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Comparison of Cytokine Patterns (IL-6, IL-8, and IL-10) in Influenza and Respiratory Syncytial Virus Infections: An Age-Based Comparative Study

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ABSTRACT

Background: *Respiratory viruses such as influenza and respiratory syncytial virus (RSV) remain a global challenge due to the respiratory infections they cause. While both viruses exhibit somewhat similar clinical symptoms, they may elicit different immune responses. Therefore, we compared the patterns of cytokines (IL-6, IL-8, and IL-10) in patients infected with influenza and respiratory syncytial virus (RSV) across different age groups.* ***Methods:*** *220 samples were collected from patients with respiratory symptoms, 110 of whom were infected with influenza and 75 with RSV. The samples were collected from October 2024 to April 2025 at Al-Zahraa Hospital and Al-Hakim Teaching Hospital, Samples were classified into four groups according to age (≤ 5 years), (6 - 18 years), (19 - 50 years), (≥ 50 years), depending on the maturity of the immune system, the severity of the inflammatory response, and the clinical nfection patterns of each virus. Cytokine levels were measured by ELISA, and statistical analyses were performed using SPSS version 26. Statistical significance was set at a p-value of <0.05.* ***Results:*** *The study results showed a significant difference in elevated levels of IL-6 and IL-8 in patients infected with respiratory syncytial virus (RSV), especially in children under 5 years of age (P < 0.0001), while a significant increase in IL-10 levels was observed in patients infected with influenza virus, particularly in those over 50 years of age (P < 0.01).* ***Conclusion:*** *The differential cytokine patterns imply different immune processes associated with these respiratory viral infections. Influenza appears to induce a greater number of anti-inflammatory processes (IL-10), while RSV induces a greater number of anti-inflammatory processes (IL-8/IL-6). These findings are important for targeted therapeutic approaches and improved clinical management of respiratory viral infections.*

Keywords: Influenza virus, Respiratory syncytial virus (RSV), Cytokines, IL6, IL8, and IL10.

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INTRODUCTION

Viral respiratory infections are among the most important global health problems.[1] Viruses account for the majority of upper respiratory tract infections, which are considered to be trivial infections that may resolve on their own. Lower respiratory tract infections are slightly more serious and occur in children and adults.[2] All these viruses are transmitted by infected air droplets, such as sneezing, coughing, and others, such as saliva or infected objects.[3]

The most significant viruses that cause respiratory infections are the influenza virus and the respiratory syncytial virus.[4] The influenza virus is among the most common respiratory viruses due to its rapid spread and the severity of the symptoms it causes, which can lead to serious conditions of the entire respiratory

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system. Some of these symptoms include high fever, cough, headache, and general body weakness.[5]

Respiratory syncytial virus (RSV) is a common respiratory virus that infects children under the age of two years. The disease can lead to serious, life-threatening respiratory diseases such as pneumonia and bronchiolitis.[6] The virus is transmitted through airborne droplets when coughing or sneezing.[7] The virus causes symptoms such as breathing problems and a runny nose. Both influenza and RSV can cause seasonal epidemics that range from mild to severe and can require hospitalization.[8]

Cytokine research is of utmost importance in understanding the immune mechanism that characterizes respiratory viral infections because these molecules are responsible for guiding and regulating the inflammatory immune response.[9] Cytoxins play an important part in , stimulating and inhibiting the immune response, as IL-6 enhances the inflammatory response via the NF-kB pathway, while IL-10 suppresses the inflammatory response.[10] The understanding and detailed research of these immune mechanisms demonstrate the difference in the severity of diseases and symptoms among age groups when infected with viruses.[11]

Recent scientific research also, indicates that cytokine secretion differs significantly in influenza virus infection and respiratory syncytial virus (RSV) infection, making these cytokines useful as biomarkers for differentiation, diagnosis, and prediction of disease severity. (Tan *et al*.,2025)[12] demonstrated that levels of IL-6 and IL-8 are higher in patients infected with respiratory syncytial virus (RSV) compared to influenza-infected patients, while elevated interleukin-10 levels are strongly associated with severe inflammatory disease in elderly individuals with influenza. Despite the widespread prevalence of these viruses, studies comparing cytokine levels are still limited.[13] Based on the gap in research on this comparison, this study aims to compare the levels of some cytokines (IL-6, IL-8, IL-10) in patients infected with RSV and patients infected with influenza in Iraq.[14]

MATERIALS AND METHODS

This study included 220 samples collected from Al-Zahraa Teaching Hospital and Al-Hakim General Hospital in Al-Araf, Najaf, during the period from October 2024 to April 2025. Samples were randomly collected from patients suffering from respiratory symptoms, including cough, shortness of breath, and fever, Samples were classified into four groups according to age (≤ 5 years), (6 - 18 years), (19 - 50 years), (≥ 50 years), depending on the maturity of the immune system, the severity of the inflammatory response, and the clinical infection patterns of each virus.

