

E-ISSN: 2791-8823



# CSMJ

THE JOURNAL OF BAŞAKŞEHİR ÇAM AND SAKURA CITY HOSPITAL



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December

2024 Volume: 4 Issue: 3

[www.csmedj.org](http://www.csmedj.org)

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drmerih@yahoo.com

ORCID ID: 0000-0002-7344-8637

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kamuran67@gmail.com

ORCID ID: 0000-0003-0814-5637

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ahmetguler01@yahoo.com.tr

ORCID ID: 0000-0002-0963-9658

### Alper Gümüş

Department of Biochemistry, University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, İstanbul, Turkey

dralpergumus@gmail.com

ORCID ID: 0000-0002-4453-6339

### Bekir Tuğcu

Department of Neurosurgery, University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, İstanbul, Turkey

tugcubekir@gmail.com

ORCID ID: 0000-0003-0385-0054

### İlgin Özden

Department of Hepatopancreatobiliary Surgery and Liver Transplantation, Başakşehir Çam and Sakura City Hospital, İstanbul, Turkey

iozden@hotmail.com

ORCID ID: 0000-0001-7360-628X

### Nevra Dursun Kepkep

Department of Pathology, University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, İstanbul, Turkey

durnevra@gmail.com

ORCID ID: 0000-0001-8076-7911

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Norrland Universitetssjukhus, CEntrum för Obstetrik och Gynekologi, Vasterbotten, Umea/Sverige

cetinkayanilufer@gmail.com

ORCID ID: 0000-0001-9183-3558

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Department of Emergency Medicine, University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, İstanbul, Turkey

drramazanguven@gmail.com

ORCID ID: 0000-0003-4129-8985

### Serkan Sarı

Department of General Surgery, University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, İstanbul, Turkey

drserkansari@yahoo

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Soyhan.bagci@ukbonn.de  
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## Editorial

Dear Colleagues,

It is our great pleasure to publish the last issue of Cam Sakura Medical Journal at 2024.

In this issue you will find four original articles. The first article aimed to evaluate inflammatory, cardiac and hematological parameters in children with COVID-19 infection. The second article evaluated IL-17 IgM and IgG levels in patients with viral respiratory tract infection. The third interesting article was designed to determine the effect of maternal depression on children with primary monosymptomatic nocturnal enuresis. And, the last article was about the incidence of typhoid fever in a country.

I hope you will read these interesting articles.

We wish all of you a happy and healthy new year.

Hoping to meet you in the issues of 2025.

Best regards,

**On Behalf of Deputy Editors, Associate Editors, and Editorial Secretary**

**Merih Çetinkaya**

**Editor-in-Chief**

**Cam & Sakura Medical Journal**

# Evaluation of Inflammatory, Cardiac and Hematological Parameters in Hospitalized Children with COVID-19

✉ Damla Geçkalan<sup>1</sup>, ✉ Rahmi Özdemir<sup>2</sup>, ✉ Zülal Yılmaz<sup>3</sup>, ✉ Onur Sivas<sup>3</sup>, ✉ Yasin Yılmaz<sup>3</sup>,  
✉ Cemile Hilal Çelik<sup>3</sup>

<sup>1</sup>Bakırçay University, Çiğli Training and Research Hospital, Department of Pediatrics İzmir, Turkey

<sup>2</sup>İzmir Katip Çelebi University Faculty of Medicine, Department of Pediatric Cardiology, İzmir, Turkey

<sup>3</sup>Kütahya Health Sciences University Faculty of Medicine, Department of Pediatrics, Kütahya, Turkey

## What is known on this subject?

The relationship between clinical symptoms such as inflammatory, haematological, cardiac and coagulation parameters, which are very common in adults, is still unclear in children with coronavirus disease-2019 (COVID-19).

## What this study adds?

In our study, we aimed to improve the clinical approach while evaluating coagulopathy and myocarditis in children receiving treatment for COVID-19 pneumonia. In our study, it should be kept in mind that the incidence of pneumonia increased with age, and troponin values were high in the younger age group without pneumonia. Moreover, coagulation disorder is not a common finding in pediatric patients.

## ABSTRACT

**Objective:** The relationship between clinical symptoms such as inflammatory and coagulation parameters, which are very common in adults, is still unclear in children with coronavirus disease-2019 (COVID-19). The aim of this study is to investigate the levels of inflammation and coagulation blood parameters and their correlation with pneumonia in COVID-19 pediatric patients.

**Material and Methods:** One hundred thirteen hospitalized COVID-19 pediatric patients were included in this study retrospectively. All patients' age, gender, number of hospitalization days, respiratory symptoms, laboratory parameters, thoracic computed tomography, polymerase chain reaction results were recorded. Patients were analyzed for pneumonia presence and absence.

**Results:** Gender distribution was 53% female, 47% male. Median age was 11.4 years. Hospitalization length was 4.5 days. Chest tomography was performed on 90 patients with respiratory complaints or symptoms, and COVID-19 pneumonia was detected in 62 patients (68.8%). There was a statistically significant difference in the length of hospitalization, age, white blood cell and troponin values between the patients with COVID-19 pneumonia and those without pneumonia ( $p < 0.001$ ,  $p = 0.008$ ,  $p = 0.048$ , and  $p = 0.003$ , respectively). When multivariate analysis was performed for these parameters, the probability of pneumonia was found to be 1.17 times higher for every additional year of age. Elevation of fibrinogen and D-dimer was not found to be statistically significant ( $p = 0.07$ ,  $p = 0.29$ , respectively). There was no statistical difference between coagulation and inflammatory parameters in children with COVID-19 pneumonia. No cardiac complications or thrombosis were observed.

**Conclusion:** The finding that the risk of COVID-19 pneumonia increases with age draws more attention in terms of diagnosis and treatment. Coagulopathy was not detected in patients with COVID-19 pneumonia and no treatment is required. In addition, a detailed cardiac assessment is required in patients without COVID-19 pneumonia due to elevated troponin levels.

**Keywords:** Children, coagulation, COVID-19, D-dimer, pneumonia, troponin



**Address for Correspondence:** Damla Geçkalan MD, Bakırçay University, Çiğli Training and Research Hospital, Clinic of Pediatrics İzmir, Turkey

**E-mail:** damlageckalan@gmail.com **ORCID ID:** orcid.org/0000-0001-6344-7035

**Received:** 27.06.2024 **Accepted:** 12.09.2024

**Cite this article as:** Geçkalan D, Özdemir R, Yılmaz Z, Sivas O, Yılmaz Y, Çelik CH. Evaluation of inflammatory, cardiac and hematological parameters in hospitalized children with COVID-19. Cam and Sakura Med J. 2024;4(3):76-81



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## Introduction

The coronavirus disease-2019 (COVID-19) pandemic was announced on 11 March 2020 in our country. In the literature, 1-5% of COVID-19 cases consist of pediatric patients (1,2). In the pediatric COVID-19 study conducted in China, 55% of cases were mild or asymptomatic, 40% were moderate, 5% were severe, and less than 1% were critically ill (3,4). Also, COVID-19 infection can cause significant cardiac and haematological alterations in children (5,6,7).

The relationship between laboratory parameters, particularly pneumonia and myocarditis, in COVID-19 is important. White blood cell (WBC), C-reactive protein (CRP), D-dimer, fibrinogen, and troponin-I are the most commonly used laboratory markers. In adult COVID-19 patients, increases in lymphopenia, fibrinogen and D-dimer levels, and myocarditis frequency have been reported (8,9,10). The clinical importance of these parameters in pediatric patients is not clear.

In this study, our aim was to determine the changes in cardiac and haematological parameters of pediatric patients diagnosed with COVID-19 pneumonia and without pneumonia.

## Material and Methods

One hundred thirteen COVID-19 pediatric patients, aged 0-18 years, who were admitted to the pediatric pandemic service of the Health Sciences University between March 2020-March 2021 were analyzed retrospectively. The code U07.3, defined for COVID-19 according to the "International Classification of Diseases" coding system, was used to collect data. The study was conducted in accordance with the principles of the Declaration of Helsinki and the Kütahya Health Sciences University Non-Interventional Clinical Research Ethics Committee (decision no: 2021/09-02, date: 26.05.2021). All patients' age, gender, length of hospitalization, laboratory parameters (WBC, neutrophil %, lymphocyte %, platelet, fibrinogen, D-dimer, CRP, troponin-I), thoracic computed tomography (CT), and polymerase chain reaction (PCR) were recorded. Thoracic CT was performed in patients with respiratory complaints or signs of pneumonia on physical examination or chest X-ray. Four patients who did not accept treatment were not included in the hospitalization portion of the study.

Before analysis, patients were divided into four subgroups. Groups 1 and 2 had pneumonia, while groups 3 and 4 had no pneumonia.

Group 1: Patients with both COVID-19 PCR positive with pneumonia [PCR (+), CT (+)],

Group 2: Patients with negative COVID-19 PCR test but was detected in CT with COVID-19 pneumonia [PCR (-), CT (+)],

Group 3: Patients with positive COVID-19 PCR test and without COVID-19 pneumonia [PCR (+), CT (-)],

Group 4: Patients with positive COVID-19 PCR test and no respiratory system complaints and findings [only PCR (+)]. CT was not performed in group 4 patients because of the absence of respiratory system complaints and findings.

Patients with clinically impaired general condition, persistent fever, abnormal blood parameters, respiratory distress, or COVID-19 pneumonia were hospitalized. Patients with respiratory failure or indication for intensive care unit hospitalization were excluded. COVID-19 pediatric patients were divided into two groups according to their clinical and radiological results: those with pneumonia and those without pneumonia. Patients with mild to moderate pneumonia were hospitalized and treated in accordance with the Turkish Ministry of Health Guidelines (11,12). Pediatric patients were classified as mild-moderate pneumonia in the guideline recommendation if they had a fever  $<38.5$  °C, a respiratory rate  $<50$  per minute, and mild respiratory distress the Turkish Ministry of Health's Pediatric Patient Treatment Protocol recommends 5 days of favipiravir treatment for COVID-19 pneumonia patients aged 15 years and older.

## Statistical Analysis

Epidemiological, clinical, laboratory, and imaging characteristics of the patients were recorded with standard descriptive statistics. Statistical Package for the Social Sciences (version 25, SPSS Inc., Chicago, IL, USA) was used to analyze the data. The descriptive statistics of the numerical parametric variables were calculated as mean  $\pm$  standard deviation, non-parametric variables as the median (25%-75% quartiles), and categorical variables as a percentage. We evaluated the normal distribution of the study parameters using the Shapiro-Wilk test. Subsequently, Student's t-test or Mann-Whitney U test was used to compare the groups. Laboratory parameters were compared between groups with and without respiratory system involvement by One-Way ANOVA or Kruskal-Wallis test. For the pairwise comparisons of the subgroups, a post-hoc test with Tukey honestly significant difference correction was used. P values based on two-sided tests were considered statistically significant at less than 0.05. Variables from the univariate logistic regression analysis with a statistical result of  $p < 0.250$  were included in the multivariate logistic regression analysis.

## Results

In the epidemiological analysis of 113 COVID-19 pediatric patients, 60 (53%) were female and 53 (47%) were male. The median age was 11.4 (0.8-18) years and the hospital stay was 4.5 (1-19) days (Table 1).

When the laboratory values of all patients were evaluated, lymphopenia was found in 25% of patients, and fibrinogen, D-dimer, CRP, and troponin-I were higher than the normal reference range in 44%, 46%, 48%, and 13% of patients, respectively (Table 2). When the fibrinogen, D-dimer, and CRP values were evaluated in the subgroups, no statistically significant difference was found between the subgroups (Table 1).

As the subgroup laboratory values were evaluated, a statistically significant difference was found in age, WBC, and troponin-I values ( $p < 0.001$ ,  $p = 0.006$ , and  $p = 0.003$  respectively) (Table 1). Additionally, we evaluated the comparison results in the subgroups; there was a statistically

significant difference in WBC and troponin-I values between groups 1 and 4, with  $p = 0.011$  for WBC and  $p = 0.008$  for troponin-I, respectively (Table 1).

Chest tomography was performed in 90 patients with respiratory complaints or symptoms, and COVID-19 pneumonia was detected in 66.6% of patients who required tomography.

In the analysis of 113 COVID-19 pediatric patients according to the presence of pneumonia, there was a statistically significant difference between the length of hospital stay and age ( $p < 0.001$ ,  $p = 0.008$ , respectively). Mean age was 13.9 years, length of hospitalization was 5.2 days in the pneumonia groups (Table 3). Mean age and length of hospitalization were higher in the pneumonia groups. When fibrinogen, D-dimer, and CRP were evaluated according to pneumonia, there was a statistically significant difference in WBC and troponin-I levels ( $p = 0.048$  and  $p = 0.003$ , respectively) (Table 3). When multivariate analysis was performed for these parameters, the probability of pneumonia was found to be 1.17 times higher with increasing age (Table 4).

**Table 1. Epidemiological and laboratory parameters of COVID-19 pediatric patients**

	Group 1 (n=40)	Group 2 (n=20)	Group 3 (n=28)	Group 4 (n=25)	p value
Age (years)	15.4 [2.0; 18.0]	15.2 [1.7; 17.9]	14.4 [3.1; 18]	2.7 [0.1; 17.1]	<0.001
Hospitalization day	5.1 [1; 19]	4.6 [1; 18]	3.1 [1; 16]	3.1 [1; 8]	0.071
WBC ( $\times 10^3$ )	6.0 [4.7; 8.2]	7.4 [5.2; 13.3]	6.3 [4.9; 10.6]	9.8 [7.0; 12.5]	<b>0.006<sup>b</sup></b>
Neutrophil (%)	57.8 $\pm$ 16.3	61.0 $\pm$ 22.3	60.8 $\pm$ 15.4	50.2 $\pm$ 23.6	0.187 <sup>a</sup>
Lenfocyte (%)	31.9 $\pm$ 12.7	30.3 $\pm$ 21.6	29.0 $\pm$ 14.7	39.6 $\pm$ 23.0	0.168 <sup>a</sup>
Thrombocyte ( $\times 10^3$ )	233.2 $\pm$ 60.6	366.0 $\pm$ 270.3	256.7 $\pm$ 67.2	268.3 $\pm$ 71.3	0.160 <sup>a</sup>
CRP (mg/L)	4 [1.2; 15.9]	10.2 [2.8; 87.8]	4.7 [2.0; 13.9]	7.1 [1.4; 19.6]	0.463 <sup>b</sup>
Fibrinogen (mg/dL)	358 [272; 418]	383.5 [342.5; 567]	338.2 [302.2; 360]	318 [291.4; 353.7]	0.07 <sup>b</sup>
D-dimer (ng/mL)	420 [262; 798]	850 [345.5; 1829]	367 [317; 757]	679.5 [380; 1098]	0.289 <sup>b</sup>
Troponin-I (ng/L)	1.4 [0.5; 2.8]	3.2 [1.8; 13.8]	2.6 [1.7; 6.2]	5.5 [2.1; 11.7]	<b>0.003<sup>b</sup></b>

Values are presented as median [minimum; maximum], p values were calculated with Kruskal-Wallis test. The significant results were represented as bold; values are presented as mean  $\pm$  SD, median [25-75% quartiles], p values were calculated with <sup>a</sup>: One-Way ANOVA or <sup>b</sup>: Kruskal-Wallis test. The significant results represented as bold and pairwise group comparison results were as represented below; for WBC: 1 vs. 4:  $p = 0.011$  (post-hoc test: Tukey HSD), for troponin: 1 vs. 4:  $p = 0.008$  (post-hoc test: Tukey HSD), COVID-19: Coronavirus disease-2019, n: Number, WBC: White blood cell, CRP: C-reactive protein, SD: Standard deviation

**Table 2. Evaluation of laboratory parameters of all patients**

Laboratory parameters	Mean + SD (reference range)	Laboratory parameters	Median [IQR] (reference range)
Thrombocyte ( $10^3/\mu\text{L}$ )	254.1 $\pm$ 77.6 (130-400)	CRP (mg/L)	6.8 [32.6] (<5)
Neutrophil %	57.7 $\pm$ 19.2 (41-73)	Fibrinogen (mg/dL)	352 [105.1] (180-350)
Lymphocyte %	32.4 $\pm$ 17.7 (19-44)	D-dimer (ng/mL)	568.5 [588.5] (170-550)
		Troponin-I (ng/L)	2.1 [3.8] (0-19.8)
		WBC ( $10^3/\mu\text{L}$ )	6.2 [5.4] (5.2-12.4)

SD: Standard deviation, CRP: C-reactive protein, WBC: White blood cell, IQR: Interquartile range

**Table 3. Evaluation of epidemiological and laboratory parameters of patients with and without COVID-19 pneumonia**

	COVID-19 pneumonia (n=60)	COVID-19 without pneumonia (n=53)	p value
Age (year)	15.2 [13.1; 16.8]	8.6 [3; 14.8]	<b>&lt;0.001<sup>b</sup></b>
Hospitalization (day)	5.2 [3; 6]	3.1 [1; 5]	<b>0.008<sup>b</sup></b>
WBC (10 <sup>3</sup> /uL)	6.2 [4.4; 8.9]	7.7 [5.2; 12.2]	<b>0.048<sup>b</sup></b>
Neutrophil (%)	58.9±18.3	56.3±20.3	0.474 <sup>a</sup>
Lenfocyte (%)	31.3±15.8	33.6±19.8	0.489 <sup>a</sup>
Thrombocyte (10 <sup>3</sup> /uL)	245.3±84	264.3±69.1	0.195 <sup>a</sup>
CRP (mg/L)	4.6 [1.5; 19.8]	6.2 [1.9; 18.9]	0.795 <sup>b</sup>
Fibrinogen (mg/dL)	375.2 [291; 448]	330 [302; 363]	0.108 <sup>b</sup>
D-dimer (ng/mL)	476 [262; 889]	526 [331; 894.5]	0.671 <sup>b</sup>
Troponin-I (ng/L)	2 [0.8; 4.5]	3.1 [2; 9.2]	<b>0.024<sup>b</sup></b>

Values are presented as mean ± SD, median [25-75% quartiles], p values were calculated with <sup>a</sup>Student's t-test or <sup>b</sup>Mann-Whitney U test. The significant results represented as bold. COVID-19: Coronavirus disease-2019, n: number, WBC: White blood cell, CRP: C-reactive protein

**Table 4. Multivariate logistic regression analysis of epidemiological parameters of patients with and without COVID-19 pneumonia**

	Xep (β)	95% CI		p value	Wald statistic
		Lower	Upper		
Age	1.138	0.981	1.321	0.089	2.894
Hospitalization day	1.177	1.086	1.275	<b>&lt;0.001</b>	15.955

Variables from the univariate logistic regression analysis with a statistical result of  $p < 0.250$  were included in the multivariate logistic regression analysis. Age groups, sex, hospitalization day, lymphocyte count, neutrophil count, platelet count, D-dimer, fibrinogen, C-reactive protein, and troponin levels were evaluated in the analysis. COVID-19: Coronavirus disease-2019, CI: Confidence interval

## Discussion

Leukopenia, lymphocytopenia, high CRP level, high D-dimer, and fibrinogen levels were detected in most of the studies conducted on COVID-19 infection (13,14,15). Especially in pediatric patients, more detailed clinical studies are required to determine the relationship between these parameters and age, pneumonia, myocarditis, and coagulopathy.

In some review studies, it was reported that: 56% of the patients were male; mean age was  $8.9 \pm 0.5$  years; 86.5% were PCR positive; and the length of hospital stay was  $11.6 \pm 0.3$  days (16). In our study, it was observed that the gender distribution was similar, the average age was higher, and the length of hospitalization was shorter than reported in the literature. The difference in the length of stay was thought to be because the ministry's guideline recommended the treatment period as 5 days (11,12).

