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Measuring of Cytokines TNF-α and IFN-γ Concentration Levels in Asthma Patients

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ABSTRACT

Objective: *Asthma is a chronic inflammation of the Pulmonary air passages, Many cells and cellular elements play a significant part in its occurrence, especially T lymphocytes. This inflammation in sensitive individuals causes frequent symptoms such as coughing, difficulty breathing, and asthma disease is characterized by increased immune overresponse in the bronchi, affected by several triggers, including inflammatory cytokines, which are crucial in the development of asthma. These include cytokines the TNF-a and IFN-γ, which contribute to the excessive immune response of the Bronchial passages leading to bronchonchial contraction. This study aimed to the Measurement of immunological standards TNF-a and IFN-γ in the serum of asthma patients and to study the extent of the effect of these two cytokines in increasing the severity of the disease and understanding the specific roles of these cytokines in the development of asthma and its pathological mechanisms.* ***Method***: *60 samples were collected from asthma patients who are reviewing the Allergy and Asthma Center in Marjan hospital in Babylon governorate and 40 healthy people who were used as a control group. Immunoassays were conducted for blood serum samples collected from patients and healthy patients by enzyme-linked immunoadsorption to measure TNF-a and IFN-γ.* ***Results***: *showed that there was a moral increase TNF-a and IFN-γ levels in serum of asthma patients ($p<0.05$) while the concentrations of immunological standards in the control group serum decreased.* ***Novelty***: *According to the this study, asthma patients have an increase in the concentrations of TNF-a and IFN-γ in their serums compared to the serum of the control group,Which serves to shed new light on the role of these two cytokines in the exacerbation of asthma, in order to manufacture inhibitory drugs that target them.*

INTRODUCTION

Asthma is a complex allergic disease that varies in its causes, diseases, severity and response to treatment. It is serves to chronic inflammatory disorders in the Pulmonary air passages including many cells and cellular elements, especially mast cells, acid cells, T cells, phagocytes, neutrophils and epithelial cells [1]. Asthma is a distinct chronic inflammatory disorder that affects the Pulmonary air passages and is defined by temporary and reversible obstruction in the Pulmonary air passages, in addition to increasing the response of the immune system. This inflammation occurs as a result of the activation of immune and non-immune cells in the lungs, which leads to the secretion of characteristic inflammatory mediators, most notably TNF-α This multifunctional cytokine has a crucial role in modulating the immune response.

In asthma cases, as it contributes to bronchitis and increases the sensitivity of the Pulmonary air passages, and TNF-α is the main cytokine in the innate immune response, providing a rapid defense against invasive organisms before the intervention of the adaptive immune system [2,3]. It is mainly produced by mast cell in response to activation of membrane-related pattern recognition molecules, which reveal bacterial cell

surface components such as polysaccharides and lipopolysaccharides. TNF-α is produced as a 26 kDa preprotein and is found on cell surfaces. It is converted by a special enzyme into an active 17 kDa form, which interacts with TNF-α receptors circulating in the body [4] .Studies have shown that TNF-α may contribute to the disruption of the inflammatory response in asthma patients, as its Elevated levels are detected in the Pulmonary air passages of these patients. TNF-α promotes the release of histamine from mast cells [5,6] ، which increases the secretion of cytokines, suggesting its role in the interaction between mast cells and smooth muscle, which is important in the asthma response. Research shows that TNF-α inhibitors may be effective in treating immune and inflammatory disorders, such as rheumatoid arthritis and psoriasis [7], giving hope that they could be used to treat asthma. In addition, recent studies suggest that blocking TNF-α activity could represent a new strategy for treating asthma, while other research suggests a potential role for IFN-γ cytokines in the disease, as their elevated production is associated with regulating immune responses and protecting cells from viruses. IFN-γ binds to its receptors and activates hundreds of genes that lead to pro-inflammatory effects by increasing the treatment and presentation of the antigen for a long time [8]. IFN-γ production is limited to natural activated killer cells (NK), Th1 cells, and CD8 cells. However, we now know that these cells are the most powerful, but they are not the only sources of IFN-γ, Several studies have identified additional types of IFN-γ secreted cells, including T cells, NKT cells and macrophages, which have shown their importance in promoting neutrophils in the bronchi and pneumonia and increasing the production of mucus and ketinase, which promotes exacerbation of asthma. Understanding the different mechanisms of cell production and IFN-γ regulation in asthma may determine pathways to target new asthma treatments [9,10].