The samples were divided into two groups according to laboratory diagnostic results:

1. A group infected with influenza virus, (n110) samples.

2. A group infected with respiratory syncytial virus (RSV), (n75) samples.

3. control group (n 30)

Based on previous studies and to provide sufficient statistical power (80%, with a 5% margin of error), the sample size was chosen accordingly. Patients who had received a seasonal influenza or respiratory syncytial virus (RSV) vaccine within three months of the study were excluded. Those with a bacterial infection or chronic immune disease were excluded.

Sample Collection

5 ml of blood was drawn from the patients, and 3 ml was collected in anticoagulant (EDTA) tubes and 2 ml in gel tubes. separated serum by centrifugation at 3,000 rpm for 15 minutes at 4°C. Blood samples were stored at -80°C, and serum samples at -20°C.

Laboratory Diagnosis

Influenza virus and RSV were diagnosed using the Enzyme-Linked Immunosorbent Assay (ELISA) Due to its high sensitivity in detecting infection during the acute phase as stated in the WHO-approved protocols of 2023, improperly stored samples were excluded to ensure the accuracy of the results.

Cytokine Levels Measurement

The Enzyme-Linked Immunosorbent Assay (ELISA) technique:

IL6 (R&D Systems) Human IL-6 Quantikine ELISA Kit, IL8 (Abcam) Human CXCL8/IL-8 ELISA Kit, IL10 (Thermo Fisher Scientific) Human IL-10 ELISA Kit

Data Analysis

Statistical analysis software was used: SPSS v.26 with a statistical significance of *p*-value < 0.05.

RESULTS AND DISCUSSION

A total of 220 samples were randomly collected from people with respiratory symptoms. (110) of these cases were found to be infected with influenza virus and (75) with respiratory syncytial virus (RSV). The samples were divided according to age: ≤ 5 years (12 samples infected with the influenza virus) and (33 with RSV). The other age group, between (5 _18 years), was found (28 to be infected with the influenza virus) and (18 with RSV). The most active age group, between (19 _ 50) years, was found to have (32 people infected with the influenza virus), while (14 people were infected with RSV). The last age group, (≥50 years), the group most susceptible to influenza complications, was found to have (30 people infected), and (10 people were found to be infected with RSV).

The study results showed clear differences in the immune response between influenza patients and respiratory syncytial virus (RSV) patients, particularly in the levels of cytokines associated with the inflammatory response and immune regulation. Our study also demonstrated differences in infection with these viruses across age groups: RSV was more prevalent among children under five years of age (44% of cases), while influenza was more prevalent among older age groups (25-29%) in adults and the elderly. This study is consistent with (Zheng, Z *et al.*, 2022)[15], which indicated that more than 66,700 cases hospital admissions were recorded for children infected with respiratory syncytial virus (RSV).

Table 1: Showing the age groups and infection rates.

Age groups	Influenza n (%)	RSV n (%)	Scientific reason
≤ 5 years	12 (10.9%)	33 (44%)	RSV is most common among children and infants.
(6 _18 years)	28 (25%)	18 (24%)	RSV is most common among children and infants.
(19 _ 50 years)	32 (29%)	14 (18.6%)	This age group is considered to be the active youth group, so influenza is the most common virus among them.
(≥50 years)	30 (27%)	10 (13%)	The elderly are the most vulnerable group to complications from influenza infection.
Total	110	75	

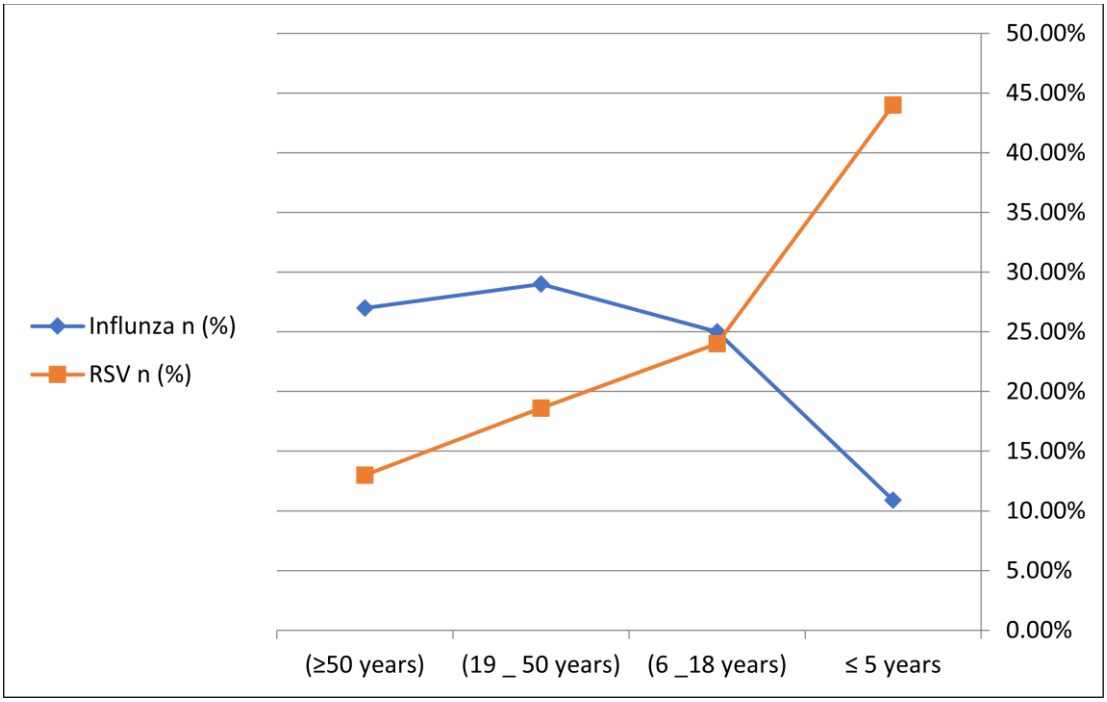


Figure 1: Showing different age groups infected with (influnza virus and RSV).

The study results also showed that in the age group (≥50 years), the influenza virus is more prevalent than the respiratory syncytial virus (RSV), at a rate of (27%). This study is largely consistent with the study (Javanian, M *et al*., 2021)[16], which indicated that the influenza virus is widespread among adults and the elderly, exposing them to serious complications.

The significantly higher incidence of influenza virus infection in older age groups may be attributed to travel, social interaction, and exposure to respiratory syncytial virus (RSV) infection. This is due to developed immune systems in adults than in children, consistent with (Principi, *et al.*, 2023)[17].

Comparison levels of interleukin-6 (IL6) between influenza virus and respiratory syncytial virus (RSV) :

This study focused on measuring a set of immune parameters and comparing their levels between influenza virus and respiratory syncytial virus infections according to the age groups proposed in this study. Interleukin 6 (IL6) levels and standard deviations were measured, which are one of the most important parameters for comparing infections between the two viruses.

Table 2: Comparison of IL6 levels between influenza and respiratory syncytial virus infection.

Age groups	Level IL6 pg/ml influenza patient (mean ±SD)	*n*	Level IL6 pg/ml RSV patient (mean ±SD)	*n*	Level IL6 pg/ml RSV control (mean ±SD)	*n*	*P value anova*
≤ 5 years	(76±20)	12	(120±35)	33	(13±4)	7	< 0.0001
(6 _18 years)	(55± 17)	28	(85±26)	18	(15±5)	7	< 0.0001
(19 _ 50 years)	(48±13)	32	(65±20)	14	(18±6)	8	< 0.0001
(≥50 years)	(66± 25)	30	(96± 28)	10	(20±8)	8	< 0.0001
Total		**110**		**75**		30	

The results showed that interleukin-6 (IL6) levels were higher in patients infected with respiratory syncytial virus (RSV) than in those infected with influenza virus. The highest interleukin-6 levels were found in those under five years old with RSV (120 ± 35 pg/ml), followed by those over 50 with RSV (96 ± 28 pg/ml). Interleukin-6 levels were highest in those under five years old, followed by those over 50 years old with influenza virus (76 ± 20 pg/ml) and (66 ± 25 pg/ml), respectively, our study results also showed significantly lower levels compared to the control group across all age groups, (13±4 pg/ml), (15±5 pg/ml), (18±6 pg/ml) and (20±8 pg/ml) respectively.

