INTRODUCTION

The throat is an area where microorganisms are most abundantly found. It is known to permit the passage of organisms through the epithelium which may be deficient at places, into the lymphatic tissues and bear the brunt of all individual attacks of disease ***(Agrawal et al., 2014)***.

The range of organisms cultured from the throat both in health and disease is extremely variable, the organism most commonly identified from the throat in disease is the group A beta haemolytic streptococcus (GAβHS). Up to 40 percent of asymptomatic individuals will also have a culture positive for this organism. In recurrent tonsillitis the samples grew a range of pathogens but the predominant organisms were Haemophilus Influenza and S. aureus. A mixed flora was also common. Beta haemolytic streptococci were less common ***(Al-Hameed et al., 2014)***.

The prevalence of group A BHS carriage in the throat of school children varies from 13 to 50% depending upon the population studied, season and other factors ***(Sumanta et al., 2015)***.

Commonest organisms isolated include Staphylococcus aureus, Haemophylus influenza, Alpha-haemolytic streptococci, Pneumococcus, Enterococcus, non-pathogenic Neisseria species,

Bacteroidsfragilis group and Corynebacterium species. No anaerobes are identified ***(Agrawal et al., 2014)***.

Throat swabs are often used as a guide in identifying the organism and the proper selection of therapy in acute and recurrent tonsillitis, however, their use may lead to incorrect conclusions ***(El Galil et al., 2014).***

A study from Libya reported that out of the total isolates, Staphylococcus aureus was the most prevalent organism, followed by Streptococcus pyogenes and Klebsiella pneumonia (17.71, 12.34, and 11.27% respectively). Pseudomonas aeruginosa represented 6.26%. Serratia marcescens and Morganella morganii were the least isolated organisms. Staphylococcus aureus was the most prevalent organism in males (21.16%) while in females Strept. Pyogenes was the most prevalent organism (14.29%). Also, the study revealed that Staphylococcus aureus was the most frequent isolate in age groups between 1-20, 21-40 and 41-60 years old (20.85%, 17.02% and 16.67% respectively). However, both Staphylococcus aureus and Klebsiella pneumoniae were isolated with equal incidences, 12% each, in elder patients (more than 60 years) ***(Eldeeb and Khashan, 2006)***.

In another study ***El Galil et al. (2014)***, carried on Egyptian subjects, Bacterial isolates from throat swabs revealed that *Staph aureus* was the commonest isolate, this was in

agreement with the findings of *Abdulrahman et al. and Yildirim et al.* ***(Abdulrahman et al., 2004; Yildirim et al., 2003).***

A study from India that out of total 375 throat swabs reports 30 coagulase staphylococcus and 87 staphylococcal aureus pathogenic organisms were isolated. 62 cultures revealed group alpha b haemolytic streptococcus. Pseudomonas aeruginosa were grown in 9 cases and klebsiella pneumoniae were seen in 16 reports. Escheresia coli was grown in only 6 culture. In 125 cases no pathogenic organisms were grown. And no growth was obtained in 40 cases. Diphtheroid was grew in 8 cases. Thus total number of reports showing known pathogens were ***(Pramod et al., 2013).***

This study is therefore done to know the prevalence of throat carriage of different bacteria common in Egyptians as compