RESEARCH

The prevalence of ultra-low total IgE level among Egyptian population: impact of age, sex, and socioeconomic class

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Abstract

Background: Immunoglobulin E (IgE) is the least prevalent antibody type; it plays a key role in host immunity against parasitic infections and allergic diseases. Association between IgE deficiency and higher malignancy rates has been suggested in many studies.

Objectives: The goal of our study was to determine the prevalence of ultra-low total IgE levels and their variations according to sex and age among the Egyptian population.

Methodology: This multicenter retrospective cross-sectional study included serum total IgE and CBC records of 1099 children and 993 adults recruited from private and public hospitals in Egypt between 2015 and 2021. Total IgE levels were classified into ultra-low, normal, high, and very high.

Results: Of all included subjects, 0.8% had ultra-low IgE levels and 74.4% had normal IgE levels. High and very high serum total IgE levels were 24.1% and 0.7%, respectively. IgE levels were significantly higher among adults than children 45 (16.5–113.25) IU/ml vs. 20 (10–75) IU/ml; $p < 0.001$ and among private hospital's patients than the public one (40 (15–98.4) IU/ml vs. 25 (10–98.4) IU/ml; $p = 0.002$. No significant difference between total IgE serum levels regarding gender ($p = 0.825$). Total IgE levels were higher among young adults, with a gradual decline among older patients and a peak among the 50 s and 60 s patients. Pearson correlation between IgE and absolute eosinophilic count showed positive correlation but did not reach significant level $r = 0.04$, $p = 0.367$.

Conclusion: Age and socioeconomic class have impacts on total IgE levels with a relatively low prevalence of ultra-low IgE among the Egyptian population.

Keywords: Sex, Socioeconomic class, Total IgE, Ultra-low

Introduction

Despite being the least common antibody type, immunoglobulin E (IgE) plays a critical function in host protection against parasitic infestations. Furthermore, IgE antibodies created following exposure and sensitization to environmental allergens play a role in allergy disorders [1, 2]. Serum total IgE levels help in diagnosis, evaluation

of disease severity, and treatment evaluation [3]. Compared to other immunoglobulin types, the normal level of IgE in the blood is very low (< 240 ng/ml) [4]. IgE exists in two forms, free and bound. The major part of IgE is bound to cells through its receptors, while free IgE represents only a small proportion [5]. The half-life of free IgE is only 2–3 days. On the other hand, bound IgE is stable for several weeks [6]. IgE bound to the high-affinity receptor FcεRI on mast cells or basophils. FcεRI is also expressed but at a lower level on dendritic cells, Langerhans cells, monocytes/macrophages, eosinophil, and

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platelets [7]. Total serum IgE concentration is influenced by multiple modifiable and non-modifiable factors. Independent studies have demonstrated contradictory data. Total IgE serum levels are higher in males than females. Some studies demonstrated a decrease in serum total IgE with aging [8]; other studies reported an increase in total IgE levels with the advancing age among non-atopic individuals [9]. Various modifiable factors are associated with increased total serum IgE concentrations, including helminthic infection, alcohol consumption, obesity [10], and smoking [11]. Many medical conditions have been shown to be associated with altered serum IgE levels, ranging from ultra-low to elevated serum IgE titers. Elevated IgE has been considered a biomarker for allergic/atopic conditions [4]. Atopic dermatitis and hyper-IgE syndrome are the medical conditions with the highest serum IgE levels, followed by asthma, parasitosis, and allergic rhinitis [12, 13]. Despite the fact that most research focus on high IgE serum levels, less studies investigate the significance of IgE deficiency and its links to various clinical diseases. Low IgE levels can be a sensitive and specific indicator of common variable immunodeficiency [14]. Association between IgE deficiency and higher rates of malignancy has been suggested in many studies [15, 16]. The purpose of this study was to investigate the differences in total IgE serum levels among Egyptian individuals based on sex, socioeconomic status, and age, as well as to determine the prevalence of ultra-low total IgE among them.