This study is consistent with a study by (Liu, S., *et al.*,2023)[18], which indicated that interleukin-6 levels are higher in children under five years of age due to intense activation of the NF-kB and JAK/STAT pathways, which increases IL-6 production in those infected with respiratory syncytial virus (RSV), unlike influenza virus, which has a mechanism that inhibits the activity of the NF-kB pathway, reducing IL-6 production. This may be due to the immature immune systems of children under five years of age, which causes immunological shock upon infection with the virus, leading to elevated levels of this interleukin, a condition known as immunodeficiency agree with (Anderson, *et al*., 2021).[19] Statistically, the results indicate a highly significant difference between age groups (p <0.0001), respectively, at the probability level (p≥ 0.05). This supports the robustness and strength of our findings. This highlights the urgent need to study IL6 markers in children infected with respiratory syncytial virus (RSV) as a primary indicator of infection severity, which will enable the development of new therapeutic approaches that modulate the immune response.

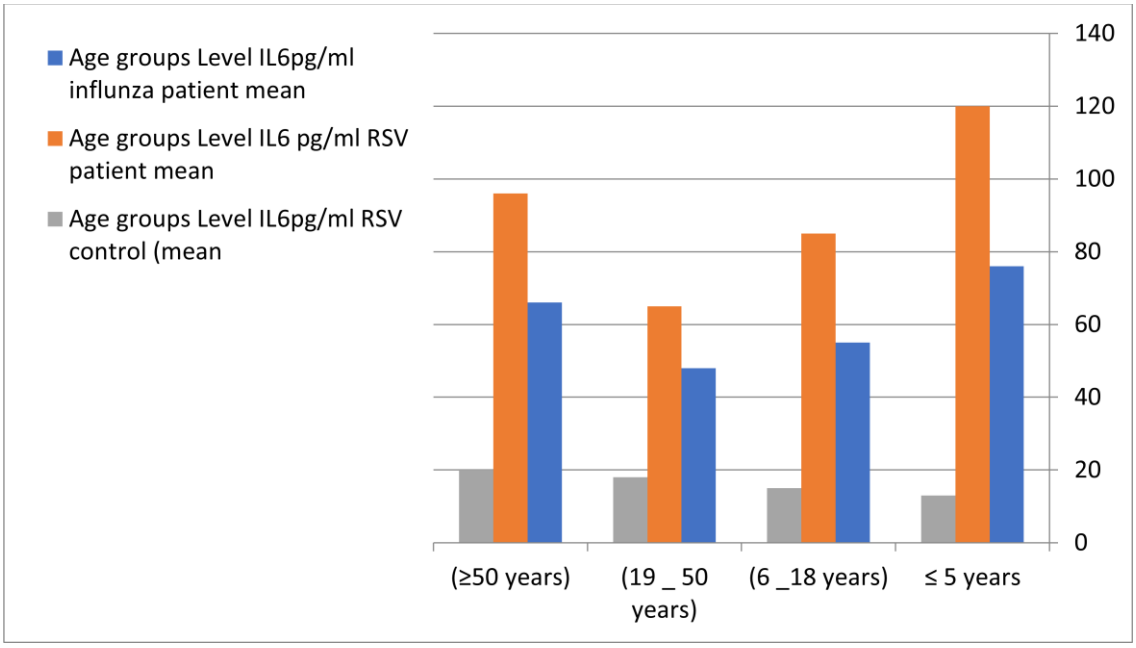


Figure 2: Shows a comparison of IL6 levels between influenza patients and respiratory syncytial virus (RSV).

