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Serum Level of IL-10 and IL-33 among Iraqi patients with sinusitis

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Abstract

Objective; objective of the present research is the evaluation of the roles of IL-10 and IL-33 indicators in pathophysiology of sinusitis patients

Methods; The conducted investigation occurred inside the capital Bagdad during time period from March to July 2022, thirty-six blood samples had from patients suffering from sinusitis that attending outpatients clinics after screening them by specialist physician. Additionally, thirty-two blood samples were collected from individuals without disease and considered them as control group. Study ages were ranged from 17 - 60 years All markers were quantified in all participants by utilizing enzyme linked immunosorbent assay (ELISA) with kits provided from Bio-Sources International (Camarillo,USA) Results of current investigation were calculated by SPSS v. 21.0 and Prism v.6 statistical software programs.

Results Findings of our investigation showed the age groups 30-50 years appeared highest percentages in patients (43.75%) and controls (50.00%). Our research showed the most patients were it found the most patients were females (62.5%) compared to males (37.50%)and controls (36.11% and 63.89%) Our results showed a highly significant increase ($P \leq 0.01$) in IL-10 level in patients compared to controls and a significant increase ($P \leq 0.05$) in IL-33 level was observed in patients compared to controls .It has been noted increased levels of IL-10 and IL-33 in patients ≤30 years and decrease levels in patients 30-50 and >50 years with significant differences ($p<0.05$).As for gender show increased levels of IL-10 and IL-33 in males higher than in females (127.61 ±4.01 , 16.22 ±1.68) and (124.29 ±1.56 , 15.97 ±2.08) respectively. don't showed significant differences ($p>0.05$) with gender patients.

Conclusion According to the study's findings, males had a higher incidence of sinusitis than females. Sinusitis patients had higher levels of IL-33 and IL-10 than controls, but as they grew older, their levels declined due to decreased protein synthesis, inflammation, organ dysfunction, and chronic illness. All of these traits play a part. IL-10 and IL-33 levels are decreasing with increasing age.

Keywords: sinusitis , IL-10, IL-33, , Iraqi

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Introduction

One of the most prevalent and significant serious issues is sinusitis, a condition that affects the mucous membrane in the sinuses and nasal cavity [1] Viruses, bacteria, and fungi are among the causes of sinusitis, and viruses with, as well as the presence of a number of bacteria that Parainfluenza virus, Rhino virus Importance and impact Staphylococcus aureus infects humans and causes inflammation, including Klebsiella pneumoniae and occurs in patients with a weak immune system [2], and among the types of fungi that cause sinusitis is Aspergillus Rhizopus [3]. It is divided into inflammation. Acute sinusitis causes inflammation of the respiratory system and includes a number of symptoms such as cough, nasal congestion, pressure and pain in the face, loss or difficulty of smell, and its duration is shorter from (12) weeks [4].

It i2s one of the common diseases in Iraq, according to global medical information, as it is the fifth disease among common diseases in Iraq, and studies have shown that the prevalence of sinusitis is 10.9% of the population of Europe [5], and in the United States it has shown that it is 11.9% of the population. The population has CRS with a peak prevalence (15.9%) in the 50-59 age group [6],

Chronic sinusitis is a recurrent infection that lasts for a period of time more than (12) weeks and is characterized by inflammation of the sinuses and nasal mucosa [7] The psychological condition of the patient is affected by chronic sinusitis, which is characterized by a set of symptoms and the presence or absence of nasal polyps (CRSwNP). These include headaches, ear pressure, olfactory impairment, and blockage of the nasal passages. The diagnosis is made by nasal endoscopy followed by a CT scan [8]. There are a group of factors that increase the chances of developing a sinus infection, such as smoking and some medical conditions, including the modern use of decongestant sprays. Long-term nasal blockage from polyps, a deviated nasal septum, asthma, some face-related disorders, allergies, and other conditions such lung cystic fibrosis, variations Anything that raises the danger of infection, such as flying, diving, or air pollution Sinusoids [9].

