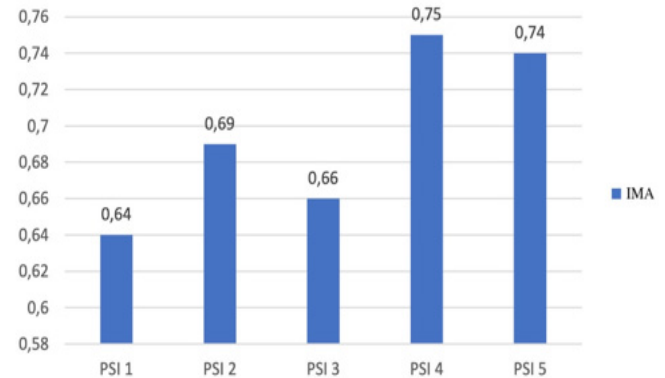


Figure 3. Average IMA values according to PSI stages
IMA: Ischemia-modified albumin, PSI: Pneumonia Severity Index

total thiol ratio in the pneumonia group was statistically lower than in the control group ($p < 0.05$) (Table 5).

When examining the relationship between native thiol values, total thiol values, disulphide values, and PSI stages, a significant difference was found between native thiol values and PSI stages between stage 1 and stage 4.5, and between stage 2 and stage 4.5, and between total thiol values and PSI stages, a significant difference was found between stage 1 and stage 4.5 and between stage 2 and stage 4 ($p < 0.05$). No statistical difference was found between disulphide values and PSI stages in the pneumonia group ($p > 0.05$) (Table 6, Figure 3).

When IMA levels were evaluated in pneumonia, the IMA level was found to be significantly higher in the pneumonia group compared to the control group ($p < 0.05$). The mean IMA value in the pneumonia group was 0.71 ABSU, while the mean IMA in the control group was 0.65 ABSU (Table 7).

In the pneumonia group, IMA and troponin levels were significantly increased compared to the control group, and a weak but significant positive correlation was found between them ($p < 0.05$) (Figure 4).

Table 7. IMA values for the pneumonia group and control group

IMA	n	Rank average	Total of rows	U	Z	p
Pneumonia	100	116.32	11632.00	3418	-3.866	.000
Control	100	84.68	8468.00			

IMA: Ischemia-modified albumin

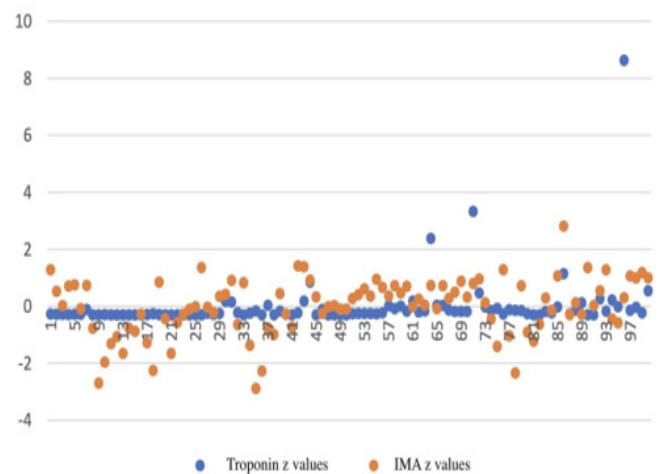


Figure 4. Distribution of IMA-troponin values in the pneumonia group
IMA: Ischemia-modified albumin

Table 5. Thiol disulphide balance values for the pneumonia group and control group

Groups	n	Native tiyol	Total tiyol	Disulfit	Rank average		
					Disulfit/native tiyol	Disulfit/total tiyol	Native tiyol/total tiyol
Pneumonia	100	278.25	336.27	23.76	120.01	118.03	89.97
Control	100	377.83	427.41	23.98	80.99	82.98	111.03

DISCUSSION

In this study, serum troponin and IMA levels were found to be significantly higher in patients with pneumonia compared to the control group. Native thiol, total thiol levels, and the native thiol/total thiol ratio were lower than in the control group, while the disulphide/total thiol and disulphide/native thiol ratios were statistically higher than in the control group.

Elevated cTn levels can be observed in approximately 50% of patients with heart failure, both during the acute decompensation phase and in the chronic compensation period. Increased cTn levels are a common finding in patients with sepsis. Although the reason for the increase in cTn in sepsis is not precisely known, factors such as cytotoxic endotoxins, inflammatory mediators (IL, TNF, heat shock protein, etc.), septic microemboli, vasoactive drugs, accompanying hypotension, and myocarditis are thought to be responsible. Elevated cTn levels are reported more frequently in patients with severe left ventricular systolic dysfunction accompanying sepsis.⁵ In patients hospitalized with sepsis in the intensive care unit, cardiac troponin T levels are independently associated with length of hospital stay and short-term mortality.¹⁴ Although elevated troponin levels are used as a marker in acute coronary syndromes, they are also elevated in some patients presenting with causes other than acute coronary syndrome.¹⁵ This situation can lead to misdiagnosis and unnecessary interventions. Troponin release from the myocardium indicates temporary or permanent myocardial damage. This damage may be due to many causes, such as ischaemia, inflammation, infection, toxins, or increased ventricular wall tension. Elevated troponin levels may be associated with pulmonary embolism, central nervous system diseases (intracranial haemorrhage, increased intracranial pressure, ischaemic stroke), aortic dissection, pneumothorax, acute cholecystitis, acute or chronic renal failure, pancreatitis, etc.^{16,17}

Early deaths due to myocardial injury occur in sepsis patients, and this condition can be used independently of rehabilitation morbidity after discharge.^{18,19} To our knowledge, there are no studies on cTn elevation in pneumonia. We thought that cTn elevation in pneumonia could be due to cytokines released due to inflammation, accompanied by hypotension, hypoxia, and cardiac pathologies other than acute coronary syndrome. Specifically, in our study, cTn levels were found to be higher in patients with left ventricular systolic dysfunction during cardiac evaluation in pneumonia compared to patients with normal cardiac function. Therefore, it is considered necessary to perform a cardiac evaluation if elevated cTn is detected in a patient with pneumonia.

In our study, patients with renal dysfunction and those suspected of having acute coronary syndrome were excluded from the pneumonia group; however, as with patients with the same renal dysfunction, a cut-off value for cTn can be determined in the pneumonia patient group, and it can help us distinguish whether the elevated cTn is due to pneumonia or ischaemia. Further studies are needed in this area.

There are many biological markers that can be used in the diagnosis and follow-up of pneumonia. CRP and PCT

are some of these. These markers indicate the severity of pneumonia, and CRP is frequently used. PCT, which is used less frequently, can also be a guide in distinguishing between bacterial and viral infections.²⁰ In our study, when examining the relationship between cTn levels in pneumonia and CRP and PCT, which are useful in diagnosis and follow-up, a positive correlation was found between cTn and CRP values in the pneumonia group and between PCT values. It has been suggested that cTn levels could be a biomarker used in the diagnosis and follow-up of infectious processes such as pneumonia, similar to CRP and PCT.

Prediction rules (CURB-65, PSI) have been developed for the classification of patients with pneumonia based on mortality risk prediction. As the CURB-65 and PSI scoring systems are only moderately sensitive and specific in determining risk in patients with pneumonia, additional risk factors and prognostic markers are needed to improve the prognostic performance of risk scores.²¹ In our study, there was a significant difference in troponin values according to PSI stage, and cTn may be a marker for deciding on follow-up between the outpatient (PSI 1-2) patient group and the ward and intensive care unit (PSI 3-4-5) groups.

Studies have been conducted showing impaired thiol disulphide balance in cardiovascular diseases and pulmonary thromboembolism.^{7,22} Studies have also been conducted showing changes in the dynamic thiol-disulphide balance in community-acquired pneumonia.^{8,23} In all of these studies, native thiol and total thiol levels in the thiol-disulphide balance were reduced compared to the control group. Another study conducted on paediatric community-acquired pneumonia cases also found that disulphide levels were low in pneumonia cases. The disulphide/native thiol, disulphide/total thiol, and native thiol/total thiol ratios were significantly higher in the pneumonia group. In our study, native thiol and total thiol levels were also significantly lower than in the control group, while the disulphide/native thiol ratio and disulphide/total thiol ratio were higher. It has been stated that the thiol-disulphide balance shifts towards disulphide bond formation, and that oxidative stress therefore increases in community-acquired pneumonia.²⁴

In our study, when IMA levels were evaluated, they were higher in the pneumonia group compared to the control group. Similarly, in a prospective case-control study conducted by Bolatkale and colleagues,²⁵ serum IMA levels were shown to be significantly increased in patients with pneumonia compared to healthy control subjects. To our knowledge, this study is the first to investigate serum IMA levels in adult patients presenting to the emergency department with TGP and has demonstrated that IMA may be a sensitive and specific new biomarker for the diagnosis of pneumonia in emergency department patients.

When the correlation between cTn values, an acute coronary syndrome marker, and IMA was evaluated in the pneumonia group, a weak but significant positive correlation was found. The evaluation of IMA and cTn in acute coronary syndrome, as in pneumonia, may guide us in the differential diagnosis of pneumonia and ischaemia.

Limitations

Our findings should be interpreted with certain limitations in mind. Firstly, this is a single-centre, small-scale study. It is the first study to evaluate cardiac troponin levels in adults with pneumonia. As cardiac troponin levels can increase for many reasons, it is difficult to establish specificity for pneumonia alone, and increases due to other causes must be considered. No threshold value has been established between myocardial ischaemia and other causes of elevation.

CONCLUSION

Consequently, cTn levels may be elevated for different reasons. The results of this study suggest that, when other causes are excluded, elevated levels in pneumonia indicate the need to evaluate cases for cardiac pathology and may also provide an important contribution as an indicator of pneumonia severity. It is thought that, particularly in cases of pneumonia with pre-existing cardiac pathologies, evaluating serum IMA levels alongside other factors could be useful in making decisions regarding hospital admission. Further studies could evaluate its potential use as a biomarker for the early detection of complications such as myocarditis that may develop during pneumonia. Furthermore, additional studies with larger sample sizes could determine a threshold value for cTn in pneumonia cases. It is therefore concluded that it could be more useful in practical application. However, a cost-effectiveness study is required.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study has been approved by the Clinical Researches Ethics Committee of Yıldırım Beyazıt University Faculty of Medicine (Date: 09.10.2019, Decision No: 102).

Informed Consent

Written informed consent was obtained from all individual participants prior to their inclusion in the study. Participants were fully informed about the study's aims, procedures, potential risks and benefits, and their rights—including the right to withdraw at any time without consequence. All participants voluntarily signed a written informed consent form.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions


Concept: S.Ö., A.K.; Design: S.Ö., A.K.; Control: S.Ö., A.K.; Data Collection and/or Processing: S.Ö., A.K.; Analysis and/or Interpretation: S.Ö., A.K.; Literature Review: S.Ö., A.K.; Article Writing: S.Ö., A.K.; Critical Review: S.Ö., A.K.

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Assessment of radiation knowledge, attitudes, and behaviors among hospital secretaries working near diagnostic imaging units

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ABSTRACT

Aims: This study aimed to assess radiation-related knowledge, attitudes, behaviors, and demand for radiation safety education among hospital secretaries, an occupational group frequently working in proximity to diagnostic imaging environments but rarely targeted by formal radiation safety programs.

Methods: This single-center, cross-sectional study included hospital secretaries working in radiology, emergency, outpatient, and inpatient units. Data were collected using a structured, self-administered questionnaire assessing demographic characteristics, radiation knowledge, attitudes, behaviors, risk perception, and educational preferences. Knowledge, attitude, and behavior scores were calculated, and associations were evaluated using appropriate comparative tests, Spearman correlation analysis, and multivariable logistic regression.

Results: A total of 88 hospital secretaries were included. While awareness of general radiation risks was high (cancer risk: 86.4%; increased sensitivity during pregnancy: 89.8%), correct identification of non-ionizing imaging modalities was limited (magnetic resonance imaging: 48.9%; ultrasonography: 53.4%). None of the participants reported awareness of the ALARA principle. Attitude and behavior scores were consistently high across groups. Attitude score was moderately correlated with behavior score ($\rho=0.53$), whereas knowledge score showed only weak correlations with attitude ($\rho=0.25$) and behavior ($\rho=0.22$). In multivariable logistic regression analysis, no independent predictors of demand for radiation safety education were identified.

Conclusion: Hospital secretaries demonstrate important gaps in modality-specific radiation knowledge despite favorable attitudes and self-reported safety behaviors. These findings highlight the need to extend structured, role-specific radiation safety education to hospital secretaries to strengthen occupational safety and promote a more inclusive radiation protection culture in healthcare settings.

Keywords: Radiation safety, hospital secretaries, occupational exposure, radiation awareness, education needs

INTRODUCTION

The rapid expansion of diagnostic imaging modalities in modern medicine has substantially increased occupational exposure to ionizing radiation within healthcare environments. While radiologists, radiologic technologists, physicians, and nurses are widely recognized as high-risk groups, radiation exposure is not confined to these professions alone. Hospital personnel who work in close proximity to imaging units—often without direct involvement in imaging procedures—may also experience unintended and largely unrecognized exposure.¹⁻⁶ Among these groups, hospital secretaries represent a particularly overlooked population.

Hospital secretaries play a critical operational role in healthcare systems, especially in radiology departments, emergency units, outpatient clinics, and inpatient wards.

Their duties frequently require physical presence near imaging areas during patient registration, scheduling, documentation, and coordination tasks. Despite this proximity, secretaries are generally not classified as radiation workers, are rarely monitored with personal dosimeters, and often do not receive structured radiation safety training.⁷⁻¹⁰ This situation places them at potential risk for cumulative low-dose radiation exposure, a risk that may remain invisible both to the individuals themselves and to institutional occupational health policies.

Existing literature demonstrates that even healthcare professionals who are formally involved in imaging procedures may have significant knowledge gaps regarding ionizing radiation and radiation protection principles.

Several studies conducted over the last decade have reported inadequate awareness of basic concepts such as ionizing versus non-ionizing radiation, radiation dose levels associated with common imaging modalities, and long-term health risks.¹¹⁻¹⁶ Misconceptions are particularly common regarding magnetic resonance imaging (MRI) and ultrasonography, which are frequently—and incorrectly—perceived as sources of ionizing radiation.¹⁷⁻¹⁹ These findings suggest that radiation awareness cannot be assumed, even among trained healthcare staff.

Education has consistently emerged as a key determinant of radiation awareness. Studies have shown that healthcare workers who receive formal or in-service radiation safety training demonstrate significantly higher knowledge levels, more appropriate attitudes toward radiation risks, and safer behaviors in clinical practice.²⁰⁻²² Conversely, lack of training is associated with poor compliance with protective measures such as maintaining distance, minimizing exposure time, and using shielding equipment when appropriate.²³⁻²⁵ From this perspective, untrained occupational groups working near imaging environments may represent an even more vulnerable population.

Despite growing recognition of radiation safety as a multidisciplinary responsibility, the literature remains heavily focused on physicians, nurses, and radiology technicians. Research specifically addressing non-clinical hospital staff—particularly secretaries—is extremely limited. To date, no comprehensive studies have systematically evaluated hospital secretaries' knowledge, attitudes, behaviors, risk perception, and demand for radiation safety education related to radiation exposure. This represents a critical gap in occupational health research, especially given the increasing volume of diagnostic imaging and the emphasis on safety culture within healthcare institutions.

Addressing this gap is essential for several reasons. First, occupational radiation protection is grounded in the ALARA (As Low as Reasonably Achievable) principle, which applies to all individuals who may be exposed, regardless of job title.²⁶⁻²⁹ Second, inadequate awareness among secretaries may indirectly affect patient safety, particularly in high-turnover areas such as emergency departments and radiology units. Third, identifying demand for radiation safety education in this group may inform the development of targeted training programs, contributing to a more inclusive and effective radiation safety culture.³⁰⁻³²

Therefore, the aim of the present study is to evaluate the levels of radiation-related knowledge, attitudes, behaviors, and risk perception among hospital secretaries, and to identify their specific demand for radiation safety education. We hypothesize that overall radiation awareness among hospital secretaries will be low, but that individuals working in radiology-related units or those who have previously received radiation education will demonstrate higher knowledge and more appropriate safety-related attitudes and behaviors. By focusing on this often-neglected occupational group, the study seeks to provide original evidence to support more comprehensive radiation safety strategies in healthcare settings.

METHODS

Ethics

This study has been approved by the Non-interventional Clinical Researches Ethics Committee of Gaziantep City Hospital (Date: 17.09.2025, Decision No: 306/2025). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design and Setting

This study was designed as a single-center, cross-sectional survey conducted to assess radiation-related knowledge, attitudes, behaviors, risk perception, and demand for radiation safety education among hospital secretaries. The study was carried out at Gaziantep Medical Point Hospital, a tertiary healthcare institution with active radiology, emergency, outpatient, and inpatient services. Data collection was performed using a structured, self-administered questionnaire.

The target population consisted of hospital secretaries working in different clinical units, including radiology, emergency department, outpatient clinics, and inpatient wards. Inclusion criteria were: (1) age ≥ 18 years, (2) employment as a hospital secretary, (3) active employment at the institution for at least one month, and (4) voluntary participation with written informed consent. There were no restrictions regarding sex, educational level, or length of professional experience. Exclusion criteria included: (1) non-secretarial administrative or healthcare staff, (2) refusal to participate or failure to provide informed consent, (3) inability to complete the questionnaire due to cognitive or health-related limitations, and (4) employment duration of less than one month at the institution. Participants who left a substantial portion of the questionnaire unanswered or failed attention control items were excluded from the final analysis.

Data Collection Tool: Questionnaire Structure

Data were collected using a structured questionnaire developed by the researchers based on a comprehensive review of the literature on radiation awareness and occupational radiation safety. No previously validated or copyrighted scale was used; therefore, no external permission was required. The questionnaire was pilot-tested for clarity and comprehensibility before full implementation. Prior to the main data collection, the questionnaire was pilot-tested on 10 hospital secretaries who were not included in the final analysis. Based on feedback obtained during the pilot phase, minor wording revisions were made to improve clarity and comprehensibility of several items; however, no items were removed or added, and the overall structure of the questionnaire remained unchanged.

The questionnaire consisted of eight sections:

- Demographic and occupational characteristics (age group, gender, education level, working unit, duration of employment, and frequency of proximity to radiology areas).
- Knowledge assessment regarding ionizing and non-ionizing radiation, health risks, pregnancy-related sensitivity, dosimeter use, ALARA principle, and radiation content of common imaging modalities.

- Dose and radiation protection principles, including time–distance–shielding concepts and portable radiography safety.
- Attitude assessment, evaluated using a 5-point Likert scale ranging from “strongly disagree” to “strongly agree.”
- Behavioral practices, assessed on a 5-point frequency scale ranging from “never” to “always.”
- Scenario-based questions addressing practical decision-making during portable imaging and special risk situations.
- Risk perception and demand for radiation safety education, including preferred training topics and formats.
- Control questions, including an attention check item and a deliberately incorrect statement to assess response consistency.

Scoring of Knowledge, Attitude, and Behavior Domains

Knowledge questions were coded as correct or incorrect; responses marked as “not sure” were considered incorrect. A total knowledge score was calculated by summing correct responses. Attitude items were scored from 1 to 5, with higher scores indicating more positive attitudes toward radiation safety. Behavioral items were scored from 0 to 4, with higher scores reflecting safer radiation-related practices. Composite scores were calculated separately for knowledge, attitude, and behavior domains.

Sample Size Estimation

Sample size estimation was performed using G*Power version 3.1. Assuming a medium effect size (Cohen’s $d=0.50$), an alpha error probability of 0.05, and a statistical power of 0.80 for two-group comparisons, the minimum required sample size was calculated as 84 participants. Considering potential exclusions and incomplete responses, a target sample size of approximately 100 participants was planned to ensure adequate statistical power.

Statistical Analysis

All data analyses were performed using IBM SPSS Statistics version 30.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as frequencies and percentages for categorical variables, and as mean±standard deviation or median (minimum–maximum) for continuous variables, depending on data distribution. The internal consistency of knowledge items was assessed using the Kuder–Richardson Formula 20 (KR-20). The reliability of attitude and behavior scales was evaluated using Cronbach’s alpha coefficient, with values ≥ 0.70 considered acceptable. Normality of continuous variables was assessed using the Kolmogorov–Smirnov test. For group comparisons, independent samples t-test or Mann–Whitney U test was used for two-group analyses, and one-way ANOVA or Kruskal–Wallis test for comparisons involving three or more groups, as appropriate. Post hoc analyses were performed using Bonferroni correction when significant differences were detected. Associations between categorical variables were evaluated using the chi-square test. Correlations between knowledge, attitude, and behavior

scores were analyzed using Spearman’s rank correlation coefficient.

To identify independent predictors of educational demand, multivariable logistic regression analysis was conducted, with educational demand (yes/no) as the dependent variable and demographic variables along with knowledge, attitude, and behavior scores as independent variables. Statistical significance was set at $p<0.05$ for all analyses.

RESULTS

Half of the participants were aged 18–25 years ($n=44$, 50.0%), followed by those aged 26–35 years ($n=35$, 39.8%), while 9 participants (10.2%) were aged 36–45 years; no participants were aged 46 years or older. The study population was predominantly female ($n=80$, 90.9%), with males accounting for 9.1% ($n=8$). Regarding educational status, the majority of participants had an associate degree ($n=51$, 58.0%). High school graduates constituted 21.6% of the sample ($n=19$), while 17 participants (19.3%) held a bachelor’s degree. Only one participant (1.1%) reported postgraduate education. With respect to working units, nearly half of the participants were employed in outpatient clinics ($n=43$, 48.9%). This was followed by radiology units ($n=23$, 26.1%), emergency departments ($n=12$, 13.6%), and inpatient wards ($n=6$, 6.8%), while 4 participants (4.6%) worked in other administrative units. Most participants had been working for 1–5 years ($n=50$, 56.8%), whereas 24 participants (27.3%) had less than one year of work experience. Twelve participants (13.6%) reported 6–10 years of employment, and only 2 participants (2.3%) had more than 10 years of experience. In terms of proximity to radiology areas, 28 participants (31.8%) reported never being near radiology units, while 27 (30.7%) reported rare proximity and 17 (19.3%) reported occasional proximity. Frequent proximity was reported by 3 participants (3.4%), and daily proximity by 13 participants (14.8%) (Table 1, Figure 1).

Internal consistency analysis demonstrated acceptable reliability for all questionnaire domains. The knowledge domain showed a Kuder–Richardson Formula 20 (KR-20) coefficient of 0.74. Cronbach’s alpha coefficients were 0.81 for the attitude domain and 0.78 for the behavior domain.

Distribution of responses to radiation knowledge items among hospital secretaries were shown in Table 2. High correct response rates were observed for general radiation risk awareness. A total of 76 participants (86.4%) correctly identified that radiation exposure may increase long-term cancer risk, and 79 participants (89.8%) correctly reported that sensitivity to radiation increases during pregnancy. Knowledge regarding imaging modalities showed greater variability. Mammography was correctly identified as involving ionizing radiation by 64 participants (72.7%), whereas fluoroscopy/angiography was correctly identified by 54 participants (61.4%). In contrast, correct identification of non-ionizing imaging modalities was lower. Only 43 participants (48.9%) correctly reported that MRI does not involve ionizing radiation, and 47 participants (53.4%) correctly identified ultrasonography as a non-ionizing modality. Knowledge related to occupational radiation monitoring was also limited, as only 53 participants (60.2%) correctly stated that dosimeters were used for personnel dose

Table 1. Baseline demographic and occupational characteristics of hospital secretaries (n=88)

Variable	n (%)
Age group (years)	
18–25	44 (50.0)
26–35	35 (39.8)
36–45	9 (10.2)
Gender	
Female	80 (90.9)
Male	8 (9.1)
Educational level	
High school	19 (21.6)
Associate degree	51 (58.0)
Bachelor’s degree	17 (19.3)
Postgraduate	1 (1.1)
Working unit	
Radiology	23 (26.1)
Emergency department	12 (13.6)
Outpatient clinics	43 (48.9)
Inpatient wards	6 (6.8)
Other*	4 (4.6)
Duration of employment	
<1 year	24 (27.3)
1–5 years	50 (56.8)
6–10 years	12 (13.6)
>10 years	2 (2.3)
Frequency of proximity to radiology areas	
Never	28 (31.8)
Rarely	27 (30.7)
Occasionally	17 (19.3)
Frequently	3 (3.4)
Daily	13 (14.8)

*Other units include administrative offices such as hospital management, physician assistance, and institutional billing.

Table 2. Distribution of responses to radiation knowledge items among hospital secretaries (n=88)

Radiation knowledge item	Correct n (%)	Incorrect n (%)	Not sure n (%)
Fluoroscopy/angiography involves ionizing radiation	54 (61.4)	7 (8.0)	27 (30.7)
Mammography involves ionizing radiation	64 (72.7)	3 (3.4)	21 (23.9)
Magnetic resonance imaging (MRI) does not involve ionizing radiation	43 (48.9)	34 (38.6)	11 (12.5)
Ultrasonography does not involve ionizing radiation	47 (53.4)	27 (30.7)	14 (15.9)
Radiation may increase long-term cancer risk	76 (86.4)	3 (3.4)	9 (10.2)
Sensitivity to radiation increases during pregnancy	79 (89.8)	4 (4.5)	5 (5.7)
A dosimeter is used for personnel dose monitoring	53 (60.2)	3 (3.4)	32 (36.4)
Awareness of the ALARA principle†	0 (0.0)	—	88 (100.0)

ALARA: As Low as Reasonably Achievable. †The ALARA item was assessed as awareness (yes/no) rather than factual correctness; none of the participants reported prior awareness.

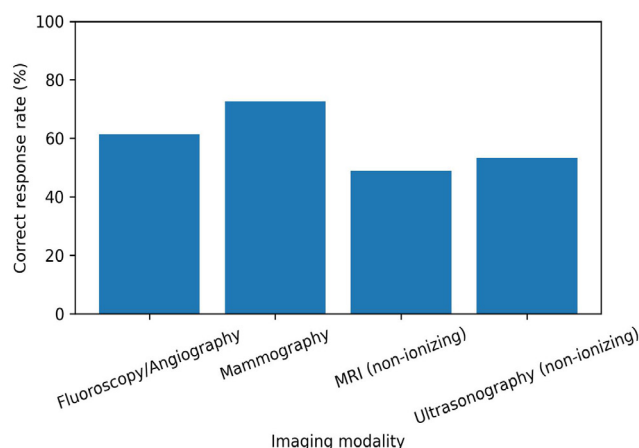


Figure 2. Correct response rates (%) for radiation knowledge items related to common imaging modalities

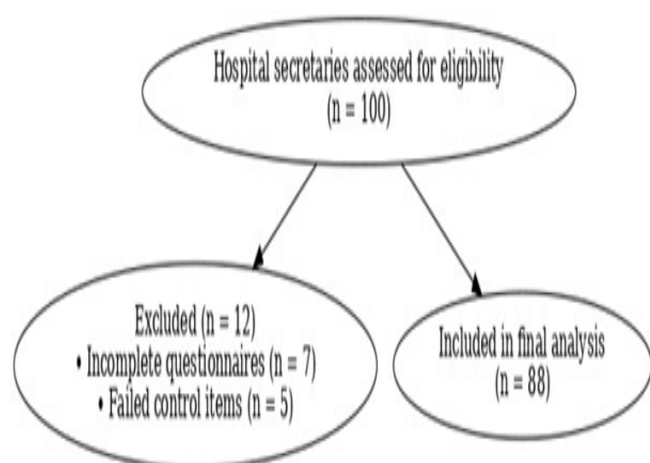


Figure 1. Flow diagram of participant inclusion and exclusion

monitoring. Notably, none of the participants reported prior awareness of the ALARA principle (Table 2, Figure 2).

Knowledge, attitude, and behavior scores according to working unit and prior radiation training were shown in Table 3. Among participants working in radiology units, those without prior radiation training (n=10) had a mean

knowledge score of 5.7±1.3, while those with prior training (n=3) demonstrated a slightly higher mean knowledge score of 6.0±1.0. Mean attitude scores in the radiology unit were 4.83±0.44 in untrained participants and 4.67±0.58 in trained participants, whereas mean behavior scores were 4.85±0.36 and 4.50±0.50, respectively. In the emergency department, untrained participants (n=6) had a mean knowledge score of 3.8±1.5, compared with 5.0±0.47 in the single participant who reported prior training (n=1). Mean attitude scores in the emergency department were 4.33±0.52 among untrained participants and 4.33±0.50 among trained participants, while mean behavior scores were 4.83±0.41 and 5.00±0.41, respectively. Among participants working in outpatient clinics, untrained individuals (n=28) had a mean knowledge score of 5.0±1.4, whereas trained participants (n=13) had a mean knowledge score of 4.23±1.60. Mean attitude scores in outpatient clinics were similar between untrained and trained participants (4.45±0.51 vs. 4.40±0.48), as were mean behavior scores (4.75±0.39 vs. 4.52±0.46). In inpatient wards and other units combined, untrained participants (n=23) demonstrated a mean knowledge score of 4.1±1.8, compared with 3.5±1.9 among trained participants (n=4). Mean attitude scores in this group were 4.39±0.55 in untrained participants and 4.50±0.58 in trained participants, while mean behavior

scores were 4.57 ± 0.49 and 4.75 ± 0.50 , respectively. Between-group comparisons did not reveal statistically significant differences in knowledge, attitude, or behavior scores across working units or training status (all $p > 0.05$) (Table 3, Figure 3). However, subgroup analyses involving trained participants in certain units were based on small sample sizes and should be interpreted cautiously.

