

**THE UTILITY OF A SINGLE ANTI STREPTOLYSIN O TITER IN THE DIAGNOSIS OF ACUTE RHEUMATIC FEVER**Anil Shetty<sup>1</sup>, Vitus D'Silva<sup>2</sup>**HOW TO CITE THIS ARTICLE:**

Anil Shetty, Vitus D'Silva. "The Utility of a Single Anti Streptolysin O Titer in the Diagnosis of Acute Rheumatic Fever". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 30, July 28; Page: 8372-8377, DOI: 10.14260/jemds/2014/3055

**ABSTRACT: BACKGROUND:** Acute Rheumatic Fever still affects millions of children in the developing world, the diagnosis of rheumatic fever is based on the Jones criteria and supporting evidence of preceding streptococcal infection from a positive throat culture or elevated ASO titers. However, some clinicians have questioned the role of a single ASO titer in the diagnosis of acute rheumatic fever. **AIMS AND OBJECTIVES:** To determine the utility of a single ASO titer level and its correlation with Jones major criteria. **MATERIAL AND METHODS:** 12 children diagnosed with rheumatic fever at our hospital in the preceding two years were included. A single ASO titer done in these children using a turbidimetric immunoassay was recorded **OBSERVATIONS:** The ASO titer levels ranged from 185 to 1691 IU/ml. The highest levels were seen with features of acute carditis and the lowest levels in association with chorea. **CONCLUSION:** A single ASO titer retains its role as a useful diagnostic tool and inversely correlates with disease progression.

**KEYWORDS:** Antistreptolysin O titer, Acute Rheumatic Fever, Carditis, Chorea, Jones Criteria.

**INTRODUCTION:** Rheumatic Fever develops two to three weeks after an antecedent streptococcal infection. It is believed that the disease results from antibody cross reactivity and affect the joints, skin, heart and brain. Acute rheumatic fever can manifest in children between the age of 5 and 14 years. In 2005 it was estimated that 15.6 million people suffer from Rheumatic Heart Disease all over the world.<sup>1</sup>A huge proportion of these cases are seen in the Indian Subcontinent.<sup>2</sup> The diagnosis of Rheumatic Fever is made using the Jones criteria.

The Jones Criteria was originally proposed by Dr T Duckett Jones and have been revised several times. The major criteria include carditis, polyarthritis, erythema marginatum, subcutaneous nodules and chorea. The minor criteria include fever, arthralgia and laboratory findings of elevated erythrocyte sedimentation rate, C-reactive protein and prolonged PR interval on ECG. Acute Rheumatic Fever is diagnosed in the presence of two major, or one major and two minor manifestations and must be accompanied by supporting evidence of antecedent group A streptococcal infection in the form of positive throat culture or elevated or rising anti-streptolysin titer. Indolent carditis, chorea and previous history of rheumatic fever or rheumatic heart disease are exceptions to Jones Criteria.<sup>3</sup>

Streptococcal antibody tests are used for the diagnosis of infections caused by group A Streptococcus and are particularly useful in the diagnosis of acute rheumatic fever and post-streptococcal glomerulonephritis.<sup>4</sup> Ideally it is recommended that the titers be done in both the acute and the convalescent phase, 14 to 28 days later with a positive result defined as a two- fold or more rise in the titer.<sup>5</sup> Often it is not feasible to get a second titer, then a single titer greater than the upper limit of normal can be considered evidence to presume streptococcal infection.<sup>6</sup>

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There is an ongoing debate among clinicians about the real utility of ASO titer levels. A study in the US concluded that in areas of low rheumatic fever incidence abnormal streptococcal antibody titers have poor diagnostic value and repeat testing has no treatment value.<sup>7</sup> In India most centers employ only a single ASO titer during first out-patient contact or at admission in making a diagnosis of acute rheumatic fever. The purpose of this study is to determine if a single ASO titer is useful in the diagnosis of acute rheumatic fever and if the clinical presentation at diagnosis has a bearing on the ASO titer levels.

