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

Zahraa Khalid Al-Kheroo[1], Khalid N. Al-Kheroo[2], Mahmood Abd Al Jabbar Al-Tobje[1]

[1]University of Mosul College of Science, Department of Biology, Mosul, Iraq
[2]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

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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±42.79 and 1493.89±874.57 ng/mL, respectively). When the level of IL-17 reached (54.48±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

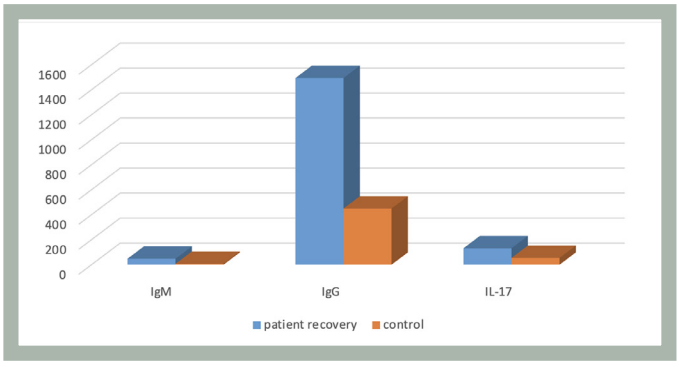

Figure 1. Compare the patient's health and recovery using a few immunological parameters

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		01.284	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

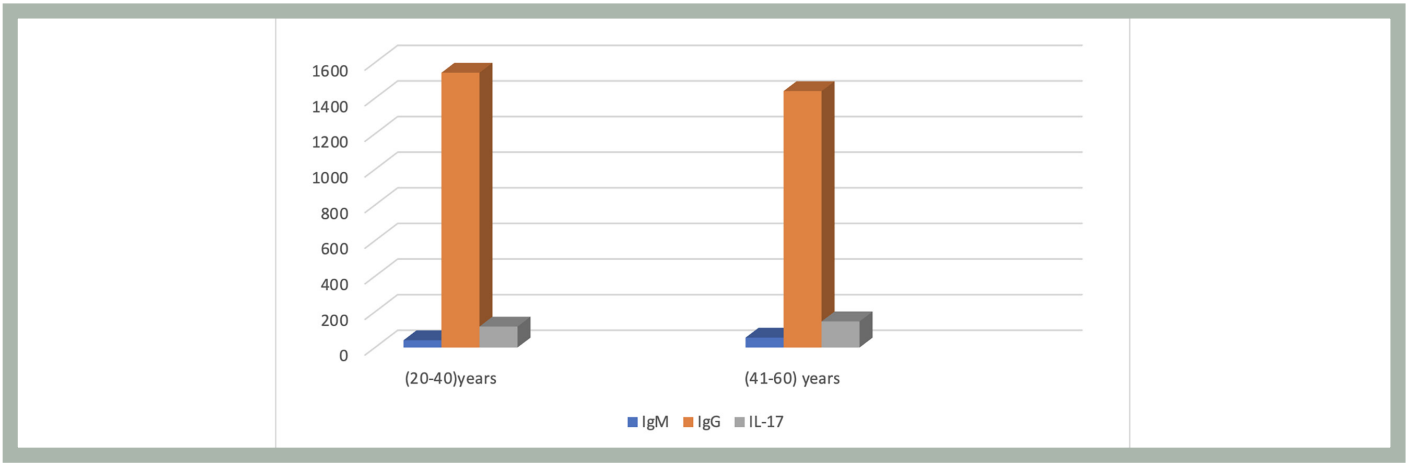

Figure 2. Show IgG, IgM, and IL-17 averages by age group
IgG: Immunoglobulin G, IgM: Immunoglobulin M, IL-17: Interleukin-17

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)-γ, IL-5, IL-6, IL-1β, IL-17, IL-10, IFN-α, and TNF-α 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) RORgt may be overexpressed in minimally recovered volunteers, as shown by Treg's enhanced production of IL-17. RORgt+ 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.

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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.

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