

# EPIDEMIOLOGY OF STREPTOCOCCAL INFECTION WITH REFERENCE TO RHEUMATIC FEVER

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## ABSTRACT

*Antistreptolysin antibodies were estimated in 787 normal children and young adults by latex test. This test detects titres of 200 IU/ml and above, which is the western cut off point, for diagnosis. Children below one year showed no antibodies. Unlike western studies where no antibodies are detected below the age of 3 years, our study revealed that 7.9% children between 1-3 years had significantly elevated antibodies. This epidemiological pattern is well reflected in the different clinical profile of younger children developing rheumatic heart disease in our country. Antibodies progressively increased with age--11.8% in 4-8 years group to 15.8% in 9-12 years age group. All these were from the lower socio-economic group. ASO was positive in 16.7% of young adults from lower socio-economic status while it was positive only in 9.2% in the upper socio-economic status. A total of 522 patients of rheumatic carditis were studied. Only 23.4% had no antibodies or less than 200 IU/ml, and 77% were positive (26.9% had >400 IU/ml and 49.7% had 200 IU/ml). Throat swab culture and ASO antibodies were done simultaneously in 76 outdoor patients, clinically diagnosed as acute bacterial pharyngitis. Group A beta hemolytic streptococci were isolated in 64% and significant antistreptolysin antibodies were seen in 62%. School health records were scanned in more*

In developing countries, the high incidence of upper respiratory infection assumes special significance due to development of rheumatic fever. The incidence of rheumatic fever may be as high as 3% during an epidemic or as low as 0.3% in endemic areas(1). Diagnosis of rheumatic fever is often presumptive, based on suggestive clinical pattern backed by the proof of antecedent streptococcal infection. Anti streptolysin O (ASO) titre is the commonest test used to detect evidence of streptococcal infection. The higher the titre more is the probability of rheumatic fever(2). Western studies have shown that ASO is very much dependent on age and socio-economic factors. ASO titre needs to be considered in the context of an existing epidemiological pattern in a particular geographic area. In the Western set up, an ASO of >200 IU/ml by latex test is consid-

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*than 50,000 school children. Point prevalence of rheumatic heart disease was estimated to be 0.17% in lower and 0.05% in upper socio-economic groups. Age and socio-economic factors are important variables in epidemiology of streptococcal infection. ASO test must be carried as paired sera in streptococcal disease and rheumatic fever where diagnosis has far reaching implications.*

**Key words:** *Epidemiology of streptococcus, Antistreptolysin titre, Throat swab culture, Rheumatic fever, Rheumatic heart disease.*

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ered a screening point(3). Since ASO persists for 4-6 months, it is likely that healthy individuals in an endemic area may have persistently high titre due to repeated exposures. It is thus necessary to collect data in our own population for any meaningful interpretation. For diagnosis of recent infection a three-fold rise in antibodies at the interval of 2-3 weeks, *i.e.*, paired sera are mandatory(4,5).

However, this is rarely done in routine practice due to cost and other factors, and clinicians tend to rely on a single ASO estimation.

To get an epidemiological background of streptococcal infection in the community, we decided to study ASO titre in health and diseased states and to find out the incidence of rheumatic fever in the city of Bombay. The aims of the study were: (i) to determine ASO antibodies in normal children compare with patients of rheumatic fever, (ii) to assess ASO antibodies in children suffering from clinically diagnosed streptococcal sore throat and correlate with bacteriological cultures of the throat, and (iii) to find out the point prevalence of rheumatic heart disease in children under 15 years.

### Material and Methods

Children between the age of 1 month and 12 years attending a general hospital for various non-infective conditions were selected to represent normal child population. Young voluntary blood donors from both lower and upper socio-economic group and free from recent infection were selected. ASO antibodies were estimated in all these, forming the normal population for this study.

Data on ASO antibodies in patients suffering from acute rheumatic carditis was collected retrospectively as well as pro-

spectively from two general hospitals. Diagnosis of rheumatic fever was made by radiological and electrocardiographical criteria,(4,6). Patients with rheumatic carditis were those who were considered by their physicians to be in the active stage of the disease and were treated by aspirin or steroids. These children represented the population of rheumatic fever patients in this study.

Children clinically diagnosed as suffering from acute bacterial throat infection were subjected to throat swab for bacteriological examination and blood examination for ASO antibodies on the same day.

ASO antibodies were estimated by using latex ASL reagent—Rapi Tex Kit manufactured by Hoechst Laboratories. The test is carried out by diluting one part of serum to 5 parts of 0.9% normal saline and then adding 1 drop of the reagent to one drop of diluted serum. Presence of marked agglutination seen after two minutes indicated positive test, and in such case, further dilution of 1 part of serum to 10 parts of 0.9% saline was done and tested similarly. Positive agglutination with 1 : 5 dilution indicated ASO antibodies of 200 IU/ml, while with 1 : 10 dilution indicate 400 IU/ml and so on.

The latex test detects titres of 200 IU/ml and above which is the western cut off point. It is reproducible and easy to perform. To maintain consistency all the tests were personally done by one of the authors. The tube dilution test is more sensitive and detects levels even below 100 IU/ml. We did not wish to establish mere positivity of ASO titre, but we wished to detect healthy individuals who harbored a significant ASO titre of >200 IU/ml. Hence, we chose the latex test.

Health records of 39,868 children attending free municipal school were scruti-

nized to collect data on presence of heart murmurs diagnosed as rheumatic in etiology. These children were examined by a team of municipally employed doctors and clinically suspected cases were further investigated at various general hospitals to confirm the etiology of the murmurs. Similar data was collected in 12,124 children attending private schools. These represented the high socio-economic group as compared to the municipal school children.

## Results

Of the 522 patients of rheumatic fever, 122 (23.4%) had either no antibodies when subjected to the latex test or insignificant antibodies when subjected to tube test. Two hundred and fifty six (49.0%) had ASO antibodies of 200 IU/ml and 144 (27.6%) had ASO antibodies of >400 IU/ml).

Children below the age of one year had no detectable ASO antibodies. A significant number of normal children showed ASO antibodies (*Table I*). They progressively increased from 7.9% in the age group of 1-3 years to 15.8% in the age group of 9-12 years. All the children below 12 years belonged to the low socio-economic group. The children above 12 years and young adults showed ASO positivity in 10%. In lower socio-economic group ASO positivity was 16.7% and in the higher socio-economic group it fell to 9.2% (*Table II*). The ASO antibodies showed 85% specificity and 80% sensitivity.

Throat swab and blood culture done on the same day in 76 patients showed rampant streptococcal infection in our set up, (*Table III*). We had 65% cases with culture positive for Group A beta hemolytic streptococci and 64% with ASO antibodies. Both culture and ASO antibodies positive were seen in 50% cases.

**TABLE I**—ASO Antibodies in Normal Population ( $n=787$ )

Age	Total	Male	Female	ASO +ve	%	% of Total
<1	67	39	28	0	0.0	0.0
1-3	114	65	49	9	7.9	1.1
4-8	153	80	73	18	11.8	2.3
9-12	165	88	77	26	15.8	3.3
>12	288	180	108	31	10.8	3.9
Total	787	452	335	84	10.7	10.7

Eighty-four (10.7%) of normal population had high ASO of >200 IU/ml, 17 (2.1%) had ASO >400 IU/ml

**TABLE II**—ASO Antibodies in Normal Population—Young Adults ( $n=288$ )

Socio-economic	No.	ASO +ve (>200 IU/ml)	ASO +ve (>400 IU/ml)	%
Low	60	7 (11.6%)	3 (5.0%)	16.6
High	228	19 (8.3%)	2 (0.9%)	9.2
Total	288	26 (9.0%)	5 (1.7%)	10.7

The point prevalence of rheumatic heart disease (*Table IV*) was significantly higher (0.17%) in the lower socio-economic group as compared to the higher socio-economic group (0.05%).

## Discussion

A review of western literature showed ASO test to have a sensitivity of 75-80%(1). Specificity in that population is also high because healthy individuals rarely demonstrate significantly high ASO antibodies, except in the slum population of San Francisco where 20-30% of normal

rheumatic carditis patients had ASO antibodies (*Table III*). It is well known that higher the antibody titre, the more is the probability of rheumatic fever(11). As high as 23% had no titres or titre of <200 units where tube test was used. Probably most were picked up late in the course of the disease when antibodies had already declined. It has also been documented that rheumatic carditis has higher ASO antibodies as compared to rheumatic carditis(8).

The effects of socio-economic factors on the incidence of rheumatic heart disease is well borne out in our study. The children of lower socio-economic status attending municipal schools had a higher point prevalence as compared to high socio-economic group. The overall incidence of 0.15 compares well with the report of Delhi children in 1958(12). Multicentric studies done in various states of India, show a wide variation. The incidence is as low as 1.23% in Madras and as high as 3% in Shimla(13). Chandigarh has an incidence of 0.16%(14). This emphasizes the need of periodic data collection from various centers.

Where streptococcus is endemic, the risk of rheumatic fever becomes less. Endemicity of streptococcus disease in our set up of Bombay city is provided by this study, by the presence of high degree of streptococcal infection and low prevalence of rheumatic fever. This is well borne out by a recent ICMR study which showed the incidence of rheumatic disease to be 1.8/1000 in Bombay children as compared to 11.2/1000 in Delhi children(15).

The results of present study in acute bacterial throat infection show how rampant streptococcal infection is in our set up. Many ICMR studies(16-18) show that 5-15% of healthy school children and 50%

of general population has positive throat cultures. Another ICMR study(19) showed that 15% children had positive throat culture of which two thirds showed ASO antibodies. A study from Vellore(20) documented that 39% of suspected pharyngitis had raised ASO antibodies without positive culture.

It is evident from our data that the western cut off point of 200 IU/ml has limitations in our set up. This 15% of normal individuals can be misdiagnosed as having recent streptococcal infection while 20% cases of rheumatic carditis can be missed. This can be overcome by use of paired sera and demonstration of more specific streptococcal antibodies by better tests.

In conclusion, our study demonstrates that over diagnosis of rheumatic fever is a distinct possibility, if the diagnosis is based on a single ASO estimation, especially on the presence of vague clinical parameters. When in doubt, a repeat ASO titre and/or additional tests for more specific antibodies should be performed. We surveyed four leading laboratories in Bombay city and found that physicians rarely ask for paired ASO titres. The waiting period and the cost is worth while if one considers the long term impact of the diagnosis and prophylaxis of rheumatic fever on the child, family and economics of society. There is need to monitor local epidemiology for meaningful interpretation of ASO titre. Use of Western cut off point of 200 IU/ml needs to be revised in relation to our local epidemiology.

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