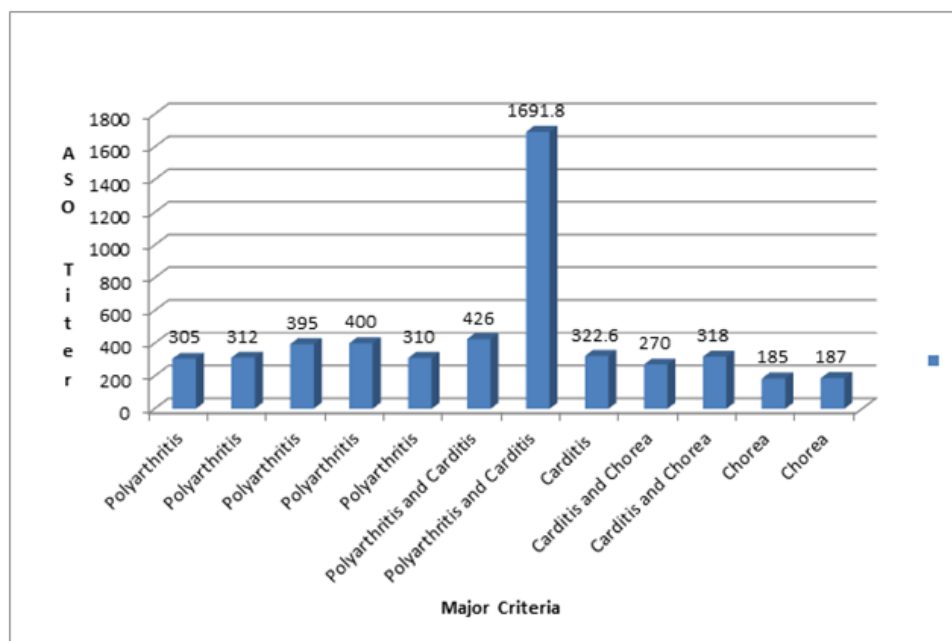
**MATERIAL AND METHODS:** The subjects included in the study were pediatric patients diagnosed with Rheumatic fever in our hospital between 2011-2013. The diagnosis was made utilizing the Duckett Jones criteria. Chorea, polyarthritis, carditis, subcutaneous nodules and erythema marginatum are the major criteria. Subcutaneous nodules and erythema marginatum were not observed in any of the patients in our study.

However the other 3 major criteria were present either in isolation or in combination among rheumatic fever patients in our study. Twelve patients were diagnosed with rheumatic fever between 2011 and 2013. A single Anti Streptolysin O titer was obtained from all patients at admission. The ASO titers were done using particle enhanced turbidimetric immunoassay.

This is based on the reactions between antibodies against streptolysin O and the values are determined photometrically. The ASO titers obtained were correlated with the major criteria.

**RESULTS:** The study collected data on all patients diagnosed with Rheumatic Fever in our Hospital in years 2012 and 2013. Three were females. The youngest child included was 5 years old and the oldest was 13 years.

Figure 1: shows the correlation of the ASO titer obtained from 12 rheumatic fever patients and the major Duckett Jones criteria observed in the same 12 cases.



**Figure 1: Correlation of ASO Titer and Major Criteria for Rheumatic Fever**

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Among the Twelve children, in five polyarthritis was the only major criteria at diagnosis, two patients had features of carditis and polyarthritis. One child had carditis alone, two others had features of carditis and chorea and two presented with isolated chorea alone. The highest ASO titer observed was 1691.8 IU and the lowest ASO titer was 185 IU. The lowest ASO titers were observed in the patients who had only chorea as major criteria. The highest ASO titer levels were observed in the child who had features of acute carditis. Except the patients who had chorea, all the others had ASO titers exceeding 300/IU.

**DISCUSSION:** An elevated ASO titer is more likely than a positive throat culture in an antecedent streptococcal infection and this provides supporting evidence in making a diagnosis of an acute rheumatic fever. In our study except in the case of isolated chorea the ASO titers were elevated. One factor that could have an influence on determining ASO levels is the geographical location. A study compared the Streptococcal antibody titers of children with rheumatic fever and without rheumatic fever in a low incidence area, Florida and a high incidence area, Grenada.

In Grenada there was no consistent difference in the mean antibody titers of rheumatic and non- rheumatic children. Where- as in Florida the streptococcal antibody titers in rheumatic children was significantly higher than non- rheumatic subjects.<sup>8</sup> A study in Portugal investigated 78 children with Acute Rheumatic Fever at admission and follow up, also 22 children with Chorea, 45 children with recurrent tonsillitis and 23 with Juvenile idiopathic arthritis were also similarly followed up and the researchers concluded that a reappraisal of the ASO titers in Acute Rheumatic Fever indicates a significant response in the acute phase and helps to distinguish it from other diseases with high ASO titers.<sup>9</sup>

There is no unanimity or consensus among clinicians about the absolute usefulness of ASO titer and different studies have provided contrary results and conclusions. A study in Poland however concluded that an increased serum antibody titers to streptolysin O is usually indicative of recent streptococcal infection and not active rheumatic fever.<sup>10</sup> A Belgian study concluded that the only practical use of ASO test is in the diagnosis of acute rheumatic fever in Pediatrics and the standardization of current automated ASLO assays is limited.<sup>11</sup> A retrospective study on 45 children below 4 years concluded that Anti-Streptolysin O titer is useful in the evaluation of tonsillitis to differentiate between those cases due to group A beta-hemolytic Streptococcus and those that are viral in origin.<sup>12</sup>

Since Rheumatic fever is more prevalent in developing countries, studies done in developing countries have included more subjects and have indicated more utility for ASO levels. An Egyptian study enrolled 660 children and divided them into six groups, Group 1 had 200 healthy children, Group 2 had 20 children diagnosed with the first attack of Acute Rheumatic Fever, Group 3 had 40 children with recurrent Rheumatic Fever, Group 4 had 100 children with Rheumatic heart disease on long acting penicillin, Group 5 had 100 children with acute follicular tonsillitis and Group 6 had 200 children with history of 3 or more episodes of follicular tonsillitis in a year. Upper limit of normal for ASO titer was 400 IU in the first group, 200 IU in group 4 and 1600 IU in group 6. Significantly high titers were seen in Group 2.<sup>13</sup>

In our study a child diagnosed with the first attack of rheumatic fever had a significantly high titer while children with carditis but diagnosed later had relatively lower ASO titers. A number of factors have a bearing on the ASO titers and various studies have indicated a variety of factors that

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can influence ASO levels. The upper limit of normal for ASO titer is influenced by the geographical location, site of infection and season.<sup>14</sup> Also, normal titers among school age children are higher than among adults.<sup>15</sup>

A study in Fiji collected 424 serum samples and determined that the higher limit of Anti Streptolysin O titre at age 10 years was 276/IU.<sup>16</sup> Since geography influences ASO levels and areas of high incidence have higher ASO levels, it is imperative to know the upper limit of normal in different areas. The upper limit of normal for streptococcal serology is defined by separating the upper 20% from the lower 80% of the group, this is due to the fact that 80% of patients with acute rheumatic fever have streptococcal titers that are above the 80th centile for the healthy control.<sup>16</sup>

Different studies in various other countries have shown a wide range of results. In an 1998 US study it was 240 IU/ml.<sup>17</sup> 326 IU/ml in an Korean study,<sup>18</sup> 200 IU/ml in Tanzania.<sup>19</sup> Studies in India also have shown a wide variation in ASO levels, 200 healthy school children in Mysore had their ASO titers tested and the upper limit of normal ASO titer was 242/IU.<sup>20</sup> In another study conducted in India it was 239 IU/ml<sup>21</sup> and 305 IU/ml in a study conducted in Mumbai.<sup>22</sup> In the present study most cases had titers exceeding 300 IU/ml and titers lower than 300 IU/ml were seen only in association with chorea.

The Egyptian study postulated that high levels of ASO titer in acute carditis may be due to the time gap between the infection and the onset of carditis, which results in the titers reaching its peak level and in contrast in patients with rheumatic chorea the long time gap between infection and onset of chorea results in a decline in the ASO titer.<sup>13</sup> In chronic Rheumatic Heart disease the ASO titer may go below even normal controls and this is attributed to the natural course of streptolysin response and the effect of penicillin.<sup>23</sup>

**CONCLUSIONS:** Our study reveals that ASO titer has a utilitarian role in the diagnosis of Acute Rheumatic Fever. Even a single ASO titer was a useful investigative tool aiding in the confirmation of the diagnosis. The ASO titers were elevated in the acute phase and show a subsequent lower titer levels as the disease progresses and reaches its nadir with the appearance of chorea. This is consistent with the findings of other studies. One major limitation of our study was the number of cases included but was probably inevitable because the incidence of rheumatic fever has shown a marked downward trend.

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Date of Submission: 07/07/2014.

Date of Peer Review: 08/07/2014.

Date of Acceptance: 15/07/2014.

Date of Publishing: 23/07/2014.