https://doi.org/10.34883/PI.2023.13.4.030

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Can IgE Level Influence the Ocular Surface Disease Index Score of Patients with Dry Eye Syndrome?

Conflict of interest: nothing to declare.
Authors' contribution: D. Jasim – conceptualization, methodology, formal analysis, resources, data curation, writing (original draft, soft wire); M. Al-Rikabi – supervision, conceptualization, investigation; writing (original draft); A. Fadil – supervision, conceptualization, writing (original draft).
The article is published in the author's edition.

Submitted: 04.09.2023
Accepted: 13.11.2023
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Abstract

Background. Dry eye syndrome (DES) is a chronic inflammatory disorder of the ocular surface. The study purposed to assess the roles of immunoglobulin IgE in DES.
Methods. A prospective comparison study was carried out from October 2022 to May 2023, enrolled 100 cases of DES. Patients were subjected to the following examination; slit-lamp examination, non-contact tonometry to measure intraocular pressure, fundus examination with 90D as routine examination along with Ocular Surface Disease Index (OSDI) questionnaire. Blood had five ml of venous blood drawn from them. The kits used is IgE (Elecsys IgE II Immunoassay) kit.
Results. The greater percentage of patients (65%) documented with OSDI score (2). The greater percentage of patients (90%) were figured with IgE level (<150 IU). There was a significant correlation between OSDI and dry eye patient's age ($p<0.0001$), BMI ($p=0.008$), IgE concentration ($p=0.003$). In severe group of DES, the IgE level was very high in severely dry eye patients (90.05±83.4 IU) when compared with mild and moderate, with a high statistical significant difference ($p=0.002$).
Conclusions. Patients with DES have higher OSDI scores. Serum immunoglobulins IgE negatively association with DES.
Keywords: dry eye syndrome, OSDI, immunoglobulin IgE, tears, conjunctivitis

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Может ли уровень иммуноглобулина Е влиять на индекс поражения поверхности глаза у пациентов с синдромом сухого глаза?

Конфликт интересов: не заявлен.
Вклад авторов: Ясим Д. – разработка, методология, формальный анализ, источник финансирования, курирование данных, написание текста; Аль-Рикаби М. – контроль, разработка, исследование, написание текста; Фадил А. – контроль, разработка, написание текста.
Статья опубликована в авторской редакции.

Подана: 04.09.2023
Принята: 13.11.2023
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Резюме

Введение. Синдром сухого глаза (ССГ) – хроническое воспалительное заболевание поверхности глаза. Целью исследования было оценить роль иммуноглобулина IgE при ССГ.

Методы. Проспективный сравнительный анализ проводился с октября 2022 г. по май 2023 г., в него было включено 100 случаев ССГ. Пациенты подвергались следующему обследованию: осмотр на щелевой лампе, бесконтактная тонометрия для измерения внутриглазного давления, исследование глазного дна с помощью офтальмологической асферической линзы 90D в качестве стандартного обследования наряду с опросником «Индекс поверхностного заболевания глаз» (OSDI). У них взяли 5 мл венозной крови для исследования. Использовался набор для иммуноферментного анализа IgE (Elecsys IgE II Immunoassay).

Результаты. У большего процента пациентов (65%) был зарегистрирован показатель OSDI (2). Больший процент пациентов (90%) был выявлен с уровнем IgE (<150 МЕ). Наблюдалась значимая корреляция между индексом поверхностного заболевания глаз (OSDI) и возрастом пациента с ССГ ($p<0,0001$), ИМТ ($p=0,008$), концентрацией IgE ($p=0,003$). В группе с тяжелой формой ССГ уровень IgE был очень высоким у пациентов с тяжелой формой сухого глаза (90,05±83,4 МЕ) по сравнению с легкой и среднетяжелой степенью с высокой статистически значимой разницей ($p=0,002$).

Выводы. Пациенты с ССГ имеют более высокие показатели индекса поверхностного заболевания глаз (OSDI). Сывороточные иммуноглобулины IgE находятся в обратной зависимости от ССГ.

Ключевые слова: синдром сухого глаза, индекс поверхностного заболевания глаз (OSDI), иммуноглобулин IgE, слезы, конъюнктивит

■ INTRODUCTION

DES is a chronic inflammatory disorder of the ocular surface occur due to hyperosmolarity of tear [1–4]. Akil and co-authors suggested that DE caused dropped tear break up time which lead to rising papillary formation of the upper tarsal conjunctiva and serum antigen specific IgE [5]. Thus an allergen come in direct contact with the conjunctiva and enhance a type I hypersensitivity reaction that interact with the IgE bound to mast cells of tissue and cause release of chemical mediators [6]. Immunoglobulin E (IgE) involve in a wide variety of immunological illnesses [7–10]. When IgE secreted in tears, it bind to fragment crystallizable (Fc) receptors on tissue mast cells [11].

The diagnosis of ocular diseases is clinical, yet laboratory tests can be helpful in support the diagnosis [7]. Thus, tests include cytological examination, skin prick tests, and total IgE antibody detection [12–14]. Unfortunately, serum IgE tests are recommended for etiology, but not for pathogenesis and disease severity [15]. In general, total and allergen-specific tear IgE levels have been studied in relation to allergic conjectivitis, but not in relation to DES [16].

The study aimed to assess the roles of immunoglobulin IgE in DES.

■ METHODS

Study design and setting

A prospective study was carried out from October 2022 to May 2023. This study was enrolled 100 (200 eyes) cases of DE symptoms. The study conducted at Ophthalmic consultant clinic.

Inclusion criteria

a) Both gender suffering from DE symptoms.
b) Aged 16 to 60 years.

Exclusion criteria

a) The age under than 16-year-old and older than 60-year-old.
b) History of corneal surgery, corneal ulcer and corneal infections.
c) Ocular diseases (glaucoma or uveitis, ocular allergy, pterygium or blepharitis).
d) Laser vision correction.
e) Current contact lens user.
f) Eye lids disease.
g) Nasolacrimal pathway disorders.

Data collection

All demographic data of patient included age, gender and BMI.

Ophthalmologic examination

Patients were subjected to the following examination; slit-lamp examination, non-contact tonometry to measure intraocular pressure, fundus examination with 90D as routine examination along with OSDI questionnaire.

Ocular Surface Disease Index (OSDI)

OSDI score was recorded after asking the patients all the 12 questions as given in the OSDI questionnaire. The OSDI questionnaire is a 12-item questionnaire used worldwide to accurately assess the symptoms of ocular irritation related to DE and vision. The OSDI overall and subscale scores range from 0 to 100. Based on their OSDI scores, patients can be categorized as having a normal ocular surface (0–12 points) or as having mild

(13–22 points), moderate (23–32 points), or severe (33–100 points) ocular surface disease. The total OSDI score was calculated using the following formula [17, 18].

Blood sample

Blood patient had five ml of venous blood drawn from them. The blood is collected in a gel tube and the serum is extracted as quickly as feasible. For 10 minutes, the blood samples were centrifuged at 3000rpm. The serum samples were then transferred into a new clean disposable plain tube to be utilized later.

Kits

The kits used in this study are IgE (Elecsys IgE II Immunoassay) kit Roche.

IgE (Elecsys IgE II Immunoassay) kit (Roche)

Principle

The Abnova IgE Quantitative Test is a solid phase enzyme-linked immunosorbent assay (ELISA) based on the sandwich principle. The test specimen (serum) is added to the IgE monoclonal antibodies immobilized on polystyrene microtiter wells (solid phase) and incubated with the Zero Buffer. If human IgE is present in the specimen, it will combine with the antibodies on the well. The well is then washed to remove any residual test specimen, and goat anti-IgE in the antibody-enzyme (horseradish peroxidase) conjugate reagent is added. The conjugate regent will bind immunologically to the IgE on the well, resulting in the IgE molecules being sandwiched between the solid phase and the enzyme-linked antibodies. After incubation at room temperature the solid phase is washed with water to remove unbound labeled antibody. A solution of 3, 3′, 5, 5′- Tetramethylbenzidine (TMB) is added and incubated for 20 minutes, resulting in the development of a blue color. The color development is stopped and the resulting yellow color is measured spectrophotometrically at 450nm [19], by Roche Cobas e 411.

Statistical analysis

Statistical analysis performed using SPSS v24 (IBM Inc., Chicago, IL, USA). Descriptive statistics consist of numbers and percentages were measured. Mean, median and SD for categorical data calculated. An association between DES clinical and biochemical parameters measured using Pearson's Chi-square test. Two– way ANOVA analysis was used to described the association between groups. A two-sided P value of less than 0.05 was considered statistically significant.

■ RESULTS

Table 1 showed the basic characteristics, immune-anti-genes of patients. Males were (30%) whereas females were (70%) (p=0.99). The higher percentage of age distribution belonged to group (51–60 years) 56 (56%). The greater percentage of patients were included in BMI group (25–29 kg/m^2) (57%). In relation to Questionnaire score (OSDI), the greater percentage of patients (65%) documented with score (2), followed by score (1) in (23%) and score (3) in (12%) (p=0.037).

In relation to IgE, the greater percentage of patients (90%) were figured with low level (<150 IU) while (10%) of patients showed normal level ranged between (150–300 IU), with no significant difference (p=0.208).

Table 1
Basic characteristics, Vitamin D and immune-anti-genes of patients in the study

Parameters	No.	%	p-value
Gender			
Male	30	30.0	0.99
Female	70	70.0	
Age groups (years)			
11–20	6	6.0	<0.0001
21–30	1	1.0	
31–40	9	9.0	
41–50	23	23.0	
51–60	56	56.0	
>60	5	5.0	
Mean ±SD		49.65±11.834	
Median		54	
Range		14–65	
BMI (kg/m^2)			
18–21	3	3.0	<0.0001
21–25	33	33.0	
25–29	57	57.0	
>29	7	7.0	
Mean ±SD		25.46±2.575	
Median		26.1	
Range		19.4-31.0	
Patients percentage according to OSDI			
Mild	23	23.0	0.037
Moderate	65	65.0	
Severe	12	12.0	
Mode		2	
Patients percentage according to IgE (IU)			
<150	90	90.0	0.208
150-300	10	10.0	
Mean ±SD		61.94±48.02	
Median		45.5	
Range		64-216	

Notes: BMI – body mass index, SD – standard deviation.