The immune system is a device specialized in defending the body against microorganisms such as bacteria, viruses, fungi, and parasites. Immunity includes the release of innate immunity (Complement Chemokines, Cytokines), which provides protection from infection with diseases or any foreign substance present in it. It produces antibodies as a response to infection [10]. Cytokines are proteins secreted by Immune cells These cells can perform multiple functions, such as transmitting intercellular signals through which the inflammatory response is regulated [11]. A member of the IL-1 cytokine family, IL-33 is a protein that triggers a Th2 inflammatory response [12]. IL-33 is crucial in controlling the immune system's reaction to inflammatory illnesses including asthma and rhinosinusitis [13]. IL-33 has been actively secreted in its entire length shape (amino acids, 1–27) through necrotic cell death, Cellular stimulation triggers ATP release or during tissue injury, it can act as an alarmin to warn the immune cells after damage to the endothelial and epithelial cells through infection, trauma or stress [14]. IL-33 releases happen mainly via the death of cells by contagious insults or response to allergens(alarmin) in many forms of the cells, such as epithelial or endothelial cells and macrophages [15]. The objective of current investigation is to know the roles of IL-10 and IL-33 in sinusitis patients.

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Materials and Techniques

Collected samples

The conducted investigation was occurred Baghdad during the period from March to July 2022, thirty-six blood samples had from patients suffering from sinusitis that attending outpatients clinics after screening them by specialist physician. Additionally, thirty-two blood samples were collected from individuals without disease and considered them as control group. Study ages were ranged from 17 - 60 years.

Techniques

The collected blood were separated using centrifuge (6000 rpm for five minutes) to get the serum. All markers were quantified in all participants by utilizeing enzyme linked immunosorbent assay (ELISA) with kits provided from Bio-Sources International (USA).

Statistical analysis

Statistical Analysis System –SAS (2018) software was used, the impact of the patient and control groups' differences in the research variables was determined. The t-test was employed to contrast means statistically. In the present investigation, the chi-square test was utilized to compare percentages (0.05 and 0.01 likelihood) statistically significant.

Results

1.Age and gender of study groups

Findings of our investigation showed the age groups 30-50 years appeared highest percentages in patients (43.75%) and controls (50.00%) with no significant variations ($p>0.05$) between study groups based on age groups.

According to gender, our research showed no significant variations ($p>0.05$) between gender and study groups. In contrast, the variations in percentages among patients and among controls, where it found the most patients were females (62.5%) compared to males (37.50%) and controls (36.11% and 63.89%) respectively (table 1)

Table 1: comparison between age and gender features with patients versus controls

			Groups			P value
			Control (n=36)	Patients (n=32)	Total	
Age groups	≤30	N	11	11	22	1.00 NS
		%	30.562	34.38	32.40%	
	30-50	N	18	14	32	0.502 NS
		%	50.00	43.75	47.10%	
	>50	N	7	7	14	1.00 NS
		%	19.44	21.85	20.59%	

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Gender	**Males**	**N**	23	20	43	0.502 NS
		%	63.89	37.50	63.24%	
	Females	**N**	13	12	25	0.869 NS
		%	36.11	62.50	36.77%	

NS: Non-Significant

2.Mean concentrations of cytokines within study groups

Our results showed a highly significant increase ($P \leq 0.01$) in IL-10 level in patients compared to controls (126.36 ±2.56 and 59.49 ±2.73) respectively, and a significant increase ($P \leq 0.05$) in IL-33 level was observed in patients compared to controls, (16.12 ±1.29 and 13.16 ±0.91) respectively (Table 2).

Table 2: comparative mean concentrations of IL-10 and IL-33 indicators between patients and controls

Group	Mean ± SE	
	IL-10 (pg/mL)	IL-33 (pg/mL)
Patients	126.36 ±2.56	16.12 ±1.29
Control	59.49 ±2.73	13.16 ±0.91
T-test	7.527 **	2.797 *
P-value	0.0001	0.0491

**** Highly Significant ($P \leq 0.01$)**

*** Significant ($P \leq 0.05$)**

3. Relation of immunological markers with age groups and gender of patients

Present outcomes mentioned increased levels of IL-10 and IL-33 in patients ≤30 years (131.92 2±6.74 a) and (18.01 ±2.40 a2) respectively , and decrease levels in patients 30-50 and >50 years (121.58 ±2.10 b , 16.44 ±2.05 ab) and (127.19 ±0.64 ab , 12.55 ±1.72 b) respectively with significant differences ($p<0.05$).As for gender show increased levels of IL-10 and IL-33 in males higher then in females (127.61 ±4.01 , 16.22 ±1.68) and (124.29 ±1.56 , 15.97 ±2.08) respectively. don't showed significant differences ($p>0.05$) with gender patients (Table 3).