Comparison of knowledge, attitude, and behavior scores by frequency of proximity to radiology areas was shown in Table 4. Participants who reported never being near radiology areas ($n=28$) had a mean knowledge score of 4.18 ± 2.00 . Knowledge scores were higher among those reporting rare proximity ($n=27$; 5.07 ± 1.30) and occasional proximity ($n=17$; 5.24 ± 1.86). The highest mean knowledge score was observed in participants reporting frequent proximity to radiology areas ($n=3$; 6.67 ± 0.58), whereas participants with daily proximity showed a lower mean knowledge score with greater variability ($n=13$; 4.08 ± 2.40). Mean attitude scores were consistently high across all proximity categories, ranging from 4.32 ± 0.87 in the “never” group to 5.00 ± 0.00 in the “frequently” exposed group. Participants reporting rare and occasional proximity demonstrated mean attitude scores of 4.43 ± 0.58 and 4.62 ± 0.57 , respectively, while those with daily proximity had a mean attitude score of 4.35 ± 1.09 . Behavior scores were also high across groups. Mean behavior scores were 4.57 ± 0.59 among participants who were never near radiology areas, 4.85 ± 0.36 among those with rare proximity, and 4.76 ± 0.50 among those with occasional proximity. Participants reporting frequent proximity demonstrated the highest behavior score (5.00 ± 0.00), whereas those with daily proximity had a mean behavior score of 4.48 ± 1.10 . Comparisons across proximity-to-radiology categories did not reach statistical significance for knowledge, attitude, or behavior scores (Kruskal–Wallis test, all $p > 0.05$) (Table 4).

Association between radiation knowledge, attitudes, behaviors, and demand for radiation safety education Table 5. Participants who expressed a demand for radiation safety education ($n=61$) had a higher mean knowledge score compared with those who did not request education (4.97 ± 1.63 vs. 4.19 ± 2.30). Similarly, the mean attitude score was higher among participants requesting education than among those without educational demand (4.55 ± 0.55 vs. 4.19 ± 1.08). Behavior scores followed a similar pattern. Participants who reported educational demand demonstrated

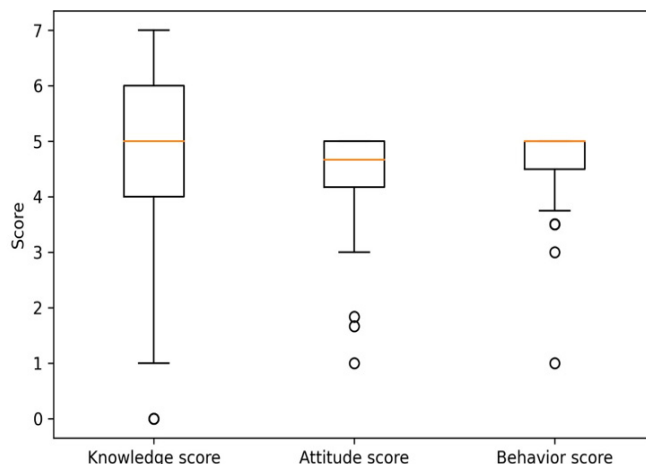


Figure 3. Distribution of knowledge, attitude, and behavior scores among hospital secretaries. Higher scores indicate better radiation-related knowledge, more positive attitudes toward radiation safety, and safer self-reported behaviors

Table 4. Comparison of knowledge, attitude, and behavior scores by frequency of proximity to radiology areas

Frequency of proximity to radiology areas	n	Knowledge score	Attitude score	Behavior score
Mean±SD				
Never	28	4.18 ± 2.00	4.32 ± 0.87	4.57 ± 0.59
Rarely	27	5.07 ± 1.30	4.43 ± 0.58	4.85 ± 0.36
Occasionally	17	5.24 ± 1.86	4.62 ± 0.57	4.76 ± 0.50
Frequently	3	6.67 ± 0.58	5.00 ± 0.00	5.00 ± 0.00
Daily	13	4.08 ± 2.40	4.35 ± 1.09	4.48 ± 1.10

Small subgroup sizes in certain proximity categories may limit the robustness of inferential comparisons, SD: Standard deviation

higher mean behavior scores compared with those who did not request education (4.80 ± 0.45 vs. 4.47 ± 0.86). Differences in knowledge, attitude, and behavior scores between participants with and without educational demand were not statistically significant (all $p > 0.05$) (Table 5).

Table 5. Association between radiation knowledge, attitudes, behaviors, and demand for radiation safety education

Demand for radiation safety education	n	Knowledge score	Attitude score	Behavior score
Mean±SD				
No	27	4.19 ± 2.30	4.19 ± 1.08	4.47 ± 0.86
Yes	61	4.97 ± 1.63	4.55 ± 0.55	4.80 ± 0.45

SD: Standard deviation

Table 3. Knowledge, attitude, and behavior scores according to working unit and prior radiation training

Working unit	Prior radiation training	n	Knowledge score	Attitude score	Behavior score
Mean±SD					
Radiology	Yes	3	6.0 ± 1.0	4.67 ± 0.58	4.50 ± 0.50
	No	10	5.7 ± 1.3	4.83 ± 0.44	4.85 ± 0.36
Emergency department	Yes	1	5.0 ± 0.47	4.33 ± 0.50	5.00 ± 0.41
	No	6	3.8 ± 1.5	4.33 ± 0.52	4.83 ± 0.41
Outpatient clinics	Yes	13	4.2 ± 1.6	4.40 ± 0.48	4.52 ± 0.46
	No	28	5.0 ± 1.4	4.45 ± 0.51	4.75 ± 0.39
Inpatient wards/other units*	Yes	4	3.5 ± 1.9	4.50 ± 0.58	4.75 ± 0.50
	No	23	4.1 ± 1.8	4.39 ± 0.55	4.57 ± 0.49

* Some subgroup analyses are based on small sample sizes; therefore, inferential interpretations should be made with caution, SD Standard deviation

Multivariable logistic regression analysis identifying independent predictors of educational demand regarding radiation safety was shown in **Table 6**. In the adjusted model, knowledge score was not independently associated with educational demand (adjusted OR [aOR]=1.17, 95% CI: 0.90–1.52; p=0.230). Similarly, attitude score did not show a significant association with demand for education (aOR=1.12, 95% CI: 0.47–2.66; p=0.792). Behavior score was also not identified as an independent predictor of educational demand in the multivariable analysis (aOR=1.92, 95% CI: 0.63–5.82; p=0.250). In addition, frequency of proximity to radiology areas, modeled as an ordinal variable, was not significantly associated with demand for radiation safety education (aOR=1.18, 95% CI: 0.81–1.70; p=0.387). Model diagnostics indicated an acceptable goodness-of-fit (Hosmer–Lemeshow test, p>0.05), and no evidence of problematic multicollinearity was observed among the independent variables (variance inflation factors <2.0) (**Table 6**).

Predictor	Adjusted OR	95% CI	p-value
Knowledge score (per 1-point increase)	1.17	0.90–1.52	0.230
Attitude score (per 1-point increase)	1.12	0.47–2.66	0.792
Behavior score (per 1-point increase)	1.92	0.63–5.82	0.250
Proximity to radiology areas (ordinal)*	1.18	0.81–1.70	0.387

OR: Odds ratio, CI: Confidence interval

Correlation matrix illustrating relationships between knowledge, attitude, and behavior scores were shown in **Figure 4**. Knowledge score showed a weak positive correlation with attitude score (Spearman’s $\rho=0.25$) and with behavior score ($\rho=0.22$). In contrast, a moderate positive correlation was observed between attitude and behavior scores ($\rho=0.53$), indicating a stronger association between these two domains. No negative correlations were identified among the evaluated variables (**Figure 4**).

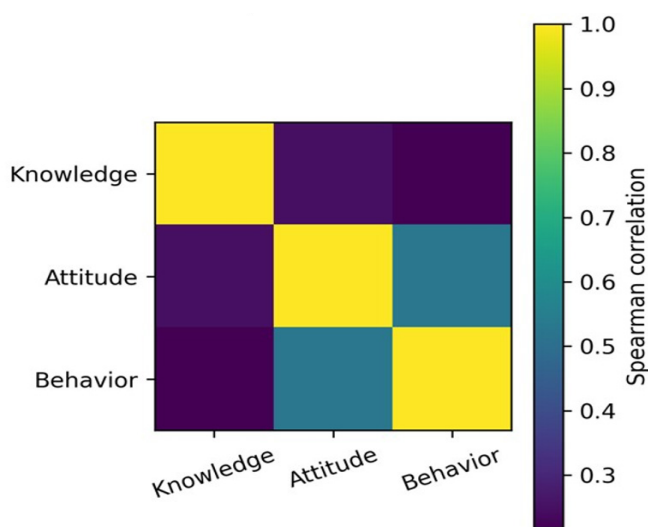


Figure 4. Correlation matrix illustrating relationships between knowledge, attitude, and behavior scores related to radiation safety. Higher scores reflect better knowledge, more favorable attitudes, and safer behaviors

DISCUSSION

This cross-sectional study provides one of the first structured evaluations of radiation-related knowledge, attitudes, behaviors, and demand for radiation safety education among hospital secretaries—an occupational group that routinely operates in imaging-intensive clinical environments but is rarely included in formal radiation safety programs. The findings indicate that, although general awareness of radiation-related health risks such as cancer and increased sensitivity during pregnancy is relatively high, important gaps persist in modality-specific knowledge, particularly regarding MRI and ultrasonography. In addition, awareness of fundamental radiation protection principles, such as the ALARA concept, appears to be absent. Despite these knowledge gaps, self-reported attitudes toward radiation safety and protective behaviors were consistently high, and attitudes were more closely aligned with behaviors than with knowledge levels. Furthermore, when these factors were evaluated simultaneously, none emerged as independent predictors of demand for radiation safety education. Taken together, these findings highlight a dissociation between knowledge and reported practice and underscore the need for structured, role-specific radiation safety education that extends beyond traditionally defined radiation workers.