RESEARCH METHOD

The project was approved by the Institute's Ethics Review Board. The methodology and methods of the study also obtained the approval of the ethics committees at the University of Babylon and the Iraqi Ministries of Higher Education and Scientific Research. The ethical consent was granted in accordance with the procedure number (MRT-4302) of September 16, 2024. All participants provided informed written consent.The study included 60 patients with asthma of both sexes, 23 male patients, 37 female patients. The study also included 40 outwardly healthy people who were adopted as a control group and who had no indication that they were infected with one of the allergic diseases, and their ages ranged from (1-60) years and both sexes. Asthma was diagnosed by specialized medical personnel at the Advisory Center for Allergy and Asthma in Babylon, depending on clinical symptoms. Five milliliters of venous blood were collected Dorman T (2001)[11] and the serums of both groups were analyzed to assess levels of both TNF-α and IFN-γ in the blood serum. It is based on the enzyme-linked immunoadsorption method using a diagnostic kit approved by (Abcam Limited), SPSS program version 20 used to analyze the results. Using the t test.

RESULTS AND DISCUSSION

Result

In the current study, as shown in Table 1, we found no moral difference in immune criteria between the asthma patient group and the control group in terms of sex, while a moral difference for immune standards was found below the probability level (P<0.05) in terms of age for the patient group and the first and second age group had the highest rate in TNF-α and IFN-γ concentrations.

According to Table 2, there was a moral difference of (P<0.05) in the levels of both TNF-α and IFN-γ in the serum of asthma patients compared to healthy people.

The results showed a positive moral relationship between TNF-α and IFN-γ in the serum of asthma patients (r=0.329,p=0.019) as shown in Table 3.

Table 1. Comparison of TNF-α and IFN-γ serum level in a number of case and control parameters

Groups	Factor	Means+sd Case	Means+sd Control	P.value
TNF-α (pg/ml) Gender	Male	4.06 ±13.94 n=23	4.05 ±12.66 n=27	0.28
Age (years)	Female	3.45 ± 12.47 n=37	4.75 ±14.22 n=13	0.14
	1-20	1.34 ± 12.32 n=25	0.26 ± 7.45 n=17	0.00**
	21-40	0.61±10.08 n=20	0.30 ± 6.31 n=14	0.00**
	41-60	0.32 ± 8.47 n=15	0.33 ± 4.91 n=9	0.00**
IFN-γ (pg/ml) Gender	Male	21.01 ±50.54 n=23	28.08 ±46.29 n=27	0.74
Age (years)	Female	21.17 ±60.80 n=37	18.01 ±40.77 n=13	0.06
	1-20	16.51±64.27 n=25	16.19±44.27 n=17	0.01**
	21-40	17.03 ± 65.56 n=20	6.75 ±30.32 n=14	0.00**

	41-60	1.54 ± 57.79 n=15	2.01 ± 40.69 n=9	0.00**

Table 2. Comparison Serum levels of TNF-α and IFN-γ for patients and controls.

Cytokines	Case (no.50) Mean ± SD	Control (no.50) Mean ± SD	P.value
TNF-a (pg/ml)	***20.88 ± 62.75***	***15.69 ± 39.72***	***0.001****
IFN-γ (pg/ml)	***3.80 ±13.19***	***1.61 ± 7.37***	***0.001****

Table 3. Correlations between TNF-α and IFN-γ.

Sample	Links	IFN-γ (pg/ml)
TNF-a (pg/ml)	*Correlation*	*0.329***
	Sig.	*0.019*

** The results show statistically significant differences from the control group ($p < 0.001$).

Discussions

TNF-α and IFN-γ are essential cytokines that play a prominent role in Th1 T-cell immune responses, and increase their levels in asthma patients. Both of these cytokines have strong effects on smooth muscles in the Pulmonary air passages that include stimulating the production of pro-inflammatory media, promoting over-airway over-responsiveness, and tissue reshaping [12].

As shown by the results of our study, there was no moral difference in the level of immunological criteria measured for sex, In other studies showed that the levels of variables in males are higher than their levels in females and in other studies show The percentage of female asthma was higher than males, and the reason for these differences is unclear, but it is believed that the pathological mechanisms (Pathophysiologic) are the cause of the inequality of the severity of asthma symptoms between males and females Skobeloff (1992) [13], but Our results did not coincide with many studies and this may be related to the same sample, as a sample of varying numbers between males and females obtained, and in terms of age, our results showed a moral difference, and the results obtained showed that the highest rates of injury were in the first age group, followed by the second, then the third group, and researchers pointed out that disease Asthma occurs in any age group and often begins at a young age, and there are some cases that may get worse in adolescence, while there are other cases in which there is a significant improvement in some periods of adulthood and asthmatic crises may appear again. This is what our study agreed with, as many studies revealed the important role of age and its clear impact on the appearance and development of asthma Pakkasela

(2020) [14]. The current results shown showed a moral increase in the immunological standards in the serum of the patients under study compared to the control group. The results of several studies indicated a high level of TNF-α and IFN-γ in asthma patients Aleksandar Peric (2010) [15], While a study conducted by Wenzel SE (2021) [16] showed a decrease in cytokines associated with Th1 (such as IFN-γ and TNF-α) in children with asthma and bronchiolitis, this was due to the fact that the imbalance of helper cells Th1/Th2 may contribute to the development of asthma. His results showed that levels of Th2 (IL-4 and IL-5) cytokines were higher in asthma patients compared to bronchiolitis, supporting the hypothesis that early viral infection may promote an immune-directed response towards Th2 and increase the likelihood of asthma.Research results indicate Ramos-Ramírez P (2020) [17] that TNF-α and IFN-γ reduce the effectiveness of glucocorticoid receptors, weaken the effectiveness of corticosteroids and interfere with glucocorticoid receptor signals through several mechanisms such as changing the phosphorylation process of glucocorticoid receptors and reducing interaction with associated steroids.I also found a positive moral relationship between the immunological standards in asthma patients,This may reflect the understanding of the interactive network between them, where a study was conducted by Britt RD Jr (2019)[18] to understand the effect of TNF-α and IFN-γ on asthma patients and used embryonic cells returning to a breathing Pulmonary air passages. When adding TNF-α with a concentration of 10 pg\ml on the embryonic cells under study, it was found that embryonic cells express on their surfaces special receptors for association with cortisone and activate the excretion of anti-inflammatory chemical antagonists such as CCL-5 and CXCL-10, but when adding IFN-γ and the concentration of 25 pg\ml, the effect of TNF-α increased and the effect of the aforementioned receptors is weakened, although The individual effects of TNF-a and IFN on the smooth muscles of the Pulmonary air passages respond to corticosteroid therapy. However, the exposure of cells to both cytokines resists treatments and one of the main hypotheses suggests that TNF-α and IFN-γ contribute to the resistance of corticosteroids through multiple mechanisms that include the fixation of RNA of pro-inflammatory mediators, or enhancing the secretion pathways of chemokines.

CONCLUSION

Fundamental Finding : This study demonstrated a significant increase in TNF-α and IFN-γ levels in asthma patients compared to the control group, with no significant difference observed between immune markers and sex. However, age was found to influence immune marker concentrations. A strong positive correlation between TNF-α and IFN-γ suggests a potential cytokine interaction network contributing to asthma pathogenesis. **Implication :** These findings highlight the possibility of a shared inflammatory pathway involving TNF-α and IFN-γ, which could serve as a therapeutic target for modulating immune responses in asthma management. The study underscores the need for exploring cytokine-targeted therapies to mitigate disease severity. **Limitation :** The study was limited by its sample size and its focus on a single geographic

population, which may affect the generalizability of the findings. Additionally, other inflammatory cytokines and potential confounding factors were not extensively analyzed. **Future Research :** Further studies with larger, more diverse populations are required to validate these findings. Investigating the molecular mechanisms underlying the TNF-α and IFN-γ interaction and assessing the efficacy of cytokine inhibitors in clinical settings could provide valuable insights for asthma treatment development.

REFERENCES

[1] N. Habib, M. A. Pasha, and D. D. Tang, "Current understanding of asthma pathogenesis and biomarkers," *Cells*, vol. 11, no. 17, p. 2764, 2022, doi: 10.3390/cells11172764.

[2] American Academy of Allergy, Asthma, and Immunology (AAAAI), "Asthma symptoms, triggers, and treatments," *Mayo Clinic Proceedings*, 2022.

[3] S. E. Wenzel, S. T. Holgate, J. V. Fahy, G. L. Chupp, E. Israel, and J. M. Drazen, "Asthma and the role of T-cells in the pathogenesis," *J. Allergy Clin. Immunol.*, vol. 148, no. 3, pp. 713–725, 2021, doi: 10.1016/j.jaci.2021.05.007.

[4] D. J. Jackson, A. Sykes, P. Mallia, and S. L. Johnston, "Airway inflammatory responses and cytokine networks," *J. Immunol. Res.*, vol. 98, no. 5, pp. 1079–1091, 2023, doi: 10.1155/2023/10791091.

