COMPARATIVE STUDY BETWEEN ANTI-STREPTOLYSIN O TITRES AND STREPTOKINASE ANTIBODY TITRES IN RHEUMATIC PATIENTS AND IN PATIENTS WITH ISCHAEMIC HEART DISEASES

M.Sc. THESIS SUBMITTED FOR PARTIAL FULFILMENT OF MASTER DEGREE IN CLINICAL AND CHEMICAL PATHOLOGY

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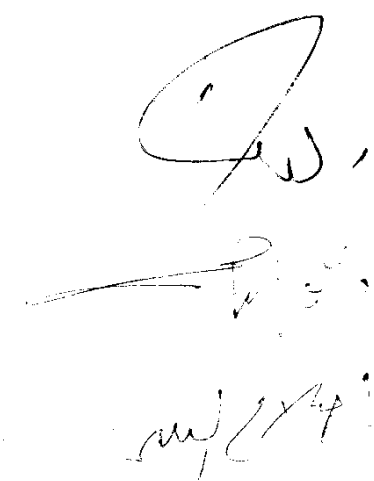

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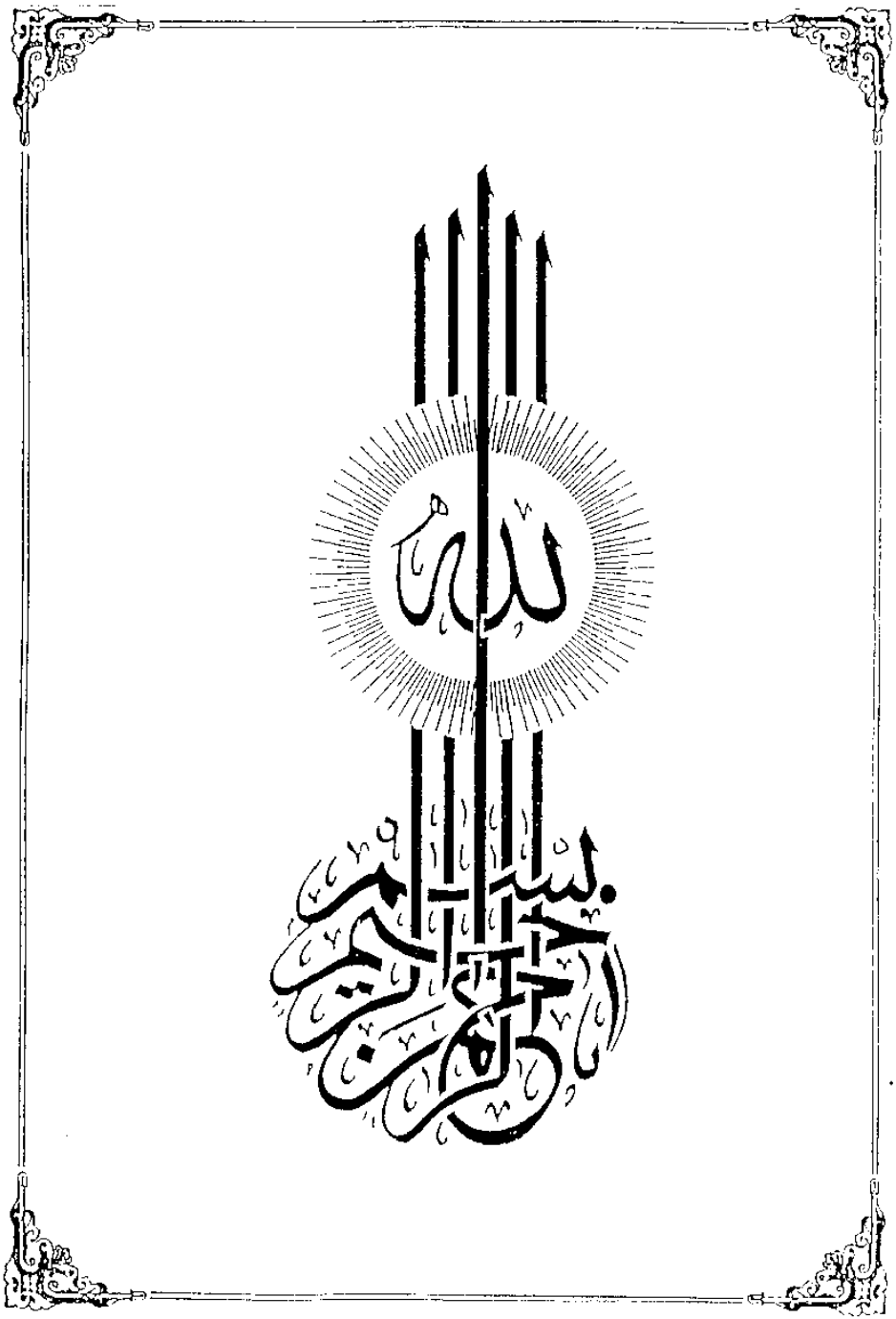

