

Normal values for Anti-Streptolysin O (ASO) titre in Saudi children

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Abstract

Measurement of Antistreptolysin O (ASO) antibodies is often necessary to confirm a clinical diagnosis of a previous group A streptococcal infection especially in patients suspected of having a non-suppurative sequel to this infection. The study was conducted to determine age-specific geometric mean titres (GMT) and upper limits of normal (ULN) of ASO antibodies in children from 5-12 years age group. ASO titres were measured in Sera by conventional laboratory methods. The geometric mean ASO titre was 192.7 Todd units and the upper limit of normal (ULN) ASO titre was 218.7 Todd units. The age-specific GMT and ULN for this group of children were higher than previously reported from our region. The highest values were obtained in children 7-9 years old.

Introduction

Diagnosis of Group A Streptococcal Infections (GAS) or the non-supportive sequelae is not always possible by medical history or bacteriological recovery of the organism. However, the appearance of antibody to streptolysin O (ASO) is usually indicative of a recent streptococcal infection [1]. Thus, the ASO test is frequently used to confirm a clinical diagnosis of a previous GAS infection. This was initially emphasized in 1965, when the revised Jones criteria for the diagnosis of rheumatic fever for the first time introduced the confirmatory role of streptococcal antibody titres in providing evidence of a previous GAS infection [2]. A positive ASO test is generally considered to be one with a two dilution rise in titre between the acute and convalescent serum specimens. However, due to practical considerations, often one single acute-phase specimen is sent to the laboratory. In such cases the 'upper limit of normal' ASO has been shown to provide a useful guideline to physicians [3]. However, ASO titres require proper interpretation in order to be useful as these antibody levels are influenced by multiple factors. These include site of infection [4], time since the onset of infection [5], age [6], geographical location [7], carrier rate [8], and treatment with antimicrobial agents [9].

In Saudi Arabia, only one study as far as we are aware, was conducted to determine 'the upper limit of normal' ASO in Saudi Children [10]. The persistence of GAS infection's and their sequelae and the lack of recent studies reporting the upper limit of normal ASO in this region, prompted the present study. We attempt to validate and compare our findings with the earlier report, which was conducted 15 years ago.

Materials and Methods

The study was conducted during the period from January 1999 to December 2001. Serum samples were collected from 397 children who attended the Outpatient clinic at King Khalid University Hospital and fulfilling the following criteria:

1. Saudi nationals
2. 5 to 12 years age group
3. Has no throat infection in the last 3 months
4. Has no current streptococcal disease (e.g. scarlet fever)

5. Has no history of acute rheumatic fever, rheumatic heart disease or post streptococcal glomerulonephritis
6. Not received antibiotics for the last 3 months
7. No current febrile illness or infection.

Consent was obtained from parents after due explanation

of the purpose of the study. Samples were obtained only from those patients whose blood was drawn for other tests (e.g. CBC).

Serum samples were separated and stored at -20°C until assayed. The antistreptolysin O (ASO) was measured using

Table 1: Upper limit of normal for ASO Titres by Age

Age	N	Geometric Mean ASO titre		ULN	
		Log	Todd Units	Log	Todd Units
5-7	132 (33.2%)	2.19	156	2.25	180
7-9	130 (32.7%)	2.34	219	2.39	247
9-12	135 (34.1%)	2.31	203	2.36	229
Total	397 (100%)	2.28	192.7	2.33	218.7

Abbreviations: ULN: Upper Limits of normal; ASO: Antistreptolysin-O

the streptolysin-O test kit from Bio Kit, S.A (08186 Lissa'd' Amunt, Barcelona - Spain). This is a haemolysis test in which the micro titration-method was used as described in the instruction manual.

Data was analysed using Statpac Gold Statistical analysis package. The ASO titres were transformed into their logarithm values and the geometric means were calculated for each age group. The 80% value of the normal distribution was used as the upper limit of normal (ULN).

Results

The study included 162 (40.8%) males and 235 (59.2%) females. The ages ranged between 5 to 12 years. The 397 subjects in the study were divided according to age, into 3 groups as shown in Table 1.

The geometric mean titre (GMT) and the upper limit of normal (ULN) were expressed both as logarithms and in Todd units. Todd units refer to the reciprocal value of the highest serum dilution, which shows no haemolysis in the test as originally described by Todd.

