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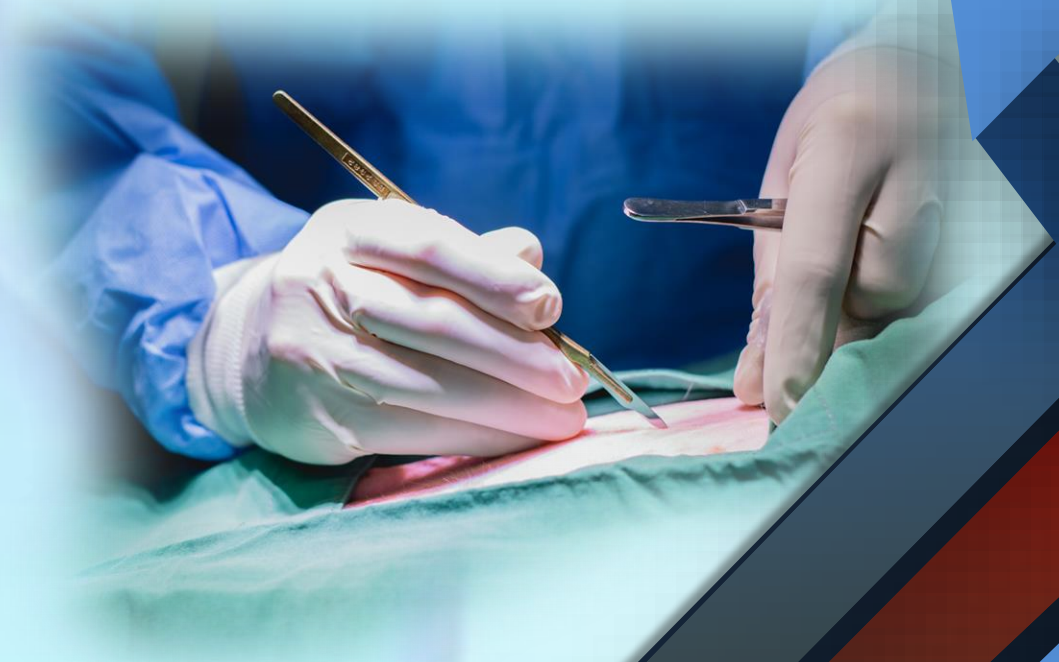

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Original article

Assessment of Anti-Streptolysin-O Titre in Healthy School Age Children in Alexandria- governorate

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ABSTRACT

Background: Serology of streptococcal [GAS] group-A is used for post-streptococcal disease diagnoses, such as acute rheumatic fever, and occasionally for streptococcal pharyngitis diagnoses. Streptococcal titers vary according to a number of factors, including age and population. In developing countries, where GAS-induced impetigo is rare, the titers in healthy people are low in early childhood, peak in children aged 6 to 15, decrease in late adolescence and early adulthood, and then flatten off afterwards.

Aim of the work: To assess Anti streptolysin-O titre in healthy school age children in Alexandria governorate.

Patients and Methods: A prospective study had been performed in Alexandria Governorate and the collected sample were tested in clinical pathology Lab [Al-Azhar University Hospital, Damietta]. A total of 3000 [1540 Males, 1460 Females] serum samples had been collected from children aged 6-15 years, had been tested for Anti-streptolysin O titer [ASO] by latex.

Results: ASO from 100-200 was higher with 1281 [42.7%] followed by <100 with 1076 [35.9%]. ASO ranged from 10-850 with mean value 91.81±93.41 and median 65.0. There was statistically significant relation between Anti-streptolysin O "ASO" titer category and age in studied group. In addition, there was statistically significant relation between Anti-streptolysin O "ASO" titer category and socioeconomic status in studied group; the high incidence of elevated ASO-titer was found in low socioeconomic status. Furthermore, the relation between ASO titer with each of weight and height reveled significant difference between different ages and height groups.

Conclusions: We concluded that upper limit of normal [ULN] ASOT is quite high in normal Egyptian children, reaching up to 850.0 IU / ml. Mapping of upper normal levels and associated factors with increased levels could provide a clue for future planning to prevent streptococcal infection and its associated complications.