Methodology
Study design and subjects
This is a multicenter retrospective cross-sectional study. We got records of 2092 people (1099 children and 993 adults) recruited from Ain Shams University Specialized Hospital (a private hospital) and El-Demerdash Hospital (a public hospital), as a proxy for socioeconomic class, Cairo, Egypt, between 2015 and 2021, independent of their age, sex, and medical status.

Data collection
All data were collected from participants' records, including age and gender. Laboratory investigations were done according to the standard methods of Ain Shams University Hospitals Central Laboratories. Complete blood count (CBC) was analyzed by Sysmex XT-1800i autoanalyzer (Sysmex, Japan), and total IgE serum levels were determined by ADVIA Centaur® XPT Immunoassay System (Siemens Healthineers, NY 10,591, USA) with a minimum detectable concentration of 1.5 IU/ml and a measuring interval of 1.5–3000 IU/ml [17].

Serum total IgE level categorization
Serum total IgE levels were classified according to Ferastraoaru et al. into four categories: ultra-low—with total IgE levels of less than 2.5 IU/ml; total IgE levels of ≥ 2.5 and < 100 IU/ml were considered normal; total IgE levels of ≥ 100 and < 1000 IU/ml were considered high; and total IgE levels of ≥ 1000 and $< 10,000$ IU/ml were considered very high [18].

Statistical methodology The results were generated using the SPSS system (version 26). Quantitative data were expressed as mean and standard deviation (SD) when parametric and median and interquartile range (IQR) when nonparametric. Qualitative variables were expressed as numbers and percentages. The Mann–Whitney U test was employed for continuous variables, whereas the chi-square test was utilized for categorical variables. A p-value of < 0.05 was considered significant.

Results
This cross-sectional study included data of 583 people recruited from a private hospital (57 children and 526 adults) and 1509 people recruited from a public hospital (1042 children and 467 adults). The age of the included subjects ranged from 1 to 87 years old. One thousand twelve (48.4%) were males, and 1080 (51.6%) were females. One thousand ninety-nine were children, and 993 were adults.

Of all included subjects, 0.8% ($n = 16$) had low total IgE serum levels while 74.4% ($n = 1556$) had normal levels. High and very high serum total IgE levels were found in 24.1% ($n = 506$) and 0.7% ($n = 14$) of the study population, respectively (Table 1, Fig. 1).

Serum IgE levels were significantly higher among adults when compared to children 45 (16.5–113.25) IU/ml vs. 20 (10–75) IU/ml; $p < 0.001$. Also, total IgE serum levels were higher among individuals recruited from the private hospital compared to those of the public one 40 (15–98.4) IU/ml vs. 25 (10–98.4) IU/ml; $p = 0.002$. On the other hand, there was no significant difference between total IgE serum levels regarding sex ($p = 0.825$) (Table 2).

Table 1 IgE level categories of the study population

	Number (present) $n = 2092$
Low IgE	16 (0.8%)
Normal IgE	1556 (74.4%)
High IgE	506 (24.2%)
Very high IgE	14 (0.7%)

Data presented as number and percentage

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Fig. 1 Percentage of total IgE level categories
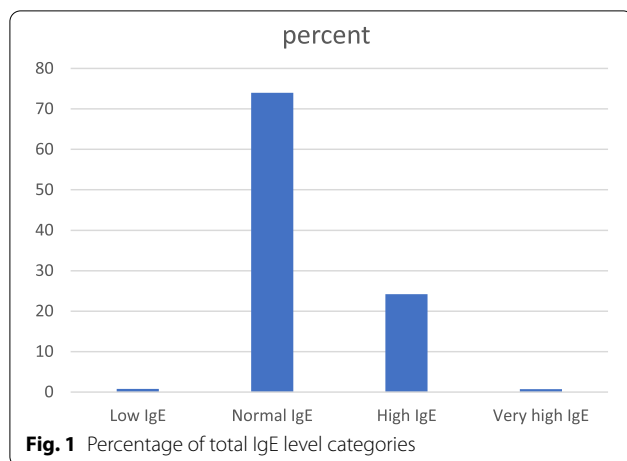
Table 2 Total IgE Levels among the different groups