Table 3: Relationship between Age groups and gender with the immunological parameters (IL-10 and IL-33) of patient's groups

Mean ± SE			
		IL-10 (pg/mL)	**IL-33 (pg/mL)**
Age groups	**≤30**	131.92 ±6.74 a	18.01 ±2.40 a
	30-50	121.58 ±2.10 b	16.44 ±2.05 ab
	>50	127.19 ±0.64 ab	12.55 ±1.72 b
	LSD	8.692 *	4.805 *
	P-value	20.0498	0.0351
($P \leq 0.05$)			

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Gender	**Males**	127.61 ±4.01	16.22 ±1.68
	Females	124.29 ±1.56	15.97 ±2.08
	T-test	7.116 NS	2.963 NS
	P-value	0.692	0.507
Non-Significant			

Discussion

A single the greatest frequent health issues that prompt medical attention worldwide is sinusitis, which also ranks among the main reasons for prescriptions for antibiotics. Individuals with sinusitis experienced up to 73 million days with minimal activity in a year, with a total of about $2.4 billion in immediate healthcare costs (not counting surgery or radiographic imaging). Furthermore, according to Shaikh, up to 14.7% of participants in a National Health Interview Survey reported having sinusitis in the twelve months prior [17]

According to the study's findings, sinusitis was more common in men than in women. These findings were consistent with those of Zielińska-Bliźniewska et al and Ravantara et al It has been hypothesized that variations in anatomic size, tobacco sensitivity, and hormonal variables raise a woman's overall risk of developing rhinosinusitis [18,19]. Because their sinus ostia are smaller, women may be more prone to blockage and consequent infection [20].

Similar findings were found in Zielińska-Bliźniewska et al study, which indicated a rise in sinusitis cases beyond the age of thirty [18]. Our findings were consistent with the high frequency of sinusitis reported by Alfallaj) in males aged 30 years and above [21]. Human bodies alter as we age. One such alteration is the nose, which becomes longer and starts to droop somewhat due to weakening surrounding cartilage. These modifications may result in a pathway that is smaller, which may lead to blockage and decreased airflow. According to earlier findings through the collected research, both the maxillary and ethmoidal sinus expand and develop between the ages of 0 and 20 years, when they reach their maximal developmental peak. There may be a noticeable drop in volume after 20 to 50 years. The volume decline is more noticeable between the ages of 50 and 65, and it accelerates even more after that [22]

The differences among studies based on age and gender are related to sample size (Table 1). Jiang et al showed increased levels of IL-33 and IL-10 in sinusitis patients than controls, [23] and these findings were compatible to results of present study.

Persons with chronic rhinosinusitis (CRS) often have persistent nasal mucosal inflammatory processes, with the potential development of nasal polyps (NP). Furthermore, inflammation caused by eosinophils is a characteristic shared by the majority of CRS with nasal polyps (CRSwNP) groups, and it is solely linked to the higher levels of IL-33 [23]. An IL-1 family cytokine is IL-33. It is a recently identified cytokine that is thought to be significant during tissue destruction linked to necrosis as well as when inflammatory is activated. Tissue-derived nuclear cytokines IL-33 is frequently produced in the epithelial cells throughout inflammatory processes and homeostasis. It is increasingly thought to be important for the etiology of CRSwNP as well as the progression of fibrosis

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or ailments, inflammatory conditions, and allergic conditions in generalLike the airways epithelium's initial line of defence towards pathogens and stimulants, IL-33 is generated. This can cause strong allergic inflammatory conditions and act as "bridges" between both adaptive and innate airways mucosa immunity. By applying these inflammatory mediator regulators to the medical management of allergic rhinitis (AR), chronic rhinosinusitis (CRS), asthma, and allergies, a thorough examination of these epithelium-derived triple inflammatory mediators will reveal a deeper comprehension of the principles fundamental type 2 respiratory inflammatory conditions [24]. According to recent research, sufferers had greater levels of IL-33 than controls, but there were no distinctions in tissues types taken from CRSsNP and CRSwNP sufferers [18]. Likewise, Song et al. reported no variation in IL-33 levels between individuals with non-eosinophilic CRSwNP and those with eosinophilic CRSwNP [25]. According to Imoto et al., IL-33 is thought to raise 15-lipoxygenase 1 levels in acute myeloid (eosinophilic) leukemia cells, a substance that is known to promote inflammatory processes in eosinophilic CRSwNP patients [25] . On the other hand, it was discovered that blocking IL-33 in a mouse model decreased the overall thickness of the oedematous mucosa, the number of Th2 cells, and the amount of subepithelial collagen. Asthma individuals' higher blood levels of IL-33 have also been validated by other investigations [26].