A striking observation was the reduced correct identification of non-ionizing modalities: only 48.9% correctly stated that MRI does not involve ionizing radiation and 53.4% correctly identified ultrasonography as non-ionizing. This pattern mirrors a broader phenomenon reported in the literature: misconceptions about MRI and ultrasound are common even among healthcare workers and students, suggesting that “radiation awareness” does not reliably diffuse through clinical environments without intentional education. Kanbayti et al.³³ documented significant gaps in MRI safety knowledge among physicians and nurses, reinforcing that MRI-related misunderstandings are widespread and not limited to patients. Similar misconceptions have been repeatedly highlighted in radiation-awareness research as a key educational target, particularly because MRI safety is often conflated with ionizing radiation risk, potentially leading to misplaced fears or inappropriate reassurance. In contrast, participants showed high correct responses for general risk statements—86.4% for cancer risk and 89.8% for increased sensitivity during pregnancy—indicating that “radiation is harmful” messaging is present, but modality-specific understanding is incomplete. This distinction matters: effective protection behaviors depend not only on generic risk awareness, but also on accurate knowledge of which settings and procedures were actually relevant to ionizing exposure.

None of the participants reported awareness of the ALARA principle. This is not merely a vocabulary issue; ALARA is a cornerstone concept that frames practical decisions (time, distance, shielding) and is embedded in institutional radiation-protection programs. International guidance has repeatedly emphasized that radiation protection training should be broadened across professional groups, including those indirectly exposed through workflow proximity.

Vassileva et al.³⁰ summarized conclusions from an IAEA meeting calling for stronger, more consistent radiation-protection education and training for health professionals across disciplines. Our finding suggests that hospital secretaries may be systematically excluded from this educational ecosystem. At the institutional level, ALARA terminology and principles are not formally incorporated into radiation safety training programs for non-radiation workers, which may partly explain the complete lack of awareness observed in this group.

Only 60.2% correctly identified the purpose of personal dosimeters, and 36.4% responded “not sure.” This aligns with the concept of secretaries being an “invisible risk group”: they were rarely designated as monitored radiation workers, so dose-tracking tools may not be familiar. Occupational monitoring trends also show that exposure patterns vary by department and job role; Baudin et al.⁷ reported trends in occupational exposure among medical staff over 2009–2019, emphasizing the importance of monitoring frameworks tailored to job categories and settings. While secretaries may not routinely exceed dose limits, lack of awareness of monitoring systems can weaken safety behaviors.

Attitude and behavior scores were consistently high across units and proximity categories. This pattern can have at least two interpretations. First, it may reflect genuine safety-mindedness and compliance with visible cues (warning lights/signage), consistent with findings in other hospital settings where staff report high adherence to basic protective measures. For example, Shubayr et al.³⁴ examined operating-room radiation safety and reported that awareness and compliance can be substantial, though variable across worker groups. Second, the pattern may reflect self-report inflation and a ceiling effect common to safety-behavior questionnaires, where respondents select socially desirable options (particularly in institutional surveys). This is precisely why coupling behavior questions with scenario-based items and control questions, as done in our instrument, is valuable—future work could strengthen this further by adding observational audits or department-level process measures. From a behavioral and occupational safety perspective, the observed association between attitude and behavior scores is consistent with the conceptual view that safety-related attitudes function as proximal determinants of self-reported safety behaviors.

Knowledge scores increased from “never” to “frequently” proximal groups but dropped in the “daily” group with larger variability. This non-linear pattern suggests that proximity alone is not a sufficient proxy for learning—daily exposure does not automatically produce correct understanding. In practice, daily proximity may coincide with routinized administrative flow, time pressure, and normalization of risk signals, which can blunt active learning. This is consistent with broader occupational safety literature, where frequent exposure may desensitize workers unless formal training reinforces correct mental models and self-protective routines.⁹

Participants requesting radiation-safety education had higher mean knowledge, attitude, and behavior scores, yet multivariable logistic regression identified no independent

predictors of educational demand. This apparent mismatch is not uncommon in survey-based occupational studies. Several methodological factors can contribute: limited sample size for multivariable modeling, collinearity among KAB domains, restricted variance in attitude/behavior (ceiling effect), and unmeasured determinants (e.g., prior incidents, leadership emphasis, department culture, perceived institutional support). A systematic review by Rodrigues et al.⁹ emphasized heterogeneity across studies and settings in radiation-protection knowledge and determinants, underscoring that training effects and predictors often depend strongly on local culture and program structure. In our context, educational demand may be shaped more by perceived institutional safety climate and personal risk perception than by knowledge score alone. Importantly, the absence of independent predictors in the multivariable regression model should not be interpreted as evidence of no effect; rather, it may reflect limited statistical power, restricted variability in knowledge, attitude, and behavior scores, or the influence of unmeasured contextual factors such as institutional culture, managerial support, or informal safety norms.

Our findings were directionally consistent with regional studies reporting knowledge gaps among healthcare staff regarding radiation and protection concepts. In Türkiye, Dönmez et al.²⁰ assessed healthcare workers’ knowledge about protection from ionizing radiation and reported notable deficiencies, supporting the need for structured education. Şenışık et al.²² evaluated radiation awareness among personnel/students in radiation environments and highlighted gaps that training could address. Although these studies focus primarily on clinical or radiation-area staff, the implication is transferable: if gaps exist among trained groups, they may be more pronounced in groups not systematically targeted—such as secretaries.

From a policy and training perspective, our results support several actionable steps. Integrate secretaries into hospital radiation-safety programs (onboarding+annual refreshers), with a focus on modality-specific knowledge (CT/fluoroscopy vs MRI/US) and “when to step out” protocols during portable imaging. Standardize micro-training modules aligned with department workflow (radiology, ED, clinics), including signage interpretation, safe waiting zones, and escalation routes. Reinforce ALARA in plain language and connect it to day-to-day actions (time–distance–shielding), consistent with international recommendations to strengthen training across health professions.³⁰ Clarify institutional monitoring practices (dosimeter policies, who is monitored, and why) to reduce uncertainty and promote consistent safety behavior. Multi-center studies are needed to determine whether these patterns generalize across hospitals with different imaging volumes and safety cultures. Intervention studies testing short, targeted training packages (e.g., 15–20-minute modules plus visual reminders) could evaluate improvements in modality-specific knowledge and scenario performance, and examine whether gains persist over time.

Limitations

Limitations include the single-center design, potential self-report and social desirability bias, and smaller subgroup sizes in some unit/training strata. Additionally, our knowledge score emphasized modality identification and selected

foundational concepts; future research could expand into dose estimation knowledge, institutional policy knowledge, and objective measures. In addition, the single-center design and the predominantly young and female composition of the study sample, as well as institution-specific organizational characteristics, may limit the generalizability of the findings to other healthcare settings or countries.

CONCLUSION

As a result, this study demonstrates that hospital secretaries, despite their close and routine proximity to imaging-intensive clinical environments, exhibit notable gaps in modality-specific radiation knowledge, particularly regarding non-ionizing imaging techniques, while simultaneously reporting high levels of safety-oriented attitudes and behaviors. The absence of awareness of fundamental radiation protection principles, such as ALARA, further underscores the need to broaden the scope of institutional radiation safety strategies. The lack of independent predictors of educational demand suggests that demand for radiation safety education may not be driven solely by measurable knowledge or behavior levels, but rather by broader factors such as safety culture and perceived occupational risk. These findings highlight the importance of implementing structured, role-specific radiation safety education programs that explicitly include hospital secretaries, thereby strengthening overall occupational safety and promoting a more inclusive radiation protection culture within healthcare institutions.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study has been approved by the Non-interventional Clinical Researches Ethics Committee of Gaziantep City Hospital (Date: 17.09.2025, Decision No: 306/2025).

Informed Consent

Written informed consent was obtained from all individual participants prior to their inclusion in the study. Participants were fully informed about the study's aims, procedures, potential risks and benefits, and their rights—including the right to withdraw at any time without consequence. All participants voluntarily signed a written informed consent form.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The author declare no conflicts of interest related to this study.

Financial Disclosure

The author received no financial support for the conduct or publication of this research.

Author Contributions

The author confirms sole responsibility for the study conception, design, data collection, analysis, interpretation, and manuscript preparation. All aspects of the work were carried out by the author.

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Current approaches to the diagnosis, treatment, and prognosis of sepsis

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ABSTRACT

Sepsis is a critical clinical condition characterized by organ dysfunction resulting from an uncontrolled host response to infection and is associated with a high risk of mortality. Its incidence is increasing due to aging populations, immunosuppression, and resistant pathogens. Although bacteria are the most common causative agents, viral pathogens such as SARS-CoV-2 have also emerged as important contributors. Advanced age, comorbidities, immune deficiencies, and nosocomial infections are the main risk factors. Diagnosis is established through a combined assessment of clinical, laboratory, radiological, and microbiological findings. Early fluid resuscitation, oxygen support, and appropriate empirical antibiotic therapy are crucial in reducing mortality. Timely initiation of appropriate treatment improves survival and plays a life-saving role.