	IgE IU/mL (median IQR)	*p*-value
Sex		0.825
Male	30 (10–100)	
Female	30 (10–96.925)	
Age group		< 0.001
Child	20 (10–75)	
Adult	45 (16.5–113.25)	
Hospital		0.002
Private	40 (15–98.4)	
Public	25 (10–98.4)	

Data presented as median, (IQR) interquartile range; significant *p*-value < 0.05

The prevalence of total IgE serum level categories was according to the age, sex, and hospital of the study population. Low total IgE serum levels were significantly associated with adults and private hospital admission ($p < 0.001$). Neither children nor adults admitted to the public hospital had low total IgE serum levels ($n = 0.0$). The prevalence of total IgE serum level categories did not change significantly according to the gender of the study population (Table 3).

Total IgE level was higher among young adults with a gradual decline among older patients with a peak elevation of IgE level among the 50- and 60-year-old patients (Fig. 2).

Pearson correlation between IgE and absolute eosinophilic count showed positive correlation but did not reach significant level $r = 0.04$, $p = 0.367$ (Table 4).

Discussion

IgE is the last to be discovered of the five immunoglobulin classes. It plays a crucial part in allergy sensitization as well as atopic illnesses such as allergic rhinitis,

Table 3 Categories of total IgE in relation to different variables

	Low IgE	Normal IgE	High IgE	Very high IgE	*p* value
Sex					0.662
Male	7 (0.7%)	750 (74.1%)	246 (24.3%)	9 (0.9%)	
Female	9 (0.8%)	806 (74.6%)	260 (24.1%)	5 (0.5%)	
Age group					< 0.001
Child	0 (0%)	861 (78.3%)	235 (21.4%)	3 (0.3%)	
Adult	16 (1.6%)	695 (70%)	271 (27.3%)	11 (1.1%)	
Hospital					< 0.001
Private	16 (2.7%)	424 (72.7%)	136 (23.3%)	7 (1.2%)	
Public	0 (0%)	1132 (75%)	370 (24.5%)	7 (0.5%)	

Data presented as number, percentage; significant *p* value < 0.05

asthma, and atopic dermatitis. The clinical manifestations of these illnesses are caused by type I hypersensitivity reactions involving IgE and other immune cells [19]. Many epidemiological investigations, as well as in vitro and in vivo studies in mouse models, have recently revealed that IgE may play a new function in tumor immune surveillance [20].

The current study aimed to detect the prevalence of ultra-low IgE levels among the Egyptian population and determine the effect of different variables, including age, sex, and socioeconomic class, on total IgE levels.

Our study showed that 0.8% ($n = 16$) of the study population had ultra-low total IgE serum levels while 74.4% ($n = 1556$) had normal levels. High and very high serum total IgE levels were found in 24.1% ($n = 506$) and 0.7% ($n = 14$) respectively.

Many studies reported different prevalence of ultra-low IgE levels ranging from 1 to 3.4% [21, 22]; another study reported that the level of ultra-low IgE was up to 10.5% [23]. Differences in total IgE level depend on many variables such as gender, ethnicity, and the age of the study population besides it is also affected by environmental factors; for example, in Egypt, we could explain the low prevalence of ultra-low IgE by the fact that Egypt might have a high level of helminthic infestations that undoubtedly have an impact on IgE level leading to high levels of total IgE.