Keywords: Group-A Streptococci [GAS]; Anti-streptolysin O [ASO]; Upper limit of normal; Children; Alexandria-Governorate.

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* Main subject and any subcategories have been classified according to the research topic

INTRODUCTION

Class A Streptococcus [GAS], the only species in this class of β-hemolytic streptococci, is synonymous with *Streptococcus pyogenes*. GAS is one of the main pathogenic bacteria that infect children and adolescents and is related to a wide variety of diseases and infections. An estimated > 600 million cases of GAS "strep throat" pharyngitis and > 100 million GAS pyoderma cases are reported worldwide[1].

Streptococcus pyogenes [GAS] is an optional, gram-positive coccus that forms in chains and induces numerous human infections, including pharyngitis, tonsillitis, scarlet fever, cellulitis, erysipelas, rheumatic fever, glomerulonephritis post-streptococcal, necrotizing fasciitis, myo-necrosis and lymphangitis. The human body 's skin and mucous membranes are the only known reservoirs for GAS in nature[2].

The most severe complication with group A streptococcal infection [GAS] is acute rheumatic fever [ARF], and rheumatic heart failure. Acute rheumatic fever [ARF] is relatively rate in developed countries. However, it had higher prevalence in developing countries and in indigenous peoples [3]. Nowadays, acute post-streptococcal Glomerulonephritis [APSGN] is the classic form of glomerulonephritis [GN] linked to bacterial infections and is the commonest type of immune complex-related GN in the past. APSGN has become much less common in recent years, mainly in developing world, after the widespread antibiotics use, and has become a rare clinical entity in the average laboratory for nephron-pathology. However, APSGN remains a frequent form of GN in the third-world countries, particularly in areas where epidemic disease occurs [4].

APSGN is an inflammatory disorder of the kidney that occurs two to three weeks after skin or throat infection with a specific type of bacteria called Group-A Streptococcus [GAS] or G Streptococcus. In specific areas, most cases pursue skin rather than throat infections, as skin infections are the most serious problems. Not all streptococcus species cause kidney issues but only those caused by 'nephritogenic' strains. Thus, the acquisition and recognition of streptococcal isolates in APSGN can better guide the response of the publics and healthcare providers [5]. Anti-Streptolysin O [ASO] is the antibody developed by most group A strains and many group G streptococci strains against streptolysin O [an immunogenic, hemolytic, oxygen-labile toxin]. The “O” in its name refers to “oxygen-labile”; the other oxygen-stable is streptolysin-S toxin. Streptolysin O mainly function to induce beta-hemolysis [the open splitting of red blood cells][6].

AIM OF THE WORK

The aim of current study was to assess Anti streptolysin-O titer in healthy school age children in Alexandria governorate.

PATIENTS AND METHODS

A prospective study was carried out in Alexandria Governorate and the collected samples were tested in Clinical Pathology Lab at Al-Azhar University Hospital [Damietta] from January 2019 till January 2020. A total of 3000 [1540 Males, 1460 Females]. The study was carried out in compliance with the Code of Ethics [Helsinki Declaration] of the International Medical Association for Human Studies.

A complete medical history has been recorded and the findings recorded in the pre-designed questionnaire. Data collected included name, age at recruitment, gender, residence, and antibiotics usage. Additionally, Clinical diagnosis, should be integrate both clinical and laboratory data. In our study we found that ASOT may be higher than the normal value in children which is <200 IU/ml despite the child was healthy. As a result, high ASOT above normal reference is not an indicator to diagnose ARF. Additionally ASOT in healthy child may reach up to 850 IU/ml.

Exclusion criteria were: echocardiogram-proven rheumatic heart disease [Because these subjects are at higher risk of acute rheumatic fever at any time]; recent GAS pharyngitis; and any other acute rheumatic fever. Systemic infection, temperature of >38°C on the day of enrollment.

Laboratory investigations including: ASO titer, which had been determined by latex agglutination method. Reference values for adults <250 IU/mL, and for children < 200 IU/mL**.**

Statistical Analysis: Information was fed to

the machine through IBM SPSS software package version 20.0. Using number and per cent, qualitative data were represented. Chi-square test was used to assess similarity between various classes over categorical variables. The findings of the significance tests are reported as two-tailed odds. The significance of reported findings was calculated at the point of 5%.