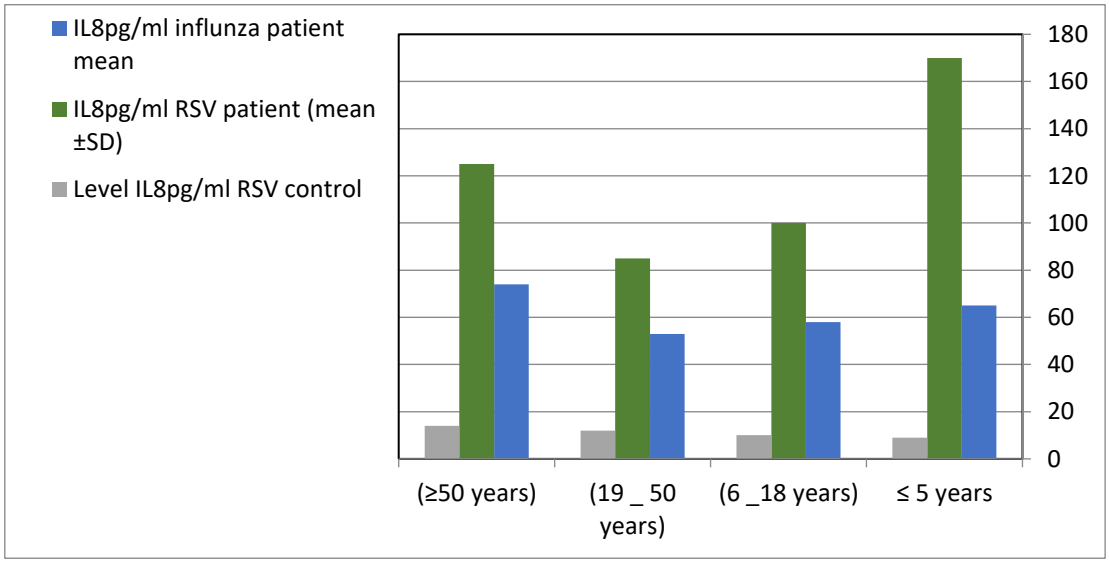
2.Comparison of interleukin-8 (IL8) levels between influenza and respiratory syncytial virus(RSV) :

The study showed significant differences in the levels of interleukin-8 in influenza and respiratory syncytial virus infections according to age groups.

The results showed higher levels of IL-8 in patients infected with respiratory syncytial virus (RSV) across all age groups compared to influenza virus. The highest levels were found in children under 5 years of age, followed by patients over 50 years of age (170 ± 44 pg/ml) and (125 ± 30 pg/ml), respectively and It was also noted that interleukin 8 levels were significantly lower in the control group (9±5 pg/ml) (10±6 pg/ml) (12±8 pg/ml) (14±10 pg/ml) respectively. agree with (Agac *et al.*, 2023)[20] RSV was found to cause damage to respiratory cells, leading to the release of large amounts of interleukin-8 to combat the virus. This is similar to the situation with influenza virus, but causes less damage to respiratory tissue. Therefore, IL-8 levels are lower during influenza virus infection, as shown in our current study. In the remaining age groups, especially among young adults and adolescents, IL-8 levels are lower, indicating a reduced overreaction, but they are still higher than influenza levels. (Bajaj F *et al.*, 2021)[21] indicated that some respiratory viruses, such as COVID-19 and similar viruses, moderately induce interleukin-8 via the PA-X protein, which regulates inflammation. This is similar to the response to influenza. There were also significant differences when comparing age groups ($p < 0.001 < 0.001 < 0.004 < 0.002$). The reason for these higher interleukin levels may be the abundance of receptors for this virus in children under five years of age, leading to an exaggerated response compared to other age groups. This proves that age is an important factor in the severity of the immune response.

Table 3: Shows a comparison of IL8 levels between influenza patients and respiratory syncytial virus.

Age groups	Level IL8 pg/ml influenza patient (mean ±SD)	*n*	Level IL8 pg/ml RSV patient (mean ±SD)	*n*	Level IL8 pg/ml RSV control (mean ±SD)	*n*	*P value*
≤ 5 years	(65±15)	12	(170±44)	33	(9±5)	7	< 0.001
(6 _18 years)	(58± 19)	28	(100±33)	18	(10±6)	7	<0.001
(19_ 50 years)	(53±17)	32	(85±27)	14	(12±8)	8	<0.004
(≥50 years)	(74± 20)	30	(125± 30)	10	(14±10)	8	<0.002
Total		110		75		30	



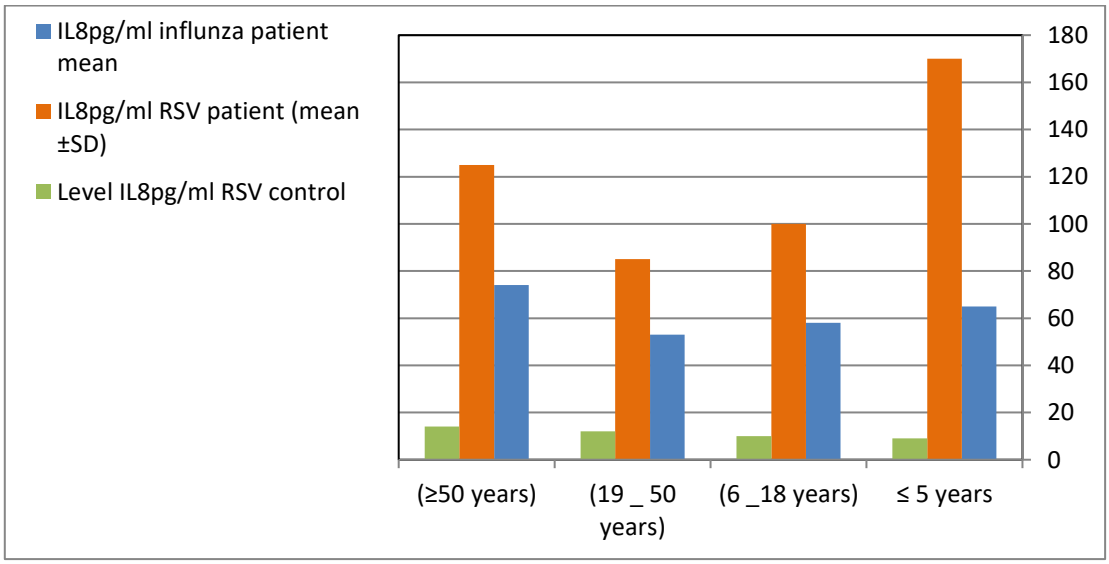


Figure 3: Shows a comparison of IL8 levels between influenza patients and respiratory syncytial virus (RSV).

3. Comparison of interleukin-10 (IL-10) levels between influenza and respiratory syncytial virus (RSV):

When measuring interleukin 10 (IL-10) levels, our study results revealed that IL-10 levels were elevated in patients with influenza virus and respiratory syncytial virus, as Table 4

The results of our study showed a statistically significant increase ($p < 0.05$) in interleukin-10 (IL-10) levels in patients infected with influenza virus compared to patients infected with respiratory syncytial virus (RSV) across all age groups, with levels gradually increasing with age. The highest levels of IL-10 were found in the age group(≥ 50 years) (53 ± 16 pg/ml).

followed by the age group (19–50 years) (45 ± 12 pg/ml). This may indicate that the immune system lost its ability to balance the inflammatory and anti-inflammatory response, according to (Franceschi *et al*., 2017)[22].

While the lower levels in patients with respiratory syncytial virus (RSV), showed the highest level in the age group (≥ 50 years)at (20 ± 8 pg/ml) , The control group also showed significantly lower levels (7±3 pg/ml), (8±4 pg/ml), (10±6 pg/ml) and (11±8 pg/ml) respectively.

The increased levels of interleukin 10 (IL10) in influenza patients, especially the elderly, indicate that this interleukin regulates the immune system against excessive stimulation of inflammatory cytokines such as (IL-1β) and (TNF-α), which can lead to a cytokine storm and develop into serious complications , This is consistent with studies by (Gu *et al.*,2021)[23] and (Rosero *et al*.,2025)[24], who indicated that immunity in the elderly is weaker (immunosenescence) making their bodies more dependent on interleukin 10 (IL10) to help suppress the inflammatory response. The low levels of interleukin-10 (IL10) in patients with respiratory syncytial virus (RSV) indicate that virus is capable of immune evasion as it stimulates the secretion of the cytokines interleukin-6 and interleukin-8 which reduces the need for interleukin-10 to regulate the inflammatory response. This is consistent with the study by (Zheng *et al*., 2023)[25].

According to study by (Oshansky *et al.*,2014)[26] children under the age of five showed lower levels of interleukin-10 (IL-10). This may indicate impaired immune regulation due to the immaturity of their immune system and their reliance on other immune pathways. Statistically, highly significant differences were found between age groups in interleukin-10 levels ($p < 0.006$, <0.001, <0.003, <0.01, respectively), indicating that the type of virus is an important factor in determining the type of immune response. Age is also a significant factor influencing the body's inflammatory and regulatory response, consistent with the findings of (Nikolich-Žugich, .2018)[27].