When we evaluate the laboratory parameters, it has been reported that leukocyte and fibrinogen levels were found to be normal, while lymphocyte, D-dimer, and CRP values were found elevated in children with COVID-19 (16). It was reported that D-dimer elevation was not found to be statistically significant

in 10 studies included in the analysis (17). Our study results were similar to those reported in the literature. In addition, although the CRP, fibrinogen, and D-dimer levels were above the normal reference range in our study, the difference was not statistically significant. None of these patients had clinical signs of a coagulopathy.

The epidemiological and laboratory values of the patients were evaluated within COVID-19 pneumonia groups. There was a statistically significant difference in age, WBC, and troponin-I values. Mean age was highest in patients with pneumonia. WBC and troponin-I values were higher in patients who had only fever and not pneumonia. Myocardial injury, also defined by increased troponin levels in patients with COVID-19, is thought to occur due to non-ischemic myocardial processes, particularly hypoxia, sepsis, systemic inflammation, and severe respiratory tract infection (8). In our study; cardiological examinations and echocardiographic findings of the patients with elevated troponin were found to be normal and no treatment was required.

In a study conducted in Turkey, it was found that 182 (42.5%) patients underwent thoracic CT imaging, and COVID-19 was confirmed in 38 (32.7%) (18). In our study, 54.8% of the hospitalized patients were found to have COVID-19 pneumonia

on CT. In both studies, the incidence of pneumonia is high because pneumonia is one of the major criteria for hospitalization. Considering the patients with pneumonia, there was a statistically significant difference found between age, hospitalization day, WBC, and troponin-I levels. In the detection of WBC elevation and troponin elevation in younger children, it is important to consider that they tend to have many viral infections. It is possible that repeated viral exposure may boost the immune system when it responds to severe acute respiratory syndrome- coronavirus-2 (SARS-CoV-2) (1,19,20). Also, the distribution and affinity of the angiotensin-converting enzyme receptor and SARS-CoV-2 are different according to age (21,22,23). When multivariate analysis was performed for these parameters, the probability of pneumonia was found to increase by a factor of 1.17 with increasing age (Table 4). In older children with pneumonia, hospitalization time was also longer. The recommendation of a 5-day favipiravir treatment for patients aged 15 years and older in the Turkish Ministry of Health pediatric patient treatment protocol was thought to be the reason for this (11,12).

It is known that D-dimer is significantly elevated in patients with severe and fatal COVID-19 (24). Although adults have high D-dimer and pulmonary embolism risk, the correlation of these factors with the severity of the disease in patients with COVID-19 pneumonia remains under investigation (13,14). However, the utility of D-dimer and its clinical effect in pediatric patients are not known. In a pediatric study from Turkey, it was reported that the mean D-dimer value was higher than the references (25). In our study, the elevation of fibrinogen and D-dimer was not found to be statistically significant. Anticoagulant therapy was not administered in these patients. No thrombotic complications were observed in this study. However, there was no correlation between coagulopathy and the severity of the disease in patients with COVID-19 pneumonia.

### Study Limitations

This study at the beginning of the pandemic-which was a major health problem at the time- comprehensively examined the issue. During the pandemic period, different treatment methods were recommended and applied by countries and clinics. We think that this study will contribute to the literature because it is a single-center study. In addition, in pediatric patients with COVID-19, there are few studies that have been evaluated in

detail in terms of coagulopathy and blood parameters, especially in patients with pneumonia. Due to the limited number of patients and the different diagnostic and treatment protocols in different countries, we think that the different results that emerged include diverse experiences and are remarkable.

## Conclusion

The finding that the risk of COVID-19 pneumonia increases with age draws more attention in terms of diagnosis and treatment. Since there was no significant difference in the COVID-19 pneumonia patients among the parameters showing a tendency to thrombosis, further investigation is warranted to understand the underlying mechanisms. It was thought that the presence of pneumonia did not increase the risk of coagulopathy. Therefore, we believe that there is no need for more aggressive anticoagulant therapy in the presence of diffuse pneumonia. Troponin-I levels may be higher in young children without COVID-19 pneumonia; therefore, it was thought that close follow-up was required for myocarditis. Also, more detailed epidemiological data are needed regarding pediatric patients related to COVID-19.

### Ethics

**Ethics Committee Approval:** The study was conducted in accordance with the principles of the Declaration of Helsinki and the Kütahya Health Sciences University Non-Interventional Clinical Research Ethics Committee (decision no: 2021/09-02, date: 26.05.2021).

**Informed Consent:** Retrospective study.

### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: D.G., R.Ö., Z.Y., O.S., C.H.Ç., Y.Y., Concept: D.G., Design: D.G., R.Ö., Data Collection or Processing: D.G., R.Ö., Z.Y., O.S., C.H.Ç., Y.Y., Analysis or Interpretation: D.G., R.Ö., Literature Search: D.G., Writing: D.G., R.Ö.

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

**Financial Disclosure:** The authors declared that this study received no financial support.



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# Determine the Level of IL-17 in People Recovering from Viral Infections of the Respiratory System

✉ Zahraa Khalid Al-Kheroo<sup>1</sup>, ✉ Khalid N. Al-Kheroo<sup>2</sup>, ✉ Mahmood Abd Al Jabbar Al-Tobje<sup>1</sup>

<sup>1</sup>University of Mosul College of Science, Department of Biology, Mosul, Iraq

<sup>2</sup>University of Mosul College of Medicine, Department of Internal Medicine, Mosul, Iraq

## What is known on this subject?

This study targets the group with elevated interleukin-17 (IL-17) levels among viral and recovered patients.

## What this study adds?

This study provides knowledge about increased IL-17 levels in patients recovering from viral infections.

## ABSTRACT

**Objective:** Numerous illnesses, such as bacterial and viral infections, affect the respiratory system. Since no known therapy for viruses directly influences health, viral infections are typically more deadly than bacterial ones. The study aimed to ascertain the degree of many immunological markers in patients recovering from viral respiratory infections. The amounts of these indicators were ascertained using the ELISA technique.

**Material and Methods:** The study includes 74 sample collections from June to September (2023), including 28 males and 46 females, aged over 18. Blood samples, overall, were taken. The study was conducted in the Research Laboratory of the Department of Biology, College of Science, University of Mosul. Seventy-four individuals were involved in the study; forty-six of them were recovering from being severe acute respiratory syndrome coronavirus-2 positive (after 6 months), and twenty-eight were not.

**Results:** The findings revealed highly variable levels of interleukin-17 (IL-17), immunoglobulin M (IgM), and immunoglobulin G (IgG) between the patient samples and the control samples. While the IgG level was higher in the first age group (20-40 years), the levels of both IgM and IL-17 were higher in older ages (41-60 years). The levels of immune markers were higher in females than in males, with IL-17, IgG, and IgM reaching 133.3 pg/mL, 1707.9 ng/mL, and 56.8 ng/mL, respectively.

**Conclusion:** According to the current study, the parameters measured in coronavirus disease-2019 recovery participants after six months were higher than those in control samples.

**Keywords:** Respiratory system, IL-17, SARS-CoV-2, IgG



**Address for Correspondence:** Mahmood Abd Al Jabbar Al-Tobje Prof. Ph.D., University of Mosul College of Science, Department of Biology, Mosul, Iraq

**E-mail:** mahmoodaltobje1967@gmail.com **ORCID ID:** orcid.org/0000-0002-0507-4469

**Received:** 03.01.2025 **Accepted:** 22.01.2025

**Cite this article as:** Al-Kheroo ZK, Al-Kheroo KN, Al-Tobje MAAJ. Determine the level of IL-17 in people recovering from viral infections of the respiratory system. Cam and Sakura Med J. 2024;4(3):82-87



## Introduction

An increase in pneumonia cases with an undetermined origin appeared throughout December 2019 in Wuhan, China (1). Research into the disease's etiology and epidemiology found a brand-new coronavirus that proceeded to spread quickly (2).

Inflammatory-promoting cytokines are crucial in the pathogenesis of many respiratory virus infections because they coordinate and activate the adaptive immunological reaction, which is a crucial part of the illness (3). The disease's progression involving lung tissue, acute respiratory distress syndrome, and/or systemic response to many organs might result from an unchecked inflammatory response (4). When the immune system's various components are balanced, disease can be cleared up with few adverse effects, but when they are out of balance, tissue damage can result (5). As potential biomarkers for viral illnesses like influenza or Middle East respiratory syndrome, cytokine profiles have been proposed (6). Additionally, results from coronavirus disease-2019 (COVID-19) studies have been linked to antibodies (7). After recovering from COVID-19, patients' T-cells respond differently to severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) because T-cells use a heterogeneous T-cell receptor to recognize many epitopes (8).

T-cell polyfunctionality of CD4+ and CD8+ refers to cells ability to produce many cytokines, at the same time, and perform a variety of functions. This is an important aspect of antigen-specific responses because, in some circumstances, resistance against the reappearance of the disease or infection may depend more on the quality of the reaction than the number (9). The stimulation of an inflammatory response and the activation of CD8+ T and B-cells depend on both Th17 and CD4+ Th1 cells. As an example, Th1 and Th17 CD4+ T, and CD8+ T-cells predominate in the immune response to the influenza A virus, resulting in both a highly inflammatory milieu and viral clearance (10,11). The immune response's initial immunoglobulin, immunoglobulin M (IgM), eliminates infections when they are still in their early stages. Especially in secondary responses, immunoglobulin G (IgG) is the predominant antibody type (accounting for 75% of all blood immunoglobulin), and its levels can be increased in a variety of circumstances, including autoimmune illnesses and infections. It can penetrate tissues to battle illness (12).

## Material and Methods

The study included 74 sample collections conducted from June to September 2023, comprising 28 males and 46 females, all aged over 18. Ethical approval was granted by the College of

Medicine, University of Mosul, with the ID [ref no: UOM/COM/MREC/2024(8), date: 06.08.2024]. Blood samples were collected, and the study was carried out in the research laboratory at the University of Mosul, Department of Biology, College of Sciences. Table 1 presents the types of kits used in this study.