Keywords: Sepsis, septic shock, organ dysfunction, MODS

INTRODUCTION

Sepsis is a life-threatening syndrome characterized by organ dysfunction that arises from dysregulated physiological, biological, and biochemical responses to infection. This condition may progress to multiple organ failure and ultimately death. Septic shock is defined as persistent hypotension requiring vasopressor therapy to maintain a mean arterial pressure of ≥ 65 mmHg despite adequate fluid resuscitation, in conjunction with a serum lactate level > 2 mmol/L.¹ Multiple organ dysfunction syndrome (MODS) refers to progressive organ failure in which homeostasis cannot be sustained without external support.² Contemporary guidelines highlight the pivotal role of early recognition of sepsis in reducing mortality and advocate the application of scoring systems such as qSOFA, SOFA, and NEWS for this purpose.³⁻⁵

INCIDENCE AND CAUSATIVE PATHOGENS IN SEPSIS

The incidence of sepsis has shown a rising trend in recent years, largely attributed to the growth of the elderly population, the increasing prevalence of immunosuppression, and the widespread emergence of multidrug-resistant infections.^{6,7} Racial and seasonal variations have also been observed; the highest incidence rates have been reported among African American men, and a seasonal increase has been noted during winter months in association with a higher frequency of respiratory infections. The majority of cases occur in individuals aged 65 years and older.⁸⁻¹⁰ Among cases with identified pathogens, bacteria remain the predominant

etioloical agents, with gram-positive microorganisms being the most prominent. Among viral pathogens, SARS-CoV-2 has emerged as a major cause of sepsis during the pandemic. Nevertheless, in approximately half of the cases, no causative microorganism can be identified.¹¹

RISK FACTORS FOR THE DEVELOPMENT OF SEPSIS

Risk factors for the development of sepsis include intensive care unit (ICU) admission, bacteremia, advanced age (≥ 65 years), immunosuppression, diabetes, obesity, cancer, prior hospitalization, and genetic predisposition. Approximately half of ICU patients develop nosocomial infections, and systemic complications are frequently observed in cases with bacteremia.^{12,13} Advanced age is an independent determinant associated with both increased incidence and mortality of sepsis.¹⁴ Conditions causing immune suppression, the use of immunosuppressive therapies, diabetes, and obesity contribute to sepsis development by impairing immune function and increasing the risk of nosocomial infections.¹⁵ Malignancy is among the most common comorbidities and may increase the risk of sepsis by nearly tenfold.¹⁶ Hospitalization, particularly following antibiotic therapy, poses a risk due to alterations in the microbiota.¹⁷ Furthermore, genetic factors such as antibody production defects, T-cell deficiencies, phagocytic dysfunction, natural killer cell impairment, or complement deficiencies can predispose individuals to infection.¹⁸

CLINICAL, LABORATORY, AND DIAGNOSTIC EVALUATION

Although no single clinical finding is specific for sepsis, patients commonly present with hypotension, tachycardia, fever, and leukocytosis. In septic shock, cold skin, cyanosis, mottling, and evidence of organ dysfunction (e.g., oliguria, altered mental status) may be observed.³ Clinical manifestations may include symptoms attributable to the infectious focus, arterial hypotension, fever or hypothermia, tachycardia, tachypnea, and signs of end-organ hypoperfusion. In the early phase, the skin may appear warm and flushed; however, as shock progresses, patients may develop cool extremities, delayed capillary refill, cyanosis, and mottling (Table).

Laboratory findings in sepsis are nonspecific and may reflect either the underlying cause or alterations related to tissue hypoperfusion.³ Common abnormalities include leukocytosis or leukopenia, increased immature neutrophils, hyperglycemia in the absence of diabetes, elevated C-reactive protein (CRP) and procalcitonin levels, arterial hypoxemia, oliguria, increased creatinine, coagulopathy, thrombocytopenia, hyperbilirubinemia, and hyperlactatemia.¹⁹ In addition, features of adrenal insufficiency (e.g., hyponatremia, hyperkalemia) and the euthyroid sick syndrome may also be observed (Table).

In sepsis, imaging modalities targeting the suspected site of infection (e.g., chest radiography, thoracic or abdominal computed tomography) are utilized. Although positive culture results support the diagnosis, they are not always obtainable and are not mandatory for diagnosis. The diagnosis of sepsis and septic shock is established through an integrated assessment of clinical, laboratory, radiological, physiological, and microbiological findings (Table). To avoid delays in treatment, the diagnosis may be made in the presence of compatible findings once alternative causes have been excluded, without awaiting culture results.

TREATMENT AND MANAGEMENT OF SEPSIS

The cornerstone of therapy in sepsis and septic shock is the prompt initiation of fluid resuscitation and antibiotics in the early phase, with the aim of rapidly restoring

perfusion. Securing the airway, correcting hypoxemia, establishing adequate venous access, and ensuring the timely administration of fluids and antimicrobial therapy constitute the essential components of effective management.³ In the presence of hypoxemia, supplemental oxygen should be administered, and oxygen saturation should be continuously monitored via pulse oximetry, generally maintained within the range of 90–96%. Noninvasive ventilation, high-flow oxygen therapy, or endotracheal intubation may be required to ensure adequate oxygenation or to reduce the increased work of breathing. While peripheral venous access may be sufficient at the initiation of fluid resuscitation, placement of a central venous catheter is recommended as soon as feasible.

Routine use of glucocorticoids in sepsis is not recommended; however, corticosteroid therapy may be considered in cases of refractory hypotension despite adequate fluid resuscitation and vasopressor therapy, particularly when critical illness–related adrenal insufficiency is suspected. In such cases, hydrocortisone is recommended as monotherapy, administered in divided doses, with a total daily dose not exceeding 400 mg.²⁰

ANTIMICROBIAL THERAPY

Early initiation of appropriate antibiotic therapy is one of the most critical prognostic factors in sepsis and may reduce mortality by approximately 50%.²¹ Empirical broad-spectrum antimicrobial therapy should be started as soon as possible, ideally within the first hour after culture collection. The choice of agents should consider recent antibiotic exposure, prior microbiological isolates, comorbidities, immune status, infection site, and local epidemiology. In most cases, empirical coverage for both gram-positive and gram-negative pathogens is recommended, with subsequent de-escalation once the causative organism is identified.

To ensure adequate tissue perfusion, crystalloid fluids should generally be initiated at 30 ml/kg based on actual body weight within the first hour, administered as rapid boluses in the absence of pulmonary edema.²² Clinical status, hemodynamic response, and pulmonary findings should be reassessed after each bolus, and fluid administration discontinued if necessary. During the first three hours, administration of 2–3 liters of fluid is generally sufficient; hemodynamic targets include a central venous pressure (CVP) of 8–12 mmHg,

Table. Diagnostic criteria and supportive findings in sepsis

Assessment domain	Key diagnostic indicators	Clinical interpretation
Clinical findings	Fever or hypothermia, tachycardia, tachypnea, altered mental status, hypotension	Indicates systemic inflammatory and hemodynamic response to infection.
Laboratory markers	Leukocytosis or leukopenia, elevated C-reactive protein and procalcitonin, hyperlactatemia, increased creatinine, thrombocytopenia	Reflects infection, tissue hypoperfusion, and organ dysfunction.
Organ dysfunction parameters (sepsis-3)	Increase in SOFA score ≥ 2 from baseline	Defines sepsis as life-threatening organ dysfunction due to dysregulated host response to infection.
Microbiological findings	Positive blood or site-specific cultures (when available)	Confirms infection source; however, culture negativity does not exclude sepsis.
Hemodynamic parameters	Mean arterial pressure < 65 mmHg despite fluids; serum lactate > 2 mmol/L	Suggests septic shock requiring vasopressor therapy.
Imaging and adjunctive tests	Radiologic evidence (chest X-ray, CT, or ultrasound) identifying infectious focus	Supports localization of infection and guides source control.

mean arterial pressure ≥ 65 mmHg, and urine output ≥ 0.5 ml/kg/hour.²³ As no mortality benefit has been demonstrated with albumin compared to crystalloids, crystalloids remain the preferred resuscitation fluid.²⁴ In patients with persistent hypotension despite adequate fluid replacement, intravenous vasopressors should be initiated, with norepinephrine as the first-line agent.²⁵

The duration of antimicrobial therapy is typically 7–10 days but may be extended in cases of slow clinical response, immunosuppression, undrainable infectious foci, or *Staphylococcus aureus* bacteremia.²⁶

PROGNOSIS IN SEPSIS

Sepsis is a life-threatening emergency with high mortality; while mortality rates are lower in younger patients without comorbidities, they increase markedly with advancing age. Overall mortality exceeds 10% in sepsis and surpasses 40% in septic shock.¹ Prognostic factors can be broadly categorized into host-related and disease-related determinants. Host-related adverse factors include advanced age (>40 years),²⁷ multiple comorbidities,²⁸ immunocompromising conditions (e.g., AIDS, immunosuppression), chronic liver disease, malignancy, alcohol dependence, heart failure, newly developed atrial fibrillation,²⁹ malnutrition, presence of indwelling catheters, prior hospitalization, as well as persistent thrombocytopenia, hyperchloremia, hyperglycemia, hypercoagulability, and elevated procalcitonin levels. The source of infection is also a critical determinant of prognosis; urinary tract–derived sepsis carries the lowest mortality, whereas infections of unknown origin or cases of pneumosepsis may reach mortality rates as high as 50–55%.³⁰ Moreover, sepsis caused by nosocomial pathogens is associated with higher mortality compared to community-acquired infections.³¹

MORBIDITY IN SEPSIS

Among survivors of sepsis, an increased risk of mortality within the first six months after hospital discharge has been reported, along with a higher frequency of recurrent hospitalizations.³² Compared with patients hospitalized for non-sepsis causes, these individuals are at greater risk of major cardiovascular and cerebrovascular events.