Our study detected different variables with statistically significant impact on total IgE, as the study showed that serum IgE levels were significantly higher among adults when compared to children 45 (16.5–113.25) IU/ml vs. 20 (10–75) IU/ml; $p < 0.001$. A study held by Amici et al. showed that total IgE level did not decrease with age, but there was a peak in the patient's age group ranging from 19 to 30 years old [24]. Another study showed that total IgE correlated with age being lowest among infants and increasing with age [25].
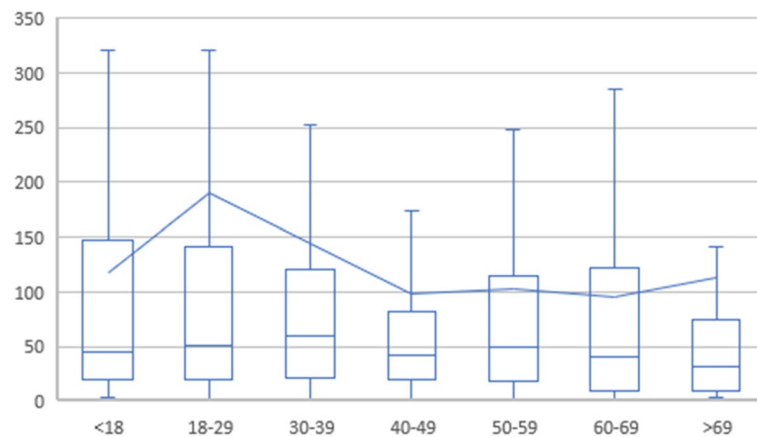
Fig. 2 Total IgE level distribution according to age of participants

Table 4 Pearson correlation between eosinophil, age, and IgE

		IgE
Eosinophil	Correlation coefficient	0.040
	Sig	0.367
Age	Correlation coefficient	− 0.080
	Sig	0.024*

* Pearson correlation is significant at the 0.05 level (2-tailed)

In contrast to our study, Warren et al. showed that total IgE level significantly declined with age regardless of the sex of the patients [26]. Another study detected a higher prevalence of IgE among children assuming that the highest level of allergic sensitization in childhood might be the cause [27]. On the other hand, a study investigated IgE level among the Dutch population detected no relation between total IgE level and age [28].

In the current study, total IgE serum levels were higher among individuals recruited from the private hospital as a high socioeconomic class compared to those of the public one, low socioeconomic class, 40 (15–98.4) IU/ml vs. 25 (10–98.4) IU/ml; $p = 0.002$.

Many European studies showed that IgE level was higher among high social class patients assuming that atopy and total IgE level is more evident at high social class with fewer family members and less exposure to microbes. Overcrowding, unsanitary circumstances, and a bigger family size, on the other hand, were linked to a lower prevalence of allergic disorders, as well as lower IgE levels [29]. Another two studies showed high IgE levels among high social class children explaining that so-called urbanization, including the increased environmental pollution, led to the high level of allergy [30, 31].

In contrast to our findings, many studies reported that higher IgE levels were found among patients with low social class, explaining that those patients were exposed to helminths more frequent than high social class, consequently leading to higher IgE levels [32, 33]. Besides those patients might be more exposed to cockroach and other mold allergens causing sensitization and high IgE level [34].

The current study showed no significant difference between total IgE serum levels regarding sex ($p = 0.825$). In agreement with our results, Omenaas et al. found that sex has no significance among younger age groups while at old females > 50 years, total IgE level seemed to be lower than males [35]. In contrast to our results, Paula et al. and Court et al. found that males showed higher IgE levels than females [27, 36]. Another large cohort study found that total IgE was higher in males than females explaining that males have a higher prevalence of smoking than females and smoking elevates IgE level. Smoking leads to a higher probability of sensitization to different aeroallergens such as house dust mites [28, 37].

The current study revealed that the total IgE level was higher among young adults with a gradual decline among older patients with a peak of IgE level among the 50- and 60-year-old patients. A finding that came in line with a study showed that total IgE levels did not decrease with age. There was a peak in the 19- to 21-year-old group, followed by a relevant increase in the 28- to 30-year-old group, with a peak in the oldest subgroup (> 85 years), implying that reduced regulatory function happening during senescence could be the origin of that observation [24].

To the best of our knowledge, it is the first study to detect the prevalence of different total IgE levels among the Egyptian population with the correlation between

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total IgE and different variables using a multicenter large study population. Our study limitation was the lack of clinical data, especially the history of allergic diseases correlating with our laboratory results.

Lastly, we concluded that age and social class impact the total IgE level with a relatively low prevalence of ultra-low IgE among the Egyptian population.

Declarations

Ethics approval and consent to participate
The current study protocol received ethical approval from the Ain Shams University Faculty of Medicine Research Ethics Committee (reference MS 274/2021). This study was conducted in accordance with the declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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