RESULTS

The distribution of the studied group regarding their age and sex **[Table 1]**, the male represents 51.3% of the cases and females was 48.7% of the cases, on comparing the male and females regarding their age, it was found that the age distribution among the two groups of sex [male and females] was matched without significant difference [p >0.05].

Anti-streptolysin O "ASO" titer category distribution among studied group. ASO from 100-200 was higher with 1281 [42.7%] followed by <100 with 1076 [35.9%]. ASO ranged from 10-850 with mean value 91.81±93.41 and median 65.0. **[Table 2].** The relation between Anti-streptolysin O "ASO" titer category and age, sex in studied group. There was statistically significant relation between Anti-streptolysin O "ASO" titer category and age in studied group [P < 0.05]. While sex there was no statistically significant relation between Anti-streptolysin O "ASO" titer category and sex in studied group [P > 0.05]. **[Table 3]**

The relation between Anti-streptolysin O "ASO" titer category and socioeconomic status in studied group. There was statistically significant relation between Anti-streptolysin O "ASO" titer category and socioeconomic status in studied group [P < 0.05] the high incidence of elevated ASO-titer was found in low socioeconomic status **[Table 4]**

The relation between ASO titer with each of weight and height in studied group reveled significant difference between different ages and height groups regarding the ASO titer **[Table 5]**

Table [1]: Distribution of the studied group regarding their demographic data.

Age group	Male		Female		Total		X^2	p
	No.	%	No.	%	No.	%		
6-8 years	227	14.7	210	14.4	437	14.6	4.82	0.065 [NS}
8-10	380	23.6	345	23.6	725	24.2		
10-12	575	33.0	482	33.0	1057	35.2		
12-15	358	29.0	423	29.0	781	26.0		
Total	1540	100.0	1460	100.0	3000	100.0		

X^2 = Chi square test; NS: not significant

Table [2]: Antistreptolysin O "ASO" titer category distribution among studied group.

ASO titer	Number [n=3000]	Percent [%]
<100	1076	35.9
100-200	1281	42.7
200-300	532	17.7
300-400	33	1.1
>400	78	2.6
Rang; mean±SD; Median	10.0-850; 91.81±93.41; 65.0	

Table [3]: Relation between Antistreptolysin O "ASO" titer category and age, sex in studied group.

		ASO titer category					X^2	p
		<100	100-200	200-300	300-400	>400		
Age group	**6-8**	329 [14.0%]	25 [17.5%]	63[15.6%]	8[24.2%]	12[15.4%]	26.50	0.003*
	8-<10	536[22.9%]	31[21.7%]	134[33.2%]	6[18.2%]	18[23.1%]		
	10-<12	840 [35.9%]	51[35.7%]	128[31.7%]	10[30.3%]	28[35.9%]		
	12-15	637[27.2%]	36[25.2%]	79[19.6%]	9[27.3%]	20[25.6%]		
Sex	**Male**	1205 [51.5%]	87[60.8%]	186[46.0%]	19[57.6%]	43[55.1%]	10.68	0.068
	Female	1137[48.5%]	56[39.2%]	218[54.0%]	14[42.4%]	35[44.9%]		

Table [4]: Relation between Antistreptolysin O "ASO" titer category and Socioeconomic status in studied group.

Socioeconomic status		ASO titer category					Total
		<100	100-200	200-300	300-400	>400	
High	No.	810	53	150	16	12	1041
	%	34.6%	37.1%	37.1%	48.5%	15.4%	34.7%
Low	No.	803	40	128	8	52	1031
	%	34.3%	28.0%	31.7%	24.2%	66.7%	34.4%
Middle	No.	729	50	126	9	14	928
	%	31.1%	35.0%	31.2%	27.3%	17.9%	30.9%
X^2		21.6					
p		0.0001*					

X^2 = Chi square test; * Not significant

Table [5]: Relation between Antistreptolysin O "ASO" titer category and anthropometric measurements.