In addition to early mortality and rehospitalization risk, the post-sepsis period is frequently associated with a constellation of long-term complications collectively referred to as post-sepsis syndrome. The pathophysiology involves persistent inflammation, immune dysregulation, microvascular injury, and metabolic derangements that may continue long after the initial infection has resolved. Survivors may develop sepsis-associated encephalopathy, manifesting as memory impairment, attention deficits, and reduced executive function. Psychiatric sequelae such as depression, anxiety, and post-traumatic stress disorder are also common, particularly among patients who required prolonged intensive care or mechanical ventilation.

Beyond neurocognitive and psychological outcomes, neuromuscular weakness, exercise intolerance, and chronic

fatigue are frequently observed, contributing to a decline in physical performance and quality of life. Functional dependency, impaired mobility, and loss of employment are additional long-term consequences that may persist for months or even years.

Furthermore, the critical illness period in the intensive care setting may result in long-term cognitive, psychiatric, and physical complications. Early multidisciplinary rehabilitation, nutritional support, and long-term follow-up are therefore crucial to mitigate these effects and enhance recovery in sepsis survivors.

CONCLUSION

Sepsis is a syndrome with high mortality and morbidity that necessitates urgent diagnosis and management. Early recognition, prompt fluid resuscitation, oxygen supplementation, and appropriate antibiotic therapy are of paramount importance in improving patient outcomes.

In recent years, there has been growing interest in the use of advanced technologies and precision medicine approaches to improve sepsis care. Artificial intelligence–based models and machine learning algorithms are being explored to facilitate earlier recognition, risk stratification, and individualized treatment strategies. Integration of clinical, laboratory, and hemodynamic data through predictive analytics may allow for real-time decision support and more accurate prognostic assessment.

Furthermore, ongoing research into host–pathogen interactions, immunomodulatory therapies, and biomarkers holds promise for more personalized interventions in the future. A multidisciplinary approach involving critical care, infectious disease, and rehabilitation teams will remain essential to optimize both short-term survival and long-term quality of life in sepsis survivors.

ETHICAL DECLARATIONS

Peer Review Process

This review was externally peer-reviewed.

Conflict of Interest

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Author Contributions






The author confirms sole responsibility for the study conception, design, data collection, analysis, interpretation, and manuscript preparation. All aspects of the work were carried out by the author.

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A case of granulomatous lymphocytic interstitial lung disease considered as sarcoidosis

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ABSTRACT

Inborn errors of immunity, formerly known as primary immunodeficiency disorders, are genetic disorders comprising 10 groups and over 500 diseases. Common variable immunodeficiency is the most common symptomatic IEI in adults and is characterised by decreased immunoglobulin levels and recurrent infections after secondary causes of hypogammaglobulinaemia have been ruled out. Granulomatous lymphocytic interstitial lung disease is a distinct clinical entity associated with common variable immunodeficiency and is characterised by lymphoid proliferation and granuloma formation in the lung interstitium. It may resemble sarcoidosis in many clinical, radiological, and pathological features. However, an important distinction is that hypogammaglobulinaemia, i.e., immunodeficiency, is rarely seen in sarcoidosis. A case of primary immunodeficiency presenting with granulomatous lymphocytic interstitial lung disease, in which hypogammaglobulinaemia was detected during follow-up for sarcoidosis, is presented.

Keywords: IEIs, GLILD, hypogammaglobulinemia, CVID, sarcoidosis

INTRODUCTION

Inborn errors of immunity (IEIs) are clinically characterized by increased susceptibility to infections, autoimmunity, autoinflammatory diseases, allergy, bone marrow failure, and malignancy. Among IEIs, primary antibody deficiencies (PADs) have a better prognosis and longer survival and are the most commonly diagnosed in adulthood. These disorders primarily involve B cell abnormalities, leading to decreased B cell numbers, impaired antibody production, or both.¹ Common variable immunodeficiency (CVID) is the most prevalent symptomatic IEIs in adults, characterized by decreased immunoglobulin levels and recurrent infections following the exclusion of secondary causes of hypogammaglobulinemia.² CVID presents with a broad clinical spectrum, encompassing not only recurrent infections but also autoimmune manifestations, malignancies, and particularly interstitial lung diseases (ILDs).³ Before establishing a diagnosis of noninfectious CVID-associated lung disease, infectious complications must be excluded. Among ILDs, granulomatous lymphocytic interstitial lung disease (GLILD) is a distinct clinical entity predominantly associated with CVID, characterized by lymphoid proliferation and granuloma formation within the lung interstitium.⁴ GLILD is a significant cause of morbidity and early mortality in CVID patients.^{5,6}

Although several large IEIs patient registries have been established globally⁷ defining the precise epidemiology of GLILD remains challenging due to various limitations.

However, cohort data estimate that GLILD occurs in approximately 8–20% of CVID patients.^{8,9} Some clinical and pathological features of GLILD resemble sarcoidosis-like conditions, as both involve granuloma formation due to immune dysregulation. Both are systemic granulomatous diseases that primarily affect the lungs and lymph nodes, making them difficult to differentiate. If radiological findings suggest GLILD, antibody deficiency can be confirmed through laboratory testing to establish the diagnosis. Here, we present a case of GLILD in IEIs, initially suspected to be sarcoidosis, highlighting the diagnostic challenges of this condition.

CASE

A 38-year-old female patient had a history of intermittent visits to a pulmonologist due to mild shortness of breath and cough persisting for 1.5–2 years. In November 2022, her respiratory symptoms worsened, leading to a diagnosis of asthma. She was prescribed inhaled corticosteroids (ICS) combined with a long-acting beta-2 agonist (LABA) and a montelukast/antihistamine combination, which provided partial symptom relief. A lung computed tomography (CT) scan performed during this period revealed ground-glass opacities and nodules, prompting a preliminary diagnosis of pneumonia and the initiation of antibiotic therapy. Concurrently, oral corticosteroids (OCS) were prescribed due to suspected asthma exacerbation. The patient also received



OCS for 1.5 months, starting in February 2023, reporting partial symptomatic improvement during this period. Her medical history was unremarkable, and she had no history of smoking, atopic conditions, or frequent infections. In a follow-up CT scan conducted in August 2023, non-pathological axillary lymph nodes, mediastinal lymph nodes (maximum diameter: 7 mm), bronchovascular thickening, and ground-glass nodules were observed in both lung parenchymal areas (**Figure 1**). Retrospective analysis of previous CT scans revealed that these lesions were present but had partially regressed in the most recent scan. To establish a definitive diagnosis, the patient underwent diagnostic video-assisted thoracoscopic surgery (VATS) with lung wedge resection and lymph node sampling for pathological examination. Histopathological analysis revealed sharply demarcated nodular infiltration areas in the lung parenchyma, containing multinucleated giant cells and perialveolar lymphocytes forming small nodules. Additionally, granulomatous infiltration with histiocytes and multinucleated cells was noted. Immunohistochemical staining demonstrated zonal CD3 and CD20 positivity in lung nodular lymphocytic infiltration, with B-cell lymphoma-2 (BCL-2) negativity in germinal centers. CD1a staining was negative. The final pathology report described non-necrotizing granulomatous inflammation consistent with interstitial lung disease. Given these findings, the patient was initially suspected of having sarcoidosis. However, upon further immunological evaluation, an antibody deficiency inconsistent with sarcoidosis was detected, and laboratory tests confirmed hypogammaglobulinemia. She was subsequently referred to immunology and allergy departments. Laboratory values and flow cytometry results are detailed in **Table 1, 2**. Abdominal ultrasonography performed for lymphoproliferation screening revealed hepatosplenomegaly. Consequently, intravenous immunoglobulin (IVIg) at 0.6 mg/kg every three weeks and trimethoprim/sulfamethoxazole prophylaxis were initiated. Radiological and pathological findings were considered consistent with GLILD, and additional investigations were conducted. A re-evaluation of the VATS pathology samples confirmed the initial findings. Pulmonary function tests at diagnosis showed a forced expiratory volume in 1 second (FEV1) of 2.38 liters (88%), forced vital capacity (FVC) of 3.02 liters (96%), and FEV1/FVC ratio of 78%. While the patient was under observation without infection, an increase in respiratory symptoms and pancytopenia was noted (**Table 3**). A follow-up high-resolution CT (HRCT) scan revealed the emergence of new pulmonary lesions, with some prior lesions regressing and others progressing, indicative of radiological disease progression (**Figure 2**). Additionally, spleen size increased from 200 mm to 260 mm, and signs

of portal hypertension were detected. Bone marrow biopsy performed due to pancytopenia and splenomegaly showed normocellular bone marrow. A carbon monoxide diffusion test (DLCO) was 39%, while pulmonary function tests revealed FEV1 of 2.06 liters (78%), FVC of 2.7 liters (87%), and FEV1/FVC of 76%. A multidisciplinary council recommended upper gastrointestinal endoscopy, colonoscopy, and a repeat bone marrow biopsy. No significant findings were noted in gastrointestinal endoscopic examinations. Consequently, the patient was started on cyclosporine at 50 mg twice daily. After one month of treatment, pulmonary function tests showed FEV1 of 2.14 liters (81%), FVC of 2.7 liters (91%), and DLCO improvement to 57%. Whole-exome sequencing was performed, and results are awaited. The patient remains under follow-up with IVIG and immunosuppressive therapy, maintaining stable health status. A summary of the patient's clinical course is presented in **Figure 3**.