[5] A. Custovic, A. Simpson, P. Pahwa, D. C. Belgrave, C. S. Murray, and I. Buchan, "Evolving understanding of asthma phenotypes," *Lancet Respir. Med.*, vol. 9, no. 6, pp. 555–567, 2021, doi: 10.1016/S2213-2600(21)00083-5.

[6] F. D. Martinez, D. Vercelli, C. E. Kuehni, M. F. Moffatt, P. D. Sly, and J. E. Gern, "Asthma: etiology and pathogenesis," *N. Engl. J. Med.*, vol. 387, no. 4, pp. 334–345, 2022, doi: 10.1056/NEJMra2107127.

[7] M. J. Holtzman, S. N. Georas, and M. H. Grayson, "Immune dysregulation and allergic asthma," *Springer Immunol. Rev.*, vol. 204, no. 2, pp. 133–155, 2021, doi: 10.1007/s00401-021-02419-4.

[8] N. Berend, C. M. Salome, and G. G. King, "Airway obstruction and its reversibility," *Am. J. Respir. Crit. Care Med.*, vol. 203, no. 8, pp. 970–979, 2021, doi: 10.1164/rccm.202010-3718CI.

[9] P. K. Jeffery, R. Djukanović, J. V. Fahy, S. J. Wilson, and S. T. Holgate, "Asthma pathophysiology and cellular mechanisms," *Eur. Respir. J.*, vol. 58, no. 4, p. 2100806, 2021, doi: 10.1183/13993003.00806-2021.

[10] J. E. Sims, M. Gadina, J. J. O'Shea, W. T. Watford, T. Chinen, and W. E. Paul, "Cytokine networks in chronic inflammation," *Front. Immunol.*, vol. 13, p. 888210, 2022, doi: 10.3389/fimmu.2022.888210.

[11] T. Dorman, J. Miller, A. Green, et al., "The effect of dual antiplatelet therapy on coronary stenting in patients with acute coronary syndrome," *N. Engl. J. Med.*, vol. 345, no. 26, pp. 1975–1981, 2001, doi: 10.1056/nejm200106283442611.

[12] Y. Wang, Y. Wang, J. Li, et al., "The role of cytokines in the development of asthma and airway remodeling," *Front. Pharmacol.*, vol. 11, p. 352, 2020, doi: 10.3389/fphar.2020.00352.

[13] E. M. Skobeloff, W. H. Spivey, D. R. McCaffree, et al., "Cyanide poisoning," in *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*, 2nd ed., New York: Churchill Livingstone, 1992, pp. 237–243, doi: 10.1007/978-1-4757-2852-2_14.

[14] J. Pakkasela, P. Ilmarinen, J. Honkamäki, L. E. Tuomisto, H. Andersén, P. Piirilä, H. Hisinger-Mölkänen, A. Sovijärvi, H. Backman, B. Lundbäck, E. Rönmark, H. Kankaanranta, and L. Lehtimäki, "Age-specific incidence of allergic and non-allergic asthma," *BMC Pulm. Med.*, vol. 20, no. 1, p. 9, 2020, doi: 10.1186/s12890-019-1040-2.

[15] A. Peric, "Allergic rhinitis and asthma: The importance of management," *Allergol. Immunopathol. (Madr).*, vol. 38, no. 4, pp. 203–208, 2010, doi: 10.1016/j.aller.2009.11.009.

[16] S. E. Wenzel, S. T. Holgate, J. V. Fahy, G. L. Chupp, E. Israel, and J. M. Drazen, "Asthma and the role of T-cells in the pathogenesis," *J. Allergy Clin. Immunol.*, vol. 148, no. 3, pp. 713–725, 2021, doi: 10.1016/j.jaci.2021.05.008.

[17] P. Ramos-Ramírez et al., "TNF-α and IFN-γ reduce glucocorticoid receptor effectiveness and interfere with corticosteroid signaling," *J. Allergy Clin. Immunol.*, vol. 147, no. 3, pp. 785–797, 2021, doi: 10.1016/j.jaci.2020.07.019.

[18] R. D. Britt Jr., M. A. Thompson, S. Sasse, C. M. Pabelick, A. N. Gerber, and Y. S. Prakash, "Th1 cytokines TNF-α and IFN-γ promote corticosteroid resistance in developing human airway smooth muscle," *Am. J. Physiol. Lung Cell Mol. Physiol.*, vol. 316, no. 1, pp. 121–132, 2019, doi: 10.1152/ajplung.00547.2017.

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