Additionally, it was recently shown that anti-IL-33 antibodies have therapeutic promise against allergic rhinitis [27]. In addition to dramatically reducing symptoms, these antibodies may also lower Th2-type mediators and eosinophil counts in bronchoalveolar lavage (BAL), which in turn lowers nasal discharges. This clinical observation can also be applied to IL-33's potential as a treatment for human allergies. Overall, the results of this research support earlier studies in the same area, suggesting that Th2-dependent illnesses that include allergic rhinitis are influenced by IL-33 [28].

According to Oka et al., IL-10 is a cytokine with anti-inflammatory properties that plays a crucial role in immunoregulatory processes and is implicated in inflammation and allergy disorders [29]. According to Kang et al., prior research has shown that irregular levels of IL10 are present in nose discharge fluid, the nasal2 mucosa, and peripheral blood of the two types of animals and humans with allergic rhinitis (AR) and are linked to the onset and progression of AR [30]. The frequency of innate IL10+ lymphoid cells and their activation by IL10 were shown to be correlated with the effectiveness of allergen-specific immunotherapy (AIT) in individuals with residential dust mite allergy disease [31].

Over time, the pathophysiology theories about the role of cytokines that are inflammatory in CRSwNP have changed. While eosinophilic infiltration and a Th2 cytokine milieu continue to play a major role in the formation of polyps, current research has brought attention to the involvement of additional cytokine subpopulations of IL-10 aids in preserving the state of inflammation by preventing the synthesis of inflammatory substances linked to pathogens. In contrast, TGF-β is a key factor in CRSwNP's pro-fibrotic activities.2 When together, these inflammatory cytokines strengthen the Th2 a microenvironment, which causes CRSwNP to have a distinct and intricate profile [32].

The investigators propose that IL-10 inhibits the generation of reactive oxygen species (ROS), inflammatory processes, and fibrosis. Additionally, by suppressing the downregulation of hyperpolarization-activated cyclic nucleotide-gated potassium channel 4 (HCN4), IL-10 may be a significant factor in preventing hyperglycemia-induced sinus node dysfunction (SND). Furthermore,

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STAT3 phosphorylation is necessary for IL-10-mediated suppression of p38 [33]. Prior findings suggest that increased IL-10 might be crucial in mitigating the effects of underpinning inflammation caused by allergies in allergic respiratory disorders; however, there was no discernible variation in the total amount of the mediators among the various kinds of patients. Thus, it is possible for authors to hypothesize that IL-10, an inhibitory cytokine, had a role in preserving an instance of health in wh8ich there is no inflammatory [34].

The pathogenesis of eosinophilic chronic rhinosinusitis (ECRS), which includes eosinophilia and deeper airway drainage, may be made worse by the results reported by the authors that nasal polyp (NP) reduced IL-10 generation in reaction to Staphylococcus aureus enterotoxin B (SEB) [35].

The cytokines of the IL-10 family have a variety of roles in CRSwNP, including responses to GCs, effects of allergens, and the epithelium. They may also be infected by viruses or bacteria. There haven't been many clinical trials using cytokines from the IL-10 family to treat airway inflammation. Consequently, [36] suggest that IL-10 family cytokines may be beneficial therapeutically in CRSwNP.

Finally, IL-10 and IL-33 were working in opposite, IL-33 is pro-inflammatory cytokine which lead to increase inflammation (activate immunological mediators and immune cells), while IL-10 is anti- inflammatory cytokine that lead to reduce inflammation and decrease secretions of respiratory tract (table 2).

According to effect of gender of sinusitis patients on levels of IL-10 and IL-33, present findings not reveals significant effect of males and females on levels of these cytokines , Finally, we found decrease levels of IL-10 and IL-33 in sinusitis patients with age progression due to reduce protein synthesis, inflammation, organ dysfunction, and chronic diseases [37] All of these features play role in reduce levels of IL-10 and IL-33 with age increasing (table 3).

Conclusion

According to the study's findings, males had a higher incidence of sinusitis than females. Sinusitis patients had higher levels of IL-33 and IL-10 than controls, but as they grew older, their levels declined due to decreased protein synthesis, inflammation, organ dysfunction, and chronic illness. All of these traits play a part. IL-10 and IL-33 levels are decreasing with increasing age.

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