The GMT and ULN for each group had increased from 2.19 log units (156 Todd units) in group I (5-7 years), to 2.34 log units (219 Todd units) in group II (7-9 years) and 2.31 log units (203 Todd units) in group III (9-12 years). The mean GMT for the entire group of 397 children was 2.28 log units (193 Todd units) and the ULN was 2.33 log units (219 Todd units)

Discussion

In the present study, the upper limits of normal ASO for children 5-7 years old was found to be 180 Todd units; for children 7-9 years 247 Todd units and for those aged 9-12 years 229 Todd units. Compared to the report of A Hossain, in Saudi Children the values were 100 Todd units for children <5 years, 166 Todd units for children 5-15 years and 100 Todd units for Adults. Although he grouped his subjects differently, the levels are higher in our study. This is particularly observed in our group of 7-9 years old. The age-related 'normal' values for ASO in the package insert of the commercial kit we used (Bio Kit, S.A, Barcelona, Spain) was quoted as 100 Todd units for pre-school children and between 166-250 Todd units in school age children and grown up adults. The commercial kit suggests a normal range to be established between 0 and 200 Todd units. In this study, the mean ULN of ASO for the entire group was found to be 218.7 Todd units for children between the ages of 5 and 12 years. However, age-related changes can be detected readily in our 3 groups, being highest in the 7-9 years old.

Compared to similar studies from the Gulf region; a study from Kuwait [11] revealed results in agreement with the report by Hossain from Saudi Arabia. Along the same line, Dawson [12] from United Arab Emirates reported the normal ASO value to be between 0 - < 200 units for pre-school, school children and adults while Khateeb from Jordan considered the ULN to be 200 Todd units. On the other hand, a study by Kaplan [13] from the United States reported the ULN for ASO titre to range from 120 to 320 Todd units for children aged between 3 to 12 years old. Their study revealed a clear age-associated rise in the ASO

titres. The mean value for the entire group was 240 Todd units, which is higher than the mean value of 218.7 Todd units in our study. Overall our study revealed higher value than previous reports from Saudi Arabia and other regions in the Gulf.

Conclusion

This study revealed that the ULN ASO titre for Saudi children in the age group of 5 – 12 years was 218.7 Todd units. One would suggest that interpretation of the ASO titre result should be correlated with normal value for each age group in that population. Because of the limitations of this study one would recommend that larger multi-center studies are carried out in different areas of the Kingdom to verify these results.

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References

1. Al-Saeid K, Majeed HA. Acute Rheumatic Fever: Diagnosis and treatment. *Ped Annals* 1998; 27: 295-300.
2. Committee to Revise the Jones criteria: American Heart Association. Jones Criteria (revised) for guidance in the diagnosis of rheumatic fever. *Circulation* 1965; 32: 664-668.
3. Klein GC, Baker CN, Jones WL. "Upper limits of Normal" antistreptolysin O and antideoxy-ribonuclease B titres. *Applied Microbiology* 1971; 21: 999-1001.
4. Kaplan E, Anthony B, Chapman S, Ayoub E, Wannamaker L. The influence of the site of infection on the immune response to group A streptococci. *J Clin Invest.* 1970; 49: 1405-1414.
5. Kaplan E, Ferrieri P, Wannamaker L. Comparison of the antibody response to streptococcal cellular and extracellular antigens in acute pharyngitis. *J Pediatr* 1974; 84: 21-28.
6. Kaplan EL, Anthony BF, Ayoub EM, Wannamaker LW. A 2-year longitudinal study of streptococcal infections in an isolated community: antibody dynamics. In Haver Kom MJ, ed. *Streptococcal Disease and the Community. Proceedings of the Fifth International Symposium on Streptococcus Pyogenes.* Amsterdam, the Netherlands: Excerpta Medica, 1974; 237-242.
7. Guidelines for the diagnosis of Rheumatic Fever. *JAMA* 1992; 268: 2069-2073.
8. Kaplan E. The group A streptococcal upper respiratory tract carrier state: an enigma. *J Pediatr* 1980; 97: 337-345.
9. Kilbourne DD, Loge JP. The comparative effects of continuous and intermittent penicillin therapy on the formation of antistreptolysin in hemolytic streptococcal pharyngitis. *J Clin Invest* 1948; 27: 418-424.
10. A Hossain. Tests for streptolysin-O antibodies in health and suspected streptococcal infections in Saudi Arabia. *J Tropical Medicine and Hygiene* 1987; 90: 111-115.
11. Karouri R, Majeed HA, Yousef AM, Mousa MA, Iskander S, Hussain K. The hemolytic streptococci and streptococcal antibodies in normal school children in Kuwait. *American Journal of Epidemiology* 1962; 116: 709-721.
12. Dawson KP, Nsanze H, Ameen AS, Mustafa N, Ibrahim AI, Al-Balooshi. Antibodies to streptococcal exozymes in the normal population of the United Arab Emirates. *Middle East Paediatrics* 1998; 3: 12-14.
13. Kaplan E, Rothermel CD, Johnson DR. Antistreptolysin O and Anti-Deoxyribonuclease Titres: Normal values for children ages 2 to 12 in the United States. *Paediatrics* 1998; 101: 86-88.

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