## Statistical Analysis

The data were assessed by the t-test to compare the concentration of IgG, IgM, and interleukin-17 (IL-17) between control and convalescent patients at a significance level of  $p \leq 0.05$ , utilizing SPSS version 21.

## Results

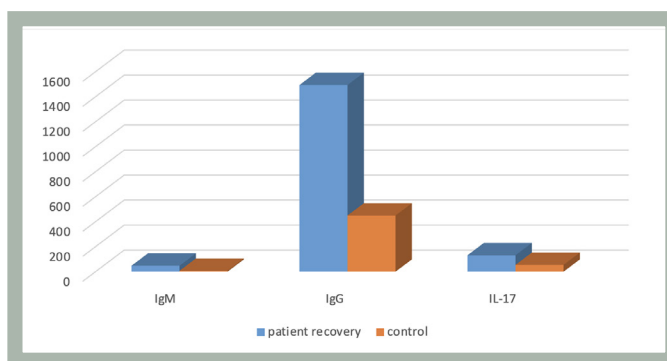
The study includes 74 samples collected from healthy people (28) and people recovering from SARS-CoV-2 after six months (46), (Table 2).

In contrast to the control group samples, the results indicate that those who recovered from COVID-19 possessed the greatest levels of IgM and IgG ( $47.77 \pm 42.79$  and  $1493.89 \pm 874.57$  ng/mL, respectively). When the level of IL-17 reached ( $54.48 \pm 5.67$ ) pg/mL, it was lower than that of the control samples (Table 3, Figure 1).

**Table 1. Description of kits used in this study**

Test kit name	Manufacturing company	Origin
IgG measurement kit	Supplier from company Sunlong	Chinese
IgM measurement kit	Supplier from company Sunlong	Chinese
IL-17, mouse	Supplier from company KOMA BIOTECH	Korea

*IgG: Immunoglobulin G, IgM: Immunoglobulin M, IL-17: Interleukin-17*



**Figure 1.** Compare the patient's health and recovery using a few immunological parameters

*IgM: Immunoglobulin M, IgG: Immunoglobulin G, IL-17: Interleukin-17*

IgM rates were (40.77±29.07 ng/mL) in the first age group and (55.41±54.56 ng/mL) in the second. In contrast, IgG and IL-17 rates were (1543.42±934.51 ng/mL, 117.74±65.70 pg/mL) in

the 20-40 age group and (1439.85±846.11 ng/mL, 146.70±21.77 pg/mL) in the 41-60 age group, (Table 4, Figure 2).

**Table 2. Comparison using some immunological parameters between the patient's recovery and health**

	Number	%	IgM ng/mL	IgG ng/mL	IL-17 pg/mL
Patient recovery	46	62.2%	47.77±42.79	1493.89±874.57	131.59±50.91
Control	28	37.8%	7.31±3.93	449.57±33.36	54.48±5.67
t value	0.031*		2.282	3.060	3.951
Significance			0.005**	0.00**	

\* $p < 0.05$ , \*\* $p < 0.01$ , Mean ± standard error. IgM: Immunoglobulin M, IgG: Immunoglobulin G, IL-17: Interleukin-17

**Table 3. IgG, IgM, and IL-17 averages by age group**

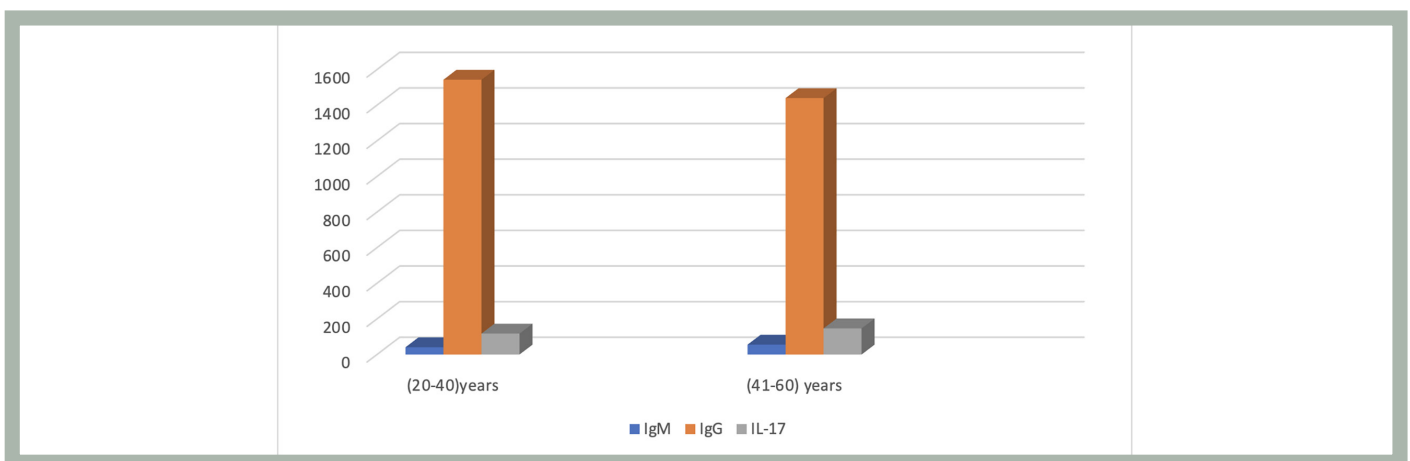
Age	Number	%	IgM (4-14.15) ng/mL	IgG (43.85-429.05) ng/mL	IL-17 (44.5-90.3) pg/mL
(20-40)	12	52.2	40.77±29.07	1543.42±934.51	117.74±65.70
(41-60)	11	47.8	55.41±54.56	1439.85±846.11	146.70±21.77
t value	0.425 n.s		0.813	0.278	1.391
Significance			0.784 n.s	0.179 n.s	

Mean ± standard error. IgG: Immunoglobulin G, IgM: Immunoglobulin M, IL-17: Interleukin-17, n.s: Non-significant

**Table 4. The levels of IL-17, IgG, and IgM by gender**

Gender	Number	%	IgM (4-14.15) ng/mL	IgG (43.85-429.05) ng/mL	IL-17 (44.5-90.3) pg/mL
Male	18	39.1	33.69±17.40	1160.87±480.71	128.94±57.27
Female	28	60.9	56.83±51.84	1707.97±1012.95	133.30±48.58
t value	0.213 n.s		0.1284	1.506	0.196
Significance			0.147 n.s	0.847 n.s	

Mean ± standard error. IL-17: Interleukin-17, IgG: Immunoglobulin G, IgM: Immunoglobulin M, n.s: Non-significant



**Figure 2. Show IgG, IgM, and IL-17 averages by age group**

IgG: Immunoglobulin G, IgM: Immunoglobulin M, IL-17: Interleukin-17

## Discussion

Convalescent patients had elevated serum levels of IgG, which may be linked to the antibody's prolonged half-life. IgM is the antibody that is initially produced by the immune system; however, if the infection persists, isotype swapping takes place IgG, which is more effective at neutralizing the pathogen, will be released. Mossa Alabassi et al. (13) observed elevated IgG levels in convalescent cases. According to Grifoni et al. (14), around 70% and 100% of COVID-19 patients who recovered developed responses involving SARS-CoV-2-specific CD8+ and CD4+ T-cells, respectively (14).

Multiple studies found memory B-cells six months after infection, and these cells may provide long-term humoral immunity (15). A few investigations found that even though their antibody titers had dropped, COVID-19 convalescents still exhibited antiviral memory T and B-cells six to eight months after infection (16). Pan et al. (17) discovered that antibodies, IgM and IgG, were detected when comparing the serum of the COVID-19 convalescent patients with that of the healthy donor group. Additionally, compared to healthy donors, IgG antibodies were more clearly seen than IgM antibodies in the individuals under observation. These data collectively imply that according to the SARS-CoV-2 molecule, both IgG and IgM responses in COVID-19 patients and that patients with the infection can continue to express IgG until at least 11 months after the disease first manifests (17), there were no discernible differences in IL-2, IL-12, interferon (IFN)- $\gamma$ , IL-5, IL-6, IL-1 $\beta$ , IL-17, IL-10, IFN- $\alpha$ , and TNF- $\alpha$  between the groups. during the follow-up, according to Pan et al. (17). These findings imply that most convalescent individuals had normal lymphocyte subsets and cytokines. However, these findings could indicate a patient's ability to neutralize the virus in COVID-19 (17).

IgG antibodies were shown to be detectable for 720 days following infection, according to one study. According to a different study, antibody levels dramatically decreased three years after infection, and 56% of convalescent patients tested positive (18). In COVID-19 patients, phorbol myristate acetate and ionomycin stimulation result in a rise in IL-17+CD4+ T-cells, similar to results has been previously described when anti-CD3 and anti-CD28 antibodies were used for stimulation. The IL-17+CD4+ T lymphocytes were remarkably sustained throughout the convalescent phase. The next aspect investigated was a correlation between any particular clinical characteristics and the increased production of IL-17 during hospitalization. Irrespective of the patient's chest X-rays being whether normal or abnormal, there is an increase in IL-17+CD4+ T lymphocytes in convalescent patients (19). Studies by Shuwa et al. (20) reveal that patients

recuperating from COVID-19 had elevated IL-17 and type 1 cytokine production.

Throughout the convalescent stage, we observed the persistence of IL-17 expression in CD4+ T-cells among activated peripheral blood mononuclear cells, regardless of clinical characteristics, following the acute illness. Therefore, it is possible that Tregs from Mild Normal levels were maintained during the acute phase and recovered at the end of the illness (20). The transcription factor (TF) ROR $\gamma$ t may be overexpressed in minimally recovered volunteers, as shown by Treg's enhanced production of IL-17. ROR $\gamma$ t+ Tregs may block Th17 differentiation, reducing the release of inflammation-causing chemicals. Previous research has shown that Tregs with TF from distinct CD4+ T subgroups contribute to the suppression of specific inflammatory patterns as part of the immune response (21).