To my husband Mr. Amr Ahmed Lotfy

"Actually his encouragment was the radical factor for the completion of this work"

Contents

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Introduction and Aim of the work

Streptococcus pyogenes has been encountered in the pathogenesis of many diseases.

The aetiology of rheumatic fever has been attributed to the presence of abnormal cellular and humoral immune response to group A haemolytic streptococci. (Zabriskie, 1985).

Serologic methods for the diagnosis of group A streptococcal infections have proved to be of considerable importance for both the physician and the clinical investigators. (Bisno, 1974)

Most clinical diagnostic laboratories perform only a single streptococcal antibody determination which is the antistreptolysin O (ASO) test. Unfortunately ; approximately 20% of patients with acute rheumatic fever have normal serum titre of ASO (Stollerman et al., 1956) and a similar percentage of rheumatic patients present with low or borderline ASO titre (250 units or less) (McCarty, 1954). This problem may be largerly overcome by measuring in addition to ASO, serum antibodies to other known extracellular products of group A streptococci (Stollerman et al., 1956).

The determination of antistreptokinase (ASK) beside ASO has proved to be valuable in 15-20% of cases with scarlet fever or epidemic exudative tonislitis who failed to develop significant rise of ASO titre (Commission on Acute Respiratory Diseases, and Kaplan, 1945).

The aim of this work is to try to detect the relationship between ASO and ASK tests and the increase in the percentage of positivity of ASO test with the additional performance of ASK test. Moreover, we aim to detect the pathologic titres of both ASO and ASK in our population since their normal upper limits are usually variable in different populations due to changes in age, economic status, season, year and other factors related to the frequency of streptococcal infections (Rantz et al., 1948).

In addition, the new trend to use the streptokinase as a successful thrombolytic therapy in the treatment of acute myocardial infarction (AMI) raise our interest to detect the possible causes of unexpected high ASK titres which lead to the clinical failure of the treatment (Lew et al., 1984). So in this work, we will try to detect the percentage of patients with AMI having high ASK titres and to detect the possible cause of such high titres which may be the presence of antecedent streptococcal infection.

Streptococcus pyogenes

The name streptococcus pyogenes was early given by Rosenbach, 1884, to the organism that grows in chains and isolated from suppurative lesion in man. Now it coincides with streptococcal strains that have the group A polysaccharide antigen (Sherman , 1937) except for few strains of streptococcus milleri (Colman, 1968).

Morphology and cultural character

They are gram positive cocci that divide in one plane to form chains. They are non motile and non spore forming. They may be capsulated but the capsule can be only demonstrated in young streptococcal culture; since , such hyaluronic capsule may be destroyed by the production of the hyaluronidase enzyme (Pike, 1949).

Streptococci are aerobes and facultative anaerobes; the optimum temprature for their growth is 35-37 ^{o}C . They grow poorly on ordinary nutrient media but the growth is rapid on media enriched with blood, serum or glucose. They produce beta haemolysis when cultured on blood agar medium as a result of production of streptolysin S (Herbert and Todd, 1944). It appears as clear zone of complete haemolysis that surround the well defined streptococcal colonies. Certain serotypes may give small zone of incomplete clearing possibly due to the production of opacity factor as it may inhibit the liberation of streptolysin S (Pinney et al, 1977)

Serological Classification of Streptococci:-

Studies of Griffith, 1934 and Lancefield, 1941, clarified the antigenic differences in these organisms and they applied firm bases for their serological classification.

Griffith, 1934, classified the heamolytic streptococci according to their T- proteins . While, Lancefield,1941, divided the streptococci into groups from A to O, according to the serologic specificity of the polysaccharide components of the cell wall, these represent the group specific polysaccharide antigens. Lancefield further subclassified the group A haemolytic streptococi, which are the main cause of infections in man and animal, according to the presence of type specific M protein antigens into more than 40 different types; now more than 80 types are recognized. (Zabriskie, 1985).

Epidemiology:-

Streptococcal infections can occur all over the year but it is more common in spring and in winter months (Murray et al, 1977). In a long term study, it was found that the attack rate of tonsillopharyngitis of different aetiology was 8.4% cases per year, 43% of such cases had streptococcal aetiology (Duben et al., 1978)

In Egypt, it was found that the attack rate of streptococcal infection among Egyptian school children is 6 per 1000 per week proved by the isolation of the organsim and the associated rise of ASO titre (El Kholy et al. 1973)

Review of Literature

Mode of Transmission:-

Respiratory streptococcal infections are transmitted mainly through the nasal discharges of a person harboring beta-haemolytic streptococci. (Jawetz et al. 1980) In addition, contaminated food may be considered as an occasional cause of explosive out break of pharyngitis (Hill et al.. 1969). However, the role of contaminated blankets or clothings is doubtful (Jawetz et al, 1980).

Pathogenicity and Virulence of group A streptococci:-

Pathogenicity denotes the ability of the organism to cause disease or to result in the production of progressive lesion, while virulence is the ability to do this with few number of organisms.

The virulence of group A streptococci could be explained in 3 main headings which are

I- The production of erythrogenic toxin .

II- The resistance to phagocytosis

III- The liberated extracellular enzymes.

I-The production of erythrogenic toxin:-

It is an antigenic toxin produced only by the group A beta haemolytic streptococci. It is responsible for the skin lesion that accompany scarlet fever (Dochez and stevens, 1927) There are three immunologically distinct erythrogenic toxins which are A,B (Hooker and Follensby, 1934) and C (Watson, 1960). This explains the

occasional occurrence of several episodes of scarlet fever in the same person. The purified form of this erythrogenic toxin is called the streptococcal pyrogenic toxin which have two distinct activities explained by Watson and Kim, 1970 as follow.

I) Primary toxicity, which is neutralized only by antisera against the homologous exotoxin; and may play a role in the pathogenesis of streptococcal infections quite independant from the ability to give rise to skin rash.

2) Secondary toxicity which arises from the induction of hypersensitivity to streptococcal products and also to other antigens. It shows cross reactivity with other types of pyrogenic exotoxins. The secondary toxicity is responsible for the characteristic rash of scarlet fever by inducing hypersensitivity of delayed type and enhancing the local arthus reaction.

However, the highly purified toxin is poorly antigenic (Watson and Kim, 1970)

II-The resistance to phagocytosis:-

The virulence of group A streptococci is mainly dependant on their ability to resist phagocytosis. This has been well correlated with the presence of the M-protein surface antigen (Lancefield, 1962, Fox, 1974). It may alter the deposition of the C_3 component of the complement and hence it hinders the phagocytic process (Fearon and wong, 1983). Another cause, may be the release of streptococcal chemotactic inactivator which delay the

polymorphonuclear neutrophil migration until the bacterial establishment is happened (Wexler et al, 1983).

III-The liberated extracellular enzymes:-

The group A beta haemolytic streptococci produces large number of enzymes which may be contributed to its pathogenecity and its virulence. These enzymes include the followings.

1) Haemolysin. (streptolysin)

The confusion concerning the haemolytic properties of the streptococci has been clarified by Todd, 1938, on the fact that streptococci produce two kinds of haemolysin, the streptolysin S and streptolysin O.

a) Streptolysin S.

It is a non antigenic enzyme or at least no antibodies could be detected against it (Stollerman and Bernheimer, 1950). It is responsible for the beta haemolysis detected on the surface of the blood agar plate (Herbert and Todd, 1944). It is produced only in the presence of serum (Weld, 1934); hence the name streptolysin S given later on by Todd, 1938. Several other agents can induce the formation of the streptolysin S such as ribonucleic acid (Bernheimer and Rodbart , 1948; Bernheimer, 1949), lipoproteins and certain detergents (Ginsburg et al., 1963). Inspite of the tight binding of the streptolysin S to streptococci, the presence of any of the previously mentioned agents in the culture media will absorb the streptolysin S from the surface of the streptococci (Ginsburg et al., 1963).