	ASO titer category					F	p
	<100	100-200	200-300	300-400	>400		
Weight [kg]						7.029	0.0001*
Range	20.0-45.0	20.0- 45.0	20.0-45.0	20.0-45.0	20.0-45.0		
Mean	32.49	32.21	30.39	31.67	32.09		
S.D.	7.39	8.37	6.70	8.37	7.59		
Height[cm]						6.558	0.0001*
Range	115.0-155.0	115.0-155.0	115.0-155.0	115.0-155.0	115.0-155.0		
Mean	135.90	135.29	132.75	134.39	135.15		
S.D.	11.49	13.24	10.66	13.25	11.93		

DISCUSSION

Rheumatic heart disease is a prevalent health problem all over the world, as about 15.6 million individuals have RHD. Special public health concern had been expressed in India, Middle East, and many countries in Africa and South America, due to high incidence in such areas. In Egypt, the RHD prevalence among school children was 5.1 per 1000 populations. In addition, ARF has been found to be severe and associated with different complications[7].

It is well-recognized that ASO upper limits of normal ASO titer frequently vary according to geographic area, season and site of infection. The determination of upper limit of normal titer of ASO is crucial to guard against over diagnosis of ARF on the basis of raised titers, which is a common encounter in daily practice [8].

Previously, the standard values were set to 200 IU/ml. In the current study the upper limit of normal is even higher than reported value, reaching 398.5 IU/ml. This increase could be explained by widespread, large untreated, streptococcal infections, affecting population of the current study. In addition, another study reported major variations could be present for specific populations due to different geographic locations. Each locality had each own climatic and socioeconomic circumstances [9].

The upper normal limit of ASO titer has been investigated in different. For example, it was 333 units in USA populations as reported by Wannamaker **and Ayoub** [10]. Also, in another analysis from different USA states, it was 240 IU/ml [11]. However, it was 326 IU/ml in Korea [12], and 305 IU/ml in India [Mumbai] [13], 239 IU/ml from another study from India [14], 200 IU/ml in Tanzania [15], and 200 units in Sweden [16].

In a systematic meta-analysis included different studies from countries with variable socioeconomic levels [low, middle and high], the pooled GAS carrier estimate was 8% [95% CI, 6%-11%]. In western Africa, the value was 2% [95% CI, 1% - 2%] was significantly different than Southern [9.0%], Eastern [7%] and Central Africa [8%]. On the other side, countries in Northern Africa had a

significantly higher estimate of 14% [95% CI, 3% - 30%] [17]. For risk factors associated with GAS colonization [e.g., age, sex, seasons, and crowding index] had conflicting results. The rate in current study was comparable to the 8.4% reported in India, and less than data from Nepal and Iraq [10% and 15% respectively] [18].

ASO titer increased with older age children in the current study. Actually, it is well-known that, GAS diseases affect all age groups. However, the extremes of age [elderly and young children] had the highest incidence. Comparable age distribution had been reported from different courtiers all over the world [19, 20].

The results of this study showed no significant relation between ASO titer and child gender. However, males had higher incidence than females. Comparable results had been reported previously [21].

In this study, it was found that there was a highly significant relation between high ASO titers and low socioeconomic levels, this result agrees with **Saini *et al*.**[8]. In addition, streptococcus pyogenes is one of the commonest bacterial pathogens found in acute pharyngitis among pediatrics living in lower socioeconomic condition[22].

In our study it was found that there was a significant relation between high ASO and low weight and height. These results agreed with **Islam *et al*.** [23]. They reported a marked significant effect of high [Positive] ASO on anthropometrics in pediatrics.

We expressed the value of ASO titer in terms of upper limit rather than as the mean values to show the maximum suitable value. Such children may not need further investigation or any type of treatment even if the levels of ASO titers are high, since they are regular and did not have any complaint at the sampling time. Re-infection usually leads to increase of ASO titers that are persistent, and previous studies have shown that the antibody response to repeated infections is more impressive [24].

We concluded that in normal children, the upper limit of normal ASO titer is quite high, reaching up to 850.0 IU/ml. At screening of ASO we must put in mind that the basal ASO titers increased with repeated attacks of acute follicular tonsillitis. Hence, isolated high ASO Titer [per se] is not appropriate for the diagnosis of ARF. During acute GAS infection, basal levels of ASOT increased with age but do not affect peak levels.

Financial and Non-Financial Relationships and Activities of Interest

None

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