Elderly people have a higher probability of experiencing severe illness, as aging impairs B-cells' capacity to produce a strong immunological response, thereby reducing the production of high-affinity antibodies. Additionally as a result of immunosenescence, older persons typically have lower cellular immunity (22).

Li et al. (23) discovered that 28 months following release, the levels of (specify substance or variable) in every study group member had returned to normal. According to one study, non-hospitalized convalescent samples had greater frequencies of expression for several activation and exhaustion markers. We found many positive associations over time when examining these markers, suggesting that the immunological dysregulation in these people did not disappear quickly. We also discovered that older people had more significant T-cell activation dysregulation and fatigue markers than younger individuals. This is the first report of COVID-19-related persistent immunological dysregulation in a sizable cohort of outpatient recuperation patients, to our knowledge (24). A recent investigation of a small cohort of patients who recovered from COVID-19 categorized immunological subgroups infected with SARS-CoV-2 and found elevated frequencies of the standard CD14+ monocyte population (25). In a separate investigation, we looked at immunity and the recovery status in 121 patients-roughly half of the Central Hospital's COVID-19 survivors. Nearly 90% of the recovered patients had 50% protection to prevent serious re-infection occurring a year following the initial infection, and, 99% of them had sustained protection against SARS-CoV-2 by anti-receptor-binding domain (anti-RBD) IgG. A year following infection, total anti-RBD antibody levels were consistent when compared to convalescent samples.

Age and antibody response were shown to be positively correlated, and persistent symptoms were discovered to be a sign of a poorer immune response. The durability of the antibody response was linked to established factors such as sex and the severity of the disease (26). A different study discovered that the elderly population had a significant degree of resistance to reinfection. Accordingly, the data point to the possibility that immunological responses associated with aging may play a role in explaining some of the variations in COVID-19 clinical manifestations between juvenile and adult patients. Many studies have shown that older individuals are more vulnerable to newly emerging viral infections. These findings are linked to both the innate and the adaptive immune system changes associated with aging, such as immunological senescence. Finding a high level of antibodies in older individuals who have recovered from an illness could help explain their capacity to heal without complications, as numerous studies have shown that different age groups have variable antibody concentrations (27).

Since hormones and the immune system are closely related and are essential to initiating the defense mechanism, females typically exhibit higher immune responses than males. In addition, when hormones are present in higher concentrations in females, we typically observe a stronger immune response than in males (28). Higher IgG and IgM antibody responses were linked to more severe COVID-19 cases compared to less severe cases (29). The IgG levels between the sexes also differed significantly. Females often have stronger adaptive immune responses than males against vaccinations and viral infections, which might explain the noted variations in SARS-CoV-2 pathogenesis between the sexes and ultimately lessen the vulnerability of women to the disease (30). Takahashi et al. (31) observed markedly increased T-cell initiation and a tendency toward larger titers of antibodies specific to SARS-CoV-2 in female patients with moderate COVID-19. Female donors were

reported to have a greater likelihood of having high (32) IgG for SARS-CoV-2 antibodies (33); however, other reports showed the opposite (33) or found no significance at all (34).

## Conclusion

According to the data, the recovery samples had higher amounts of IL-17, IgM, and IgG, than the control samples, while the IgG level was higher in those in the 20-40 age range. The levels of immunological markers were higher in females than in males.

### Ethics

**Ethics Committee Approval:** Ethical approval was granted by the College of Medicine, University of Mosul, with the ID [ref no: UOM/COM/MREC/2024(8), date: 06.08.2024].

**Informed Consent:** Obtained.

### Acknowledgments

The authors express their gratitude to the study laboratory at the University of Mosul's Department of Biology, College of Sciences.

### Footnotes

### Authorship Contributions

Surgical and Medical Practices: Z.K.A-K., K.N.A-K., M.A.A.J.A-T., Concept: Z.K.A-K., K.N.A-K., M.A.A.J.A-T., Design: Z.K.A-K., K.N.A-K., M.A.A.J.A-T., Data Collection or Processing: Z.K.A-K., K.N.A-K., M.A.A.J.A-T., Analysis or Interpretation: Z.K.A-K., K.N.A-K., M.A.A.J.A-T., Literature Search: Z.K.A-K., K.N.A-K., M.A.A.J.A-T., Writing: Z.K.A-K., K.N.A-K., M.A.A.J.A-T.

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

**Financial Disclosure:** The authors declared that this study received no financial support.

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# The Effects of Maternal Depression on Children with Primary Monosymptomatic Nocturnal Enuresis

✉ Bahar Çaran<sup>1</sup>, Duygu Hacıhamdioğlu<sup>2</sup>, Gamze Özgürhan<sup>3</sup>

<sup>1</sup>University of Health Sciences Turkey, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Clinic of Pediatric Cardiology, İstanbul, Turkey

<sup>2</sup>Bahçeşehir University Faculty of Medicine Medical Park Göztepe Hospital, Pediatric Nephrology, İstanbul, Turkey

<sup>3</sup>University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of Pediatrics, İstanbul, Turkey

## What is known on this subject?

The effect of maternal psychosocial status on quality of life of children with primary monosymptomatic nocturnal enuresis has not been investigated. The aim of this study is to investigate the effects of maternal depression and demographic variables on the quality of life of enuretic children.

## What this study adds?

This study is the first to evaluate both mothers and their enuretic children to determine how the mother's mental state can affect the child's quality of life.

## ABSTRACT

**Objective:** The effect of maternal psychosocial status on quality of life of children with primary monosymptomatic nocturnal enuresis (PMNE) has not been investigated. The aim of this study is to investigate the effects of maternal depression and demographic variables on the quality of life of enuretic children.

**Material and Methods:** The study consisted of 58 children with PMNE between the ages of 6 to12 and their mothers. Participants were asked to complete the Pediatric Quality of Life Inventory and the Beck depression inventory (BDI).

**Results:** Physical health total scores (PHTS) were correlated with psychosocial health total scores (PSHTS) ( $p=0.020$ ,  $r=0.394$ ) and mother's age ( $p=0.025$ ,  $r=0.162$ ). Maternal age was negatively correlated with the BDI score ( $p=0.012$ ,  $r=-0.328$ ). PHTS was significantly lower in the group with primary education ( $p=0.043$ ). In addition, maternal age and income were higher in the high school/university group ( $p=0.031$ ,  $p=0.042$ , respectively). PSHTS was lower in children with mothers who had moderate mood disorders/clinical depression, than children of mothers with normal BDI scores ( $p=0.032$ ).

**Conclusion:** The results of this study indicate that mothers with moderate mood disorders and clinical depression directly affected the psychosocial health of their enuretic children and indirectly affected their physical health.

**Keywords:** Enuresis nocturna, maternal depression, primary enuresis, quality of life



**Address for Correspondence:** Bahar Çaran MD, University of Health Sciences Turkey, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Clinic of Pediatric Cardiology, İstanbul, Turkey

**E-mail:** bayar818@hotmail.com **ORCID ID:** orcid.org/0000-0001-7521-2313

**Received:** 06.09.2024 **Accepted:** 16.12.2024

**Cite this article as:** Çaran B, Hacıhamdioğlu D, Özgürhan G. The effects of maternal depression on children with primary monosymptomatic nocturnal enuresis. Cam and Sakura Med J. 2024;4(3):88-94



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## Introduction

Primary monosymptomatic nocturnal enuresis (PMNE) is a common childhood disorder whose cause is often multifactorial. Nocturnal enuresis, which can seriously affect the psychosocial development of children along with their self-confidence and participation in social life, is a condition that increases rates of depression and anxiety in both children and their mothers (1,2). Active family and children's involvement in treatment is important. To the knowledge of the authors, the effects of maternal psychosocial status on the quality of life in children with PMNE have not been investigated. Therefore, the aim of this study is to investigate the effects of maternal depression scores and demographic variables on the quality of life of enuretic children between the ages of 6 and 12.

## Material and Methods

This study received approval from the Local Ethics Committee of the University of Health Sciences Turkey, Istanbul Training and Research Hospital (approval date: 04.08.2017; study no: 1057). The study was performed at the same facility and consisted of 58 children between the ages of 6 and 12 years with PMNE, along with their mothers, who were outpatients of the pediatric clinic. A diagnosis of PMNE was made based on the Diagnostic and Statistical Manual of Mental Disorders-5 criteria (3). After taking the patient's history and conducting a physical examination, blood analysis, urinalysis, urine culture, and ultrasound were performed. Patients with any chronic disease or mothers who had received medication for any disease were excluded from the study as declared by their parents.

The Pediatric Quality of Life Inventory has been validated in Turkey and is considered a reliable inventory to assess quality of life in children (4,5). Three areas comprise the total assessment: physical health total score (PHTS), psychosocial health total score (PSHTS), and scale total score (TS). The survey consists of 23 Likert-type questions, which are valued between 0 and 100 points each (100: never, 75: rarely, 50: sometimes, 25: often, 0: always). The higher the overall score, the higher the children's health-related quality of life.

Mothers in the study were asked to complete the Beck depression inventory (BDI), which was validated and found to be reliable by Hisli (6). This inventory is a depression assessment scale consisting of 21 multiple-choice questions. Each question is scored between 0-3, where a total final score between 1-10 is considered normal, 11-16 indicates a moderate mood disorder, 17-20 indicates clinical depression,

21-30 moderate depression, 31-40 severe depression, and 41-63 implies very serious depression.

Mothers were also asked to provide information about demographic data such as maternal age, education level, income level, marital status, and number of children.

## Statistical Analysis

Analyses were performed using the SPSS 22.0 software package for Windows. Results are expressed as median (interquartile range) for descriptive data. The Kolmogorov-Smirnov test was used to assess the normality of parameters, and the Mann-Whitney U test was used for comparisons of two groups in the analysis of quantitative independent data that did not show normal distribution. The chi-square test was used in the analysis of qualitative independent data, and the Fisher test was used when chi-square test conditions were not met. Spearman correlation analysis was used for the data that did not show normal distribution, and Pearson correlation analysis was used for the data that showed normal distribution. Statistical significance was defined as  $p < 0.05$ .

## Results

The median ages of the patients and mothers were 8 years and 33 years, respectively. Socio-demographic characteristics of children and mothers are shown in Table 1. A total of 58 children-29 (50%) girls and 29 (50%) boys and their mothers were included in the study. Correlation analysis of quality of life scores, BDI scores and the age of children and mothers presented in Table 2. Patient age was correlated Beck depression score (BDS) PHTS ( $p=0.025$ ,  $r=0.290$ ). PHTS was correlated with PSHTS ( $p=0.020$ ,  $r=0.394$ ) and maternal age ( $p=0.025$ ,  $r=0.162$ ). The age of mothers was negatively correlated with BDS ( $p=0.012$ ,  $r=-0.328$ ). No significant differences were observed between PHTS, PSHTS, TS, and BDS according to the mother's job status, income, number of children, and marital status. However, when the mother's education level was compared with quality-of-life scores, PHTS was found to be significantly lower in the group with primary education ( $p=0.043$ ). In addition, mothers with high school/university level education had higher maternal ages and income ( $p=0.031$ ,  $p=0.042$ , respectively). In the comparison of mothers between  $<32$  years and  $\geq 32$  years, BDS was significantly higher in the group under 32 years of age compared to the group aged 32 years or above ( $p=0.023$ ). There were no significant differences between mother's age ( $<32$  years and  $\geq 32$  years) and education level (uneducated to primary school and high school to university) ( $p=0.210$ ) (Table 3). The comparisons of mothers' BDS with socio-

**Table 1. Socio-demographic and inventory characteristics of children and mothers**

Parameter	Median (IQR)
Age (years)	8
Gender (M/F)	1 (50% F)
Mother age (years)	33±6.5
<b>Mother education status</b>	
Uneducated	n=6 (10.3%)
Primary school	n=36 (62.1%)
High school	n=7 (12.1%)
University	n=9 (15.4%)
<b>Job status</b>	
Working	n=8 (13.8%)
Unemployed	n=50 (86.2%)
<b>Income</b>	
50-100\$	n=9 (15.5%)
101-150\$	n=24 (41.4%)
>150\$	n=25 (43.1%)
<b>Number of children</b>	
1	n=4 (6.9%)
2	n=28 (48.3%)
3	n=17 (29.3%)
≥4	n=9 (15.5%)
Marital status (married/single)	n=56 (96.6%)
Physical health total score	68.75 (±18.75)
Psychosocial health total score	69.15 (±17.02)
Scale total score	71.15 (±15.48)
<b>Beck depression score</b>	
Normal (0-10)	n=20 (34.5%)
Moderate mood disorder (11-16)	n=17 (29.3%)
Clinical depression (≥17)	n=21 (36.2%)

M/F: Male/female, IQR: Interquartile range

**Table 2. Correlation analysis of quality of life scores, BDI scores and the age of children and mothers**

Parameters	Age	PHTS	PSHTS	TS	Mother age	BDS
<b>Age</b>		<b>p=0.025</b> r=0.290	p=0.287 r=0.142	p=0.071 r=0.239	p=0.254 r=0.152	p=0.795 r=0.350
<b>PHTS</b>			<b>p=0.020</b> r=0.394	<b>p=0.000</b> r=0.802	<b>p=0.025</b> r=0.162	p=-0.59 r=0.659
<b>PSHTS</b>				<b>p=0.000</b> r=0.815	p=0.253 r=-0.152	p=0.514 r=0.087
<b>TS</b>					p=0.282 r=0.144	p=0.612 r=-0.068
<b>BDS</b>					<b>p=0.012</b> r=-0.328	
<b>NoC</b>	p=0.363 r=0.120	p=0.843 r=-0.027	p=0.667 r=0.058	p=0.960 r=0.007	<b>p=0.031</b> r=0.284	p=0.347 r=-0.126

PHTS: Physical health total score, PSHTS: Psychosocial health total score, TS: Scale total score, BDS: Beck depression score, NoC: Number of children, BDI: Beck depression inventory

demographic data and children's Quality of Life Scores are presented in Table 4. There were no differences in terms of child's age, mother's age, gender, number of children, mother's education, job, income, and marital status between the normal and moderate mood disorder/clinical depression groups. In addition, there were no differences in PHTS and TS between the groups. However, PSHTS was lower in children whose mothers were in the group with moderate mood disorder or clinical depression group than in those whose mothers were in the normal group ( $p=0.032$ ).

## Discussion

The present study investigated the effect of maternal depression levels on the quality of life of enuretic children. PMNE can be uncomfortable for both children and their caregivers. The effects of maternal emotional disturbance on enuretic children have been investigated in many controlled studies (1,7,8). Childhood studies have also revealed that those diagnosed with enuresis result in more symptoms of depression and lower quality of life when compared to control groups (2,9,10,11). However, the effect of maternal depression on the child's quality of life has not been thoroughly investigated.

In a study utilizing psychometric questionnaires that included 44 mothers of children with PMNE and 45 mothers of non-enuretic children, it was found that the general psychopathology index was higher among mothers of PMNE children (1). In addition, instances of sexual abuse and physical neglect were found to be more common in mothers of children with PMNE. Interestingly, the psychiatric issues of children were not within the scope of this study. In another study, while the BDI scores were higher in mothers of children

**Table 3. Comparison analysis of maternal education level with maternal age, income levels, number of children, child quality of life scale and BDI scores**

Maternal education status	Uneducated-primary school (n=42)	High school-university (n=16)	p
Mother age (yr)	32±8.25	35±8.75	<b>0.031</b>
<b>Income</b>			
<150\$	n=33 (78.6%)	n=0	<b>0.042*</b>
≥150\$	n=9 (21.4%)	n=16 (100%)	
NoC	3±1	2±1	0.199
Age (yr)	8±3	7±1	0.212
PHTS	68.7±16.4	75.8±14.1	<b>0.043</b>
PSHTS	69.2±14.8	69.2±9.8	0.910
TS	69.5±13	73.4±9.3	0.310
BDS	14±15.25	13.5±7.25	0.525
Maternal age	<32 yr n=22	≥ 32 yr n=36	
Mother age (yr)	28.5±4.25	36±6.75	<b>0.000</b>
<b>Income</b>			
<150\$	n=2 (9%)	n=7 (19.4%)	0.459
≥150\$	n=20 (81%)	n=29 (80.6%)	
NoC	2±1	3±1	0.053
Age (yr)	7.5±2.25	8±3	0.146
PHTS	73.4±14.7	68.8±17.1	0.255
PSHTS	70.8±12.5	66.7±14.6	0.268
TS	72.3±11	66.8±12.9	0.110
BDS	15±14.75	11±10.75	<b>0.023</b>
<b>Education status</b>			
<b>Uneducated-primary school</b>	n=18 (81.8%)	n=24 (66.7%)	0.210
High school-university	n=4 (18.2%)	n=12 (33.3%)	

\*Fisher's exact test, data presented as median (±IQR), BDS: Beck depression score, PHTS: Physical health total score, PSHTS: Psychosocial health total score, TS: Scale total score, NoC: Number of children, IQR: Interquartile range, BDI: Beck depression inventory

with PMNE (n=28) than mothers of children with no health issues (n=38), there was no statistical difference in their Spielberger's state-trait anxiety inventory (STAI) scores (7). In another study that included 90 mothers of children with PMNE and 80 mothers of children without PMNE, it was found that the trait-anxiety score, a subcomponent of the STAI, and the mean BDI score were higher in mothers of children with PMNE than in mothers of children without PMNE (12). However, there was no significant correlation between STAI and BDI scores. Trait anxiety is the genetic predisposition to anxiety and is considered to be a permanent psychological characteristic (13). This finding is supported by another study which consisted of 96 children (52 enuretic children and 44 healthy children) and their mothers (14). Both child anxiety and mother trait anxiety were found to be higher for children

and mothers in PMNE group. In another study with a similar design which included 40 mothers of children with PMNE and 44 mothers of healthy children, trait anxiety scores were observed to be different between the two groups, but the BDI scores were similar between the two groups (8). It seems that mothers of children with PMNE tend to have higher levels of psychopathology, such as trait anxiety, and this can often be reflected in their children. The ability to experience negative emotions in a stable and consistent way across various situations, such as the stress of having PMNE, could be related to a heritable factor. It is not clear whether PMNE is a result of or a cause for anxiety. Another result of these studies is that anxiety is not always associated with depression, and the effect of depression on the quality of life of children is unknown.

**Table 4. Comparison of mothers' Beck depression scores with socio-demographic data and children's Quality of Life Scores**

Parameter	Normal BDS: 1-10 (n=20) Median ± IQR	Moderate mood disorder and clinical depression BDS: 11-20 (n=38) Median ± IQR	p
Age (yr)	8±2.75	8±2.25	0.543
Mother age (yr)	33.5±7.5	32±7	0.749
Gender (M/F)	12/8	17/21	0.273
PHTS	75±17.16	68.7±24.96	0.154
PSHTS	72.45±15	66.6±22.1	<b>0.032</b>
TS	73.35±12.48	67.35 ±16.5	0.092
BDS	7±3	17.5±10.75	<b>0.000</b>
	<b>n (%)</b>	<b>n (%)</b>	
<b>Mother education status</b>			
Unducated/primary school	16(80%)	26 (68.4%)	0.348
High school/university	4 (20%)	12 (31.6%)	
<b>Job status</b>			
Working	1 (5%)	7 (18.4%)	0.241
Unemployed	19 (95%)	31 (81.6%)	
<b>Income</b>			
<100\$	4 (20%)	5 (13.2%)	0.704
>100\$	16(80%)	33 (86.8%)	
<b>NoC</b>			
≤2	10 (50%)	21 (57.9%)	0.591
≥3	10 (50%)	17 (42.1%)	
<b>Marital status</b>			
Married	20 (100%)	36 (9.7%)	0.540
Single	0 (0%)	2 (5.3%)	

BDS: Beck depression score, IQR: Interquartile range, M: Male, F: Female, PHTS: Physical health total score, PSHTS: Psychosocial health total score, TS: Scale total score, NoC: Number of children

In a study by Hägglöf et al. (2) on Swedish children, pharmacological treatment was utilized for enuretic children. They determined that self-confidence values of children who underwent the treatment had significantly increased both 3 and 6 months after the treatment, compared to their pre-treatment values, and compared to the children who did not benefit from the treatment. Sahtiyanci et al. (9) studied 40 children diagnosed with primary nocturnal enuresis, whose enuresis improved after responding to 3 months of desmopressin treatment. Children and their mothers were asked to complete the BDI before and after treatment (9). While there was a statistically significant improvement in the depression scale scores for the children compared to the pre-treatment period, there was no significant change in the BDI scores of the mothers. In another study, 47 children diagnosed with PMNE were evaluated before and on the 3<sup>rd</sup> month of desmopressin treatment through administration

of the Life Quality Scale for Children then their mothers were asked to complete the short form health survey (SF-36) (10). The results revealed that both the children's and mother's scores improved. However, there was no indication whether the children's scores improved after the treatment. Naitoh et al. (11) evaluated the health-related quality of life of 139 patients with nocturnal enuresis as well as that of their mothers before and after treatment. The results indicated a higher state anxiety score for mothers triggered as a response to a stressful situation, and a similar trait anxiety score. These results also demonstrated that after treatment for enuresis, the health-related quality of life score was improved both for the enuretic children as assessed by the Kid-KINDL protocol, and for the mothers of enuretic children as assessed by the SF-36 and STAI. It can be extrapolated from these results that as enuresis improves, children's self-confidence increases, their depression levels decrease, and their quality of life

improves. Mothers who have state anxiety, possibly triggered by enuresis, can also see an improvement in their quality of life with the management of enuresis. It was also observed in this same study that mothers of enuretic children tended to be more depressed than the control group, and that the depression levels of some of these mothers did not improve even if their children's condition improved. In conclusion, it is not clear whether maternal depression is a contributing factor or a result of enuresis. Furthermore, the effect of maternal depression on the enuretic child is unknown.

In the present study, physical health scores were correlated with psychosocial health scores and maternal age. The age and income of mothers with a high school or university education were higher than those of mothers with no education or only primary school education. These results support the effect of maternal education and income level on both physical and psychosocial health. There is evidence that psychosocial health can be predicted by physical health and that lower levels of psychosocial health may be associated with physical health disorders (15,16). In this study, it was observed that BDI was inversely correlated with maternal age, and mothers with lower education status were younger. It seems that the younger and less educated mother has a higher tendency toward depression. Durmaz et al. (1) observed that mothers of enuretic children had more psychopathology, and Sahtiyanci et al. (9) concluded that there was no change in depression levels after treatment. As a result, some mothers are more disposed to depression due to factors other than enuresis. In the present study, the psychosocial health scores of the children of mothers in the moderate mood disorder group and clinical depression group were lower than those of mothers with normal BDI scores. The effect of maternal depression on child psychosocial status has been widely studied, and the association of exposure to maternal depression during year 2 of a child's life with future childhood behavioral problems has been evaluated (17). Research in these areas has concluded that exposure to maternal depression during this critical second year of life may have a negative correlation with behavioral development through age 9. Exposure to maternal depression in the early years of life can affect later life psychosocial well-being. However, there is some contradictory research. In a cross-sectional study, 111 mother-child dyads were examined for maternal depressive symptoms and their effects on children's mental health (18). This study observed that while maternal depressive symptoms were strongly related to maternal reports of children's internalizing and externalizing mental health problems, these symptoms were unrelated to children's self-reported depressive symptoms. This result does

not indicate that no relationship exists between depressive symptoms in the mother and mental health problems in children. Rather, it suggests that not only the parents' perspective, but also the children's perspective should be evaluated. The present research evaluated children's quality of life scales according to the children's own self-reports and observed that enuretic children with depressed mothers had lower scores on their psychosocial quality of life scales. Psychiatric disorders such as depression and attention deficit hyperactivity disorder have often been reported with PMNE co-morbidity. On the other hand, in another study examining the relationship between various types of enuresis, urinary incontinence, behavioral problems, and psychiatric disorders, the highest association with psychiatric disorders was found in children with delayed urination, and the lowest association was found in children with PMNE (19). Evaluation of maternal and child mental health may affect the success of treatment in patients diagnosed with PMNE, where treatment periods are at least 6 months, as patient and family involvement is important in these cases.

### Study Limitations

The presented study has some limitations. The data used in this study were cross-sectional; no control group was used; the sample size was rather small to evaluate other contributing factors; and no information about fathers was included. Chronic diseases were excluded from the study according to parental declaration. Psychiatric disorders of children or mothers were not assessed by a psychiatrist or a psychologist. We could not evaluate the situation of the mother and children after treatment; further studies are needed for evaluation of the treatment effect.

### Conclusion

Despite these limitations, this study is the first to evaluate both mothers and their enuretic children to determine how the mother's mental state can affect the child's quality of life. The results of this study show that the psychosocial and physical health of enuretic children is affected, respectively, directly and indirectly, by mothers with moderate mood disorders and clinical depression. Furthermore, the present study showed an expected correlation between maternal education and income levels and children's physical health. Although these results demonstrate the effects of maternal depression status on their children, there is further need to use a multi-informant approach to assess enuretic children's life quality.

## Ethics

**Ethics Committee Approval:** This study received approval from the Local Ethics Committee of the University of Health Sciences Turkey, Istanbul Training and Research Hospital (approval date: 04.08.2017; study no: 1057).

**Informed Consent:** Consent forms were obtained from mothers and children before the study.

## Footnotes

### Authorship Contributions

Concept: D.H., Design: D.H., G.Ö., Data Collection or Processing: B.Ç., Analysis or Interpretation: G.Ö., Literature Search: B.Ç., Writing: B.Ç.

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

**Financial Disclosure:** The authors declared that this study received no financial support.

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# Incidence of Typhoid Fever in Nineveh Province from 2018-2022

Ali Adel Dawood

University of Mosul College of Medicine, Department of Anatomy, Mosul, Iraq

## What is known on this subject?

Typhoid is regarded as one of the most serious epidemic illnesses in nations with poor economies, and it may spread quickly, causing both physical and economic harm in society.

## What this study adds?

Determining the breadth of the disease's dissemination and increasing health and treatment knowledge in society may help reduce the number of potential infections.

## ABSTRACT

**Objective:** Typhoid fever is a grave and highly contagious illness caused by *Salmonella typhi* that is primarily spread through mucosal exposure to bacteria typically found in the gastrointestinal tract. This study focused on identifying the causes of the epidemic, predicting which populations are more susceptible to the disease, and evaluating the effectiveness of health measures set in place to prevent its spread in the Nineveh province.

**Material and Methods:** The study focused on patient data collected between 2018 and 2022. The count of infected individuals belonging to the sick group was authenticated based on the clinical diagnosis and laboratory investigation. Ultimately, we used a statistical analysis tool with SPSS version 25.

**Results:** The highest number of cases was registered on the left side of Mosul, followed by cases spreading to Shekhan, Hamdaniya, and Baaj, in that order. The main proportion of the cases was among 15-45 years and older than of 45 years old people with a relatively high correlation coefficient of ( $p < 0.01$ ).

**Conclusion:** The major reason for the spread of typhoid is the combination of poor quality of life and improper activities of the health system, which eventually lead to serious public health conditions. Strengthening the health-care system and raising public awareness about the disease are the two most crucial steps to slow down the outbreak.

**Keywords:** Health, *Salmonella typhi*, typhoid

## Introduction

Typhoid fever is an infectious disease caused by the bacterium *Salmonella typhi* that is acquired through the ingestion of infected food or water. The illness is often reported to develop gradually over days, leading to persistent fever, severe headaches, and anorexia. In advanced cases, pink spots may

infiltrate the abdomen while the abdomen may become distended due to splenomegaly. Patients may also complain of abdominal discomfort with constipation or diarrhea (1,2).

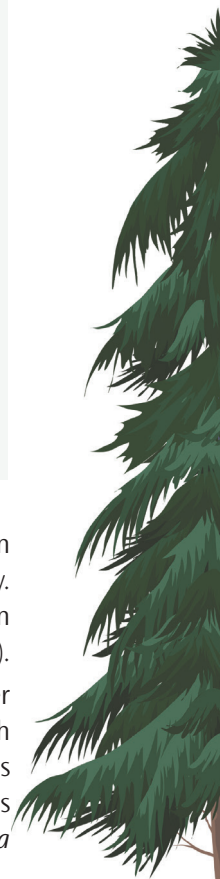
Medical management has improved over the years, but typhoid still poses a health challenge in areas that lack sanitary conditions and adequate health education, and this includes most regions of Iraq. *Salmonella*

**Address for Correspondence:** Ali Adel Dawood Assist Prof. Ph.D, University of Mosul College of Medicine, Department of Anatomy, Mosul, Iraq

**E-mail:** aad@uomosul.edu.iq **ORCID ID:** orcid.org/0000-0001-8988-5957

**Received:** 07.10.2024 **Accepted:** 27.10.2024

**Cite this article as:** Dawood AA. Incidence of typhoid fever in Nineveh province from 2018-2022. Cam and Sakura Med J. 2024;4(3):95-99



*typhi* is thought to have a high prevalence in Iraq due to poor food and water hygiene, highly populated areas, and lack of knowledge about the importance of hand washing and the need to eat cooked food. Deafness, intestinal bleeding, and bowel perforation are some of the complications of typhoid that are associated with grave consequences (3,4). In that regard, primary prevention measures include improvement of the sanitation facilities, provision of clean potable water, dissemination of health education and promotion and vaccination for typhoid fever (5).

Typhoid finds a fertile ground particularly among the poorer and slum areas since these conditions tend to facilitate its transmission. Lack of basic sewage systems, contamination of groundwater, and lack of proper health care facilities enhance the risk of acquiring the disease. Moreover, the concentration of people in these areas enhances the chance of one infected person transmitting the disease to others hence; controlling the disease turns out to be a problem (6,7).

Typhoid is generally treated by means of antibiotics. These agents destroy the pathogens of this sickness, and hence lessen the symptoms and the time these symptoms present. Apart from the antibiotics medication, the patient needs supportive treatment such as and intravenous fluids to combat dehydration and anti-pain and fever drugs (8,9). In very severe cases, the patient needs to be hospitalized so that their status can be assessed and appropriate treatment given. Ceftriaxone is a broad-spectrum antibiotic that treats a variety of bacterial illnesses, including typhoid. Trimethoprim-sulfamethoxazole, on the other hand, is a combination antibiotic used to treat salmonella, although bacterial resistance is becoming increasingly widespread (10,11).

Focusing on the prevention of typhoid is always better than the treatment of the disease. It is thus vital to seek measures that will help minimize such an outbreak, for instance, improving sanitary conditions, providing safe drinking water and promoting hygiene and sanitation education (12,13).

However, a significant obstacle in the treatment of typhoid fever is the increase in bacterial types resistant to antibiotics. Probiotic bacteria and vaccinations are examples of new and effective therapies now being investigated in an effort to reduce the need for antibiotics and reduce the likelihood of antibiotic resistance. Current research further emphasizes the need for rapid diagnosis and treatment of typhoid patients, as this improves the prospects for recovery and reduces the risk of sequelae (14,15,16).

The goal of this study was to examine the incidence of typhoid in Nineveh province during the last five years and

establish effective methods to minimize its spread. The illness prevalence was compared in Mosul and its districts.

## Material and Methods

This work was conducted in compliance with the ethical approval granted by the College of Medicine, University of Mosul, under reference number [UOM/COM/MREC/2024(8)/1a] on 6<sup>th</sup> August 2024. Typhoid patients were identified based on an initial clinical diagnosis made by medical professionals based on a set of disease-specific clinical signs. Patient information was collected via the consent form contained in the supplement file. After verifying the clinical indications, a laboratory examination using the Widal test was performed to determine the presence of antibodies against the typhoid bacterium in the patient's blood. The study sample includes all cases of typhoid confirmed clinically and in the laboratory in Nineveh province between 2018 and 2022. Gender, age, geographic area, clinical signs and symptoms, and laboratory test results were all acquired from patient records in hospitals and health clinics. Patients were categorized into five age groups: under 1 year, 1-4 years, 5-14 years, 15-45 years, and over 45 years.

### Statistical Analysis

SPSS version 25 was used to conduct statistical analysis. A series of statistical tests was performed to identify parameters related with disease transmission and to assess changes in infection rates over time. The Anova test was performed to determine correlation coefficients between the variables.

## Results

In this study, high peak cases occurred in 2021 and 2022, with no discernible difference in the number of infections between males and females. Infections are most typically observed among those aged 15-45 and the ages over 45, which are consistent with widely recognized recorded statistics.

Infections are less prevalent among children under the age of four. Table 1 and Figure 1 show a significant correlation between infection rates, age groups (3<sup>rd</sup> and 4<sup>th</sup>), and genders at ( $p < 0.01$ ).

As demonstrated in the Table 2 and Figure 2, the largest occurrence rates were concentrated in Mosul city's sectors (left) and Nineveh Governorate districts (Shekhan, Hamdaniya, and Baaj).

## Discussion

Typhoid is an endemic illness in Iraq, especially Nineveh province, as evidenced by the numbers indicated and



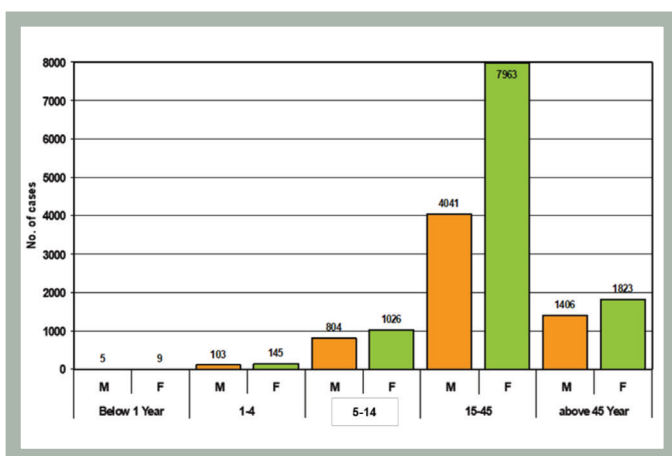
**Table 1. Typhoid fever cases by age group and gender 2018-2022**

Years	Below 1 year		1-4		5-14		15-45		Above 45 year		Total		Grand total
	M	F	M	F	M	F	M	F	M	F	M	F	
2018	0	0	15	31	188	158	953	1687	375	477	1531	2353	3884
2019	0	1	32	38	164	205	648	1240	276	210	1120	1694	2814
2020	0	2	13	12	104	142	608	1347	217	241	942	1744	2686
2021	0	0	19	42	189	225	837	1676	199	297	1244	2240	3484
2022	5	6	24	22	159	296	995	2013	339	598	1522	2935	4457
<b>Total</b>	5	9	103	145	804	1026	4041	7963	1406	1823	6359	10966	17325

M: Male, F: Female

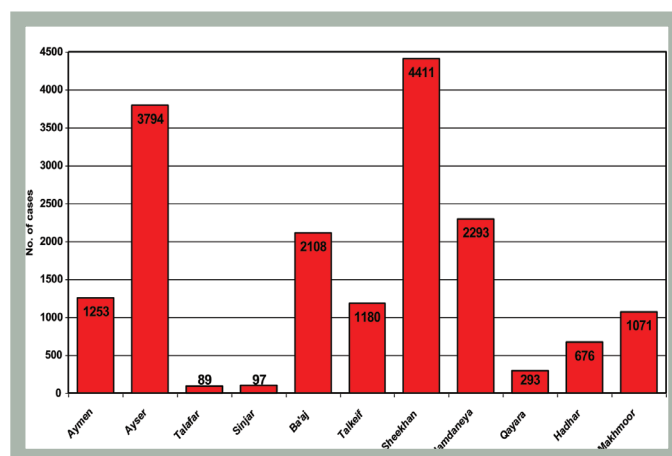
**Table 2. Typhoid fever cases by district 2018-2022**

Years	Aymen (Mosul right side)	Ayser (Mosul left side)	Talafar	Sinjar	Ba'aj	Talkeif	Sheekhan	Hamdaneya	Qayara	Hadhar	Makhmoor	Total
2018	304	894	1	10	804	181	945	331	17	98	127	3712
2019	244	898	2	9	293	120	717	400	13	115	147	2958
2020	105	537	16	7	200	178	1033	263	0	115	232	2686
2021	288	630	0	4	247	377	1103	474	0	84	295	3502
2022	312	835	70	67	564	324	613	825	263	264	270	4407
<b>Total</b>	1253	3794	89	97	2108	1180	4411	2293	293	676	1071	17265



**Figure 1. Typhoid fever cases by age group and gender 2018-2022**

M: Male, F: Female



**Figure 2. Typhoid fever cases by district 2018-2022**

documented, as well as statistics from prior years. The disease's frequency fluctuates with population size. The incidence was assessed from 2018-2022. It was observed that oscillations in incidence rates are obvious.

According to the results of the study, however, this disease still remains a health problem among the people in Nineveh Governorate. Attack rates remain consistently high. Although the infection rates tend to have multiple wastages over time, however the years 2021 and 2022 reported the highest

infection rates. The people that are majority in most risk groups are those within ages of 15 to 45 years, and that those above the age of 45 years were also at risk to the infection which is compatible with the previous report. Also the survey reported of Mosul and other areas of the governorate having unusually high number of infection cases, unlike other surveys. Such findings can be attributed to several factors which enhance the transmission of diseases such as poor sanitation facilities, pollution of water sources and poor practices. Most of the time, the outbreak is effectively managed by the local community.

Focusing on the primary prevention of typhoid under this scenario is important to achieve. Educating primary caregivers on appropriate measures to contain the spread of the disease such as practicing high standards of hygiene, drinking boiled water and washing hands after use, and immunization of children may also be effective. Similarly, local residents are able to track the progress of the disease and bring out potential disease cases (17,18,19).

For these reasons, the further spread of the disease should be contained in the most efficient way possible, which includes rebuilding medical facilities and basic utilities for the areas touched by the war, conducting thorough health education efforts, and encouraging hygienic practices including personal and food hygiene. In addition, children and other at-risk populations should be prioritized and provided with the minimum services and protection in this respect. Additionally, effective management of diseases requires integration of multi-sectors especially health, environment and agriculture (20).

Typhoid cases have a severe public health impact in numerous countries, notably Iran, Turkey, and Saudi Arabia, which border Iraq. It is expected that a large number of people are affected annually. There are many deaths documented in these nations, and despite breakthroughs in medicine and medications, illness and mortality rates remain particularly high in places with a lack of clean water and sanitation. Typhoid-related complications, such as internal bleeding and intestinal perforation, increase death rates, particularly among youngsters and the elderly.

The current study results compel all the actors concerned to work together in containing the typhus threat in Nineveh so as to protect the health status of the people. With the appropriate actions and enhanced participation of the people it is possible to achieve measurable level of elimination of such chronic infectious disease.

## Conclusion

A number of interrelated variables such as socio-economic status and inappropriate health practices influence the spread of typhoid in Nineveh, which poses a serious health risk. Older age groups are most susceptible to infection. Enhancing the healthcare system and implementing large-scale education campaigns are just two of the urgent steps that must be taken to stop the spread of the disease.

### Ethics

**Ethics Committee Approval:** This work was conducted in compliance with the ethical approval granted by the College of Medicine, University of Mosul, under reference number [UOM/COM/MREC/2024(8)/1a] on 6<sup>th</sup> August 2024.

**Informed Consent:** Obtained.

### Footnotes

**Financial Disclosure:** The author declared that this study received no financial support.

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## 2024 Referee Index

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