Table 4 shows a comparison of IL-10 levels between influenza patients and respiratory syncytial virus.

Age groups	Level IL10 pg/ml influenza patient (mean ±SD)	*n*	Level IL10 pg/ml RSV patient (mean ±SD)	*n*	Level IL10 pg/ml RSV control (mean ±SD)	*n*	*P value*
≤ 5 years	(30±7)	12	(12±5)	33	(7±3)	7	< 0.006
(6 _18 years)	(38± 9)	28	(15±4)	18	(8±4)	7	<0.001
(19_50years)	(45±12)	32	(17±6)	14	(10±6)	8	<0.003
(≥50 years)	(53± 16)	30	(20± 8)	10	(11±8)	8	<0.01
Total		110		75		30	

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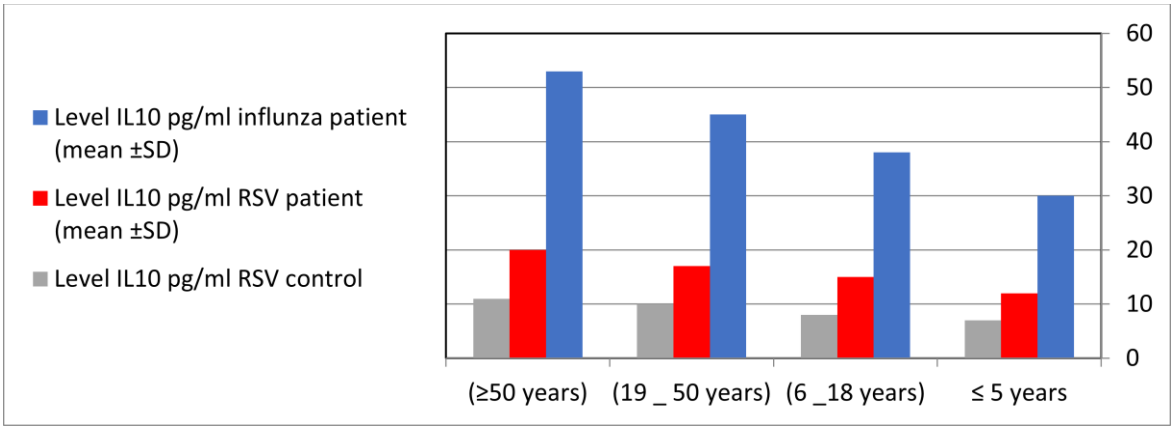

Figure 4: shows a comparison of IL10 levels between influenza patients and respiratory syncytial virus (RSV).

Elevated levels of cytokines, especially IL-6, indicate damage to respiratory epithelial cells, which stimulates these cytokines to attract neutrophils, Elevated levels of cytokines, especially IL6 and IL8, indicate damage to respiratory epithelial cells, which stimulates these cytokines to attract neutrophils. Elevated IL-10 in influenza is attributed to the body's attempt to curb excessive inflammation, especially in the elderly with weakened immune systems.[28] [29]

CONCLUSION

Our comparative study demonstrated significant differences in immune responses to viral infections of influenza virus and respiratory syncytial virus (RSV). The results showed that high levels of IL8 and IL6 proteins in patients infected with RSV, particularly those under 5 years of age, are due to severe damage to the respiratory epithelium and neutrophil activation. Conversely, high levels of interleukin 10 (IL10), particularly in patients over 50 years of age infected with influenza virus, are considered a compensatory anti-inflammatory response.

The results also indicated age-related differences. The study showed that the age group over 50 was affected by cytokine production, particularly IL10, while children under 5 years of age produced higher amounts of IL6 and IL8. The study demonstrated that the variation in cytokine production patterns serves as a biomarker and has diagnostic significance in distinguishing between viral pathogens. The study also recommends the development of direct immunomodulatory therapies, such as IL-10 modulation, in cases of influenza infection and in the life-threatening stage. The study also contributes to the development of strategies for producing new vaccines.

Limitations

This study included measuring the immune parameters IL6, IL8, and IL10, while other cytokines could have been measured to provide a more comprehensive study. Furthermore, samples were collected from a single region in Iraq, which limits the generality of the results.

The ELISA technique was used without confirming the diagnosis by RT-PCR. However, this limitation was compensated for by collecting samples at the peak time of infection (days 1-7 of infection), when antigen levels are highest.

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