Table 1. The patient's laboratory values

Parameters	Results	References
Ig G	4.1 g/L	7-16 g/L
Ig A	0.03 g/L	0.7-14 g/L
Ig M	0.2 g/L	0.4-2.3 g/L
Ig E	8 IU/ml	5-165 IU/ml
Ig G1	3.01 g/L	4.5-10.01
Ig G2	0.25 g/L	1.69-7.86 g/L
Ig G3	0.35 g/L	0.11-0.85 g/L
Ig G4	0.021 g/L	0.03-2.01 g/L
WBC	4.2x10 ³ /ml	3.8-11.8x10 ³ /ml
Hgb	13.1 g/L	10.9-14.3 g/L
Platelet	153x10 ³ /ml	179-408x10 ³ /ml
Lymphocyte	0.9x10 ³ /ml	1.1-3.1x10 ³ /ml
Calcium	8.5 mg/dl	8.8-10.6 mg/dl

Ig: Immunoglobulin, WBC: White blood cell, Hgb: Hemoglobin g: Gram, mg: Miligram, L: Liter, dl: Deciliter, U: Unit, IU: International unit, µl: Microliter

Table 2. Flow cytometry results

Parameters	Results%	References
CD45+CD19+ B cell	4	3,4-15.9
Switched memory B cell	1	5.9-34.5
CD16+/CD21 low B cell	21	1.2-14.2
Naive B cell	67	33.7-79.2
CD45+ CD16 +	11	3.5-28.9
CD45+ CD56 +	6	5.1-24.7
Memory B cell	32	11.2-66.1

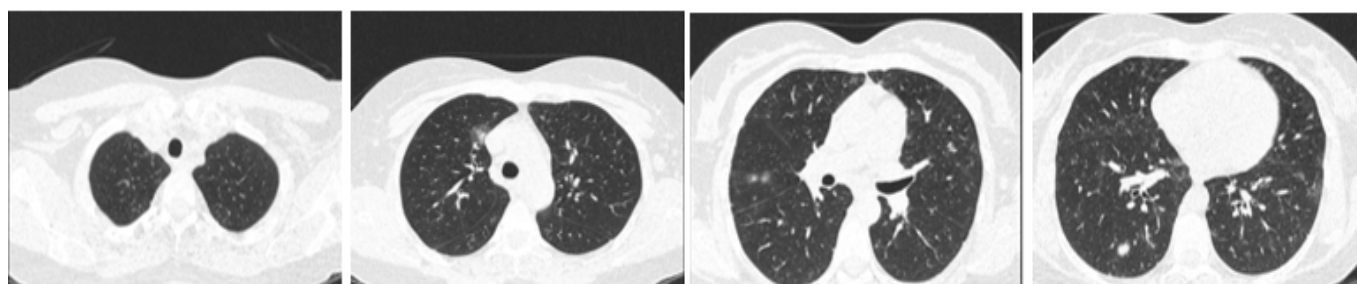


Figure 1. Images at the time of diagnosis

Table 3. Blood results from lymphoproliferative progression		
Parameters	Results	References
WBC	3.0x10 ³ /ml	3.8-11.8 x10 ³ /ml
Hgb	10 g/L	10.9-14.3 g/L
Platelet	72x10 ³ /ml	179-408 x10 ³ /ml
Lymphocyte	1.0x10 ³ /ml	1.1-3.1 x10 ³ /ml

WBC: White blood cell, Hgb: Hemoglobin, L: Liter

DISCUSSION

We present a case of a patient initially followed up with a preliminary diagnosis of sarcoidosis, who was subsequently diagnosed with CVID upon the detection of hypogammaglobulinemia. The patient exhibited clinical, radiological, and pathological pulmonary involvement consistent with granulomatous-lymphocytic interstitial lung disease (GLILD). In addition to GLILD, the patient had concurrent cytopenia and lymphoproliferation, making this an exemplary case where immunosuppressive therapy was initiated.

Sarcoidosis typically occurs in immunocompetent individuals, whereas GLILD is a pulmonary manifestation of IEs such as CVID. Therefore, in cases where radiological and clinical differentiation between these two conditions is challenging, the presence of hypogammaglobulinemia, impaired vaccine responses, and frequent recurrent infections strongly suggests an underlying IEs. Although our patient exhibited histopathological and radiological features consistent with sarcoidosis, the presence of hypogammaglobulinemia, low switched memory B cells, and impaired vaccine responses supported the diagnosis of GLILD.

GLILD is a recently recognized disease within the spectrum of IEs and has been less extensively studied than sarcoidosis. The fact that GLILD may be the initial manifestation of CVID complicates its diagnosis.¹⁰ Additionally, both diseases are systemic granulomatous conditions that primarily affect the lungs and lymph nodes, often presenting with nonspecific symptoms such as cough, exertional dyspnea, and constitutional symptoms.¹¹ The diagnosis can be easily overlooked, particularly when the clinical picture is not accompanied by frequent infections or if immune deficiency is not suspected. Notably, a significant proportion of patients with either disorder remain asymptomatic.¹²⁻¹⁴

In our case, respiratory symptoms were mild, and the findings observed on high-resolution computed tomography

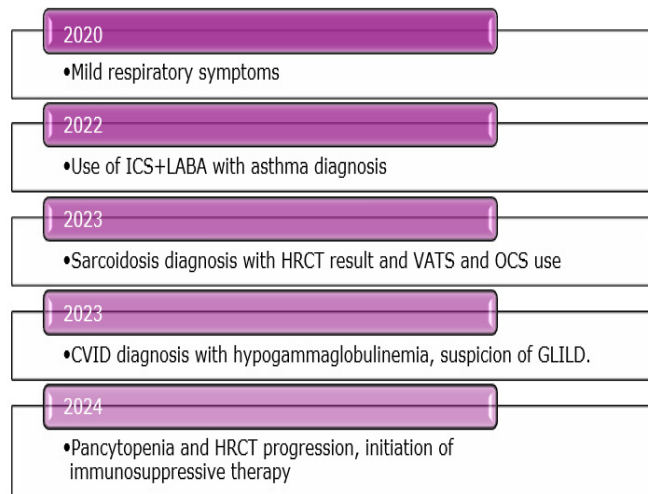


Figure 3. Chronology of the patient's clinical condition

(HRCT) prompted further investigation, aligning with existing literature. Furthermore, the lack of a linear correlation between the severity of radiological involvement and clinical symptoms was notable. While spontaneous remission is common in sarcoidosis, this phenomenon has not been described in GLILD.¹⁵ In our patient, there was no evidence of spontaneous remission, and the development of lymphoproliferative manifestations, including worsening respiratory symptoms, pancytopenia, and progressive splenomegaly, underscored the need for additional treatment.

Autoimmune cytopenia is the most frequently observed immune-mediated complication of CVID, occurring in approximately 10.4% of patients overall and in 59.6% of those with GLILD.^{16,17} In our case, cytopenia was a coexisting feature of GLILD. Although no standardized treatment protocol has been established for GLILD, oral glucocorticoids are commonly used as first-line therapy.¹⁸ However, many patients exhibit a suboptimal response to corticosteroids, and recent evidence suggests that a combination of rituximab and azathioprine may be the most effective initial treatment.¹⁹ Our patient had previously used oral corticosteroids (OCS), but treatment was discontinued during follow-up. Given the persistently low diffusing capacity of the lungs for carbon monoxide (DLCO) and worsening respiratory symptoms, additional treatment beyond intravenous immunoglobulin (IVIG) was deemed necessary. Considering the concurrent cytopenia, cyclosporine was initiated following a multidisciplinary council discussion.

Data on the long-term prognosis of CVID and GLILD remain limited. Studies have reported significantly reduced survival rates in CVID patients with GLILD compared to

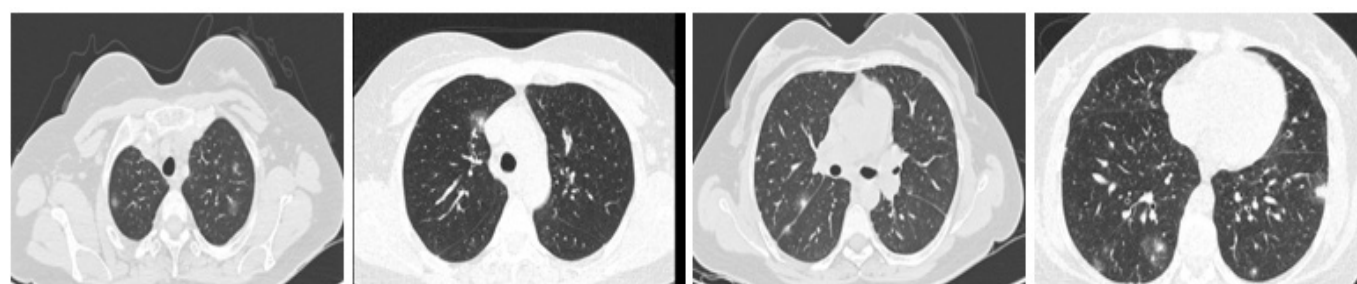


Figure 2. Images with progression

those without.¹¹ Untreated GLILD has been associated with progressive respiratory dysfunction and eventual respiratory failure. Furthermore, the presence of fibrosis has been identified as a poor prognostic factor.²⁰ The absence of fibrosis in our patient's serial HRCT scans is a promising finding in terms of long-term respiratory function and prognosis.

CONCLUSION

As a result, this case highlights the importance of considering GLILD in the differential diagnosis of sarcoidosis, as sarcoidosis remains a diagnosis of exclusion. Given the significant overlap in clinical and radiological findings, the presence of hypogammaglobulinemia should prompt further immunological evaluation. Importantly, primary immunodeficiency can be diagnosed based on ILD alone, even in the absence of frequent infections.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient included in this report. Signed consent forms are retained by the authors and are available upon request.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

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Author Contributions

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