The findings of the study as showed in Table 2, there was a significant correlation between OSDI and DE patient's age (X^2=53.536, p<0.0001), BMI (X^2=14.417, p=0.008), IgE concentration (X^2=12.117, p=0.003).

The Table 3 showed the comparison of clinical and biochemical parameters of DES according to the severity. In severe group of DES, the mean age was younger (35.75± 20.79 years) than in mild group (50.48±9.72 years) and moderate group (51.92±8.252 years), with a high statistical significant difference (p<0.0001). Regarding gender distribution and severity of disease, there was no significant difference among male and female (p=0.44). Among BMI and severity, there was no significant difference female (p=0.842).

Table 2
The correlation between OSDI with clinical and biochemical parameters

Parameters	OSDI	
	X^{2*}	p-value**
Age	53.536	<0.0001
Gender	1.64	0.415
BMI	14.417	0.008
IgE (IU)	12.117	0.003

Notes: * Pearson Chi-Square, ** Monte Carlo Sig. (2-sided), BMI – body mass index.

Table 3
The comparison of clinical and biochemical parameters of dry eye patients according to the severity of disease

Parameters		Dry eye severity (mean±SD)			p-value*
		Mild	Moderate	Severe	
Age		50.48±9.72	51.92±8.252	35.75±20.79	<0.0001
Gender	Male	17 (73.9%)	43 (66.2%)	10 (83.3%)	0.44
	Female	6 (26.1%)	22 (33.8%)	2 (16.7%)	
IgE (IU)		74.53±56.52	52.29±31.19	90.05±83.4	0.002

Notes: BMI – body mass index, SD – standard deviation.

The IgE level was very high in severely DES (90.05±83.4 IU) when compared with mild (74.53±56.52 IU) and moderate (52.29±31.19 IU), with a high statistical significant difference among the mean V-D concentration (p=0.002).

■ DISCUSSION

In term of the DE severity, there was no significant difference among male and female while Watts et al [20] concluded that female gender represented as a strong risk factor for DES.

In severe group of DES in the present study, the mean age was younger (35.75± 20.79 years) than in mild group (50.48±9.72 years) and moderate group (51.92± 8.252 years), with a high statistical significant difference (p<0.0001). This is in consistence with many studies in India by Nanda et al [21], and Jain et al [22], in Türkiye by Yildirim et al [23] and Kurtul et al [24] and in Iran by Hashemi et al [25] while disagree with other studies such as Shah and Jani [26], Jin et al [27] and Demirci et al [28].

The greater percentage of patients were belonged to BMI group (25–29 kg/m^2) (57%), with a higher statistically significant difference as those with normal weight (33%) and obese (7%) (p<0.0001). Among BMI and severity, there was no significant difference, (p=0.842). In our literature of the previous studies, we did not find any relation between BMI and DES [21, 29–32].

In the present study, the greater percentage of patients (90%) were figured with low level of IgE (<150 IU) while (10%) of patients showed normal level ranged between (150–300 IU), with no significant difference (p=0.208). In contrast, the IgE level was very high in severely DE patients (90.05±83.4 IU) when compared with mild (74.53±56.52 IU) and moderate (52.29±31.19 IU), with a high statistically significant difference among the

mean V-D concentration, (p=0.002). An agreement regards the severity of DE in this study and IgE concentration with Hom et al [33] and Dermer et al [16] studies, they reported a majority of DES cases had detectable IgE levels in their tears with great tear IgE levels that correlated with allergic seasons and exposures in the home-linked with allergies.

Dermer et al [16] in USA, observed tear IgE levels in 76% of cases, and 17.3% had high levels (>1 ng/mL) that associated with the exposure to allergic triggers as pet(s), smoke and dust. Also, they found that tears collected during spring or summer were 3.9 times great likely to have high IgE compared to those at winter.

Mimura and colleagues found a correlation between total tear IgE score and the scores for objective signs of DES [34].

A prospective, nonrandomized, cross-sectional study was enrolled subjects with allergic eye disorders to evaluated the relation between tear fluid levels of specific IgE and features of allergic conjunctivitis. Authors concluded that specific IgE measurement in tear fluid may be helpful for determining the severity of disease. Although IgE measurement is only a supplemental tool for evaluating the clinical activity of allergic conjunctivitis, the test can be helpful for detecting specific IgE antibodies responsible for this disorder [35, 36].

The assessment of IgE in tears is a very sensitive test in DES because in normal physiology, this immunoglobulin is not detectable in tear film components. In DES cases the measurement of tear osmolarity by IgE has been thought to be the most specific and sensitive test [37].

However, the total tear IgE levels can indicate the severity of ocular surface disorders more accurately than the serum total IgE [16, 38].

■ CONCLUSION

Serum immunoglobulins IgE negatively association with DES. As a result, it is accurately to measure tear total IgE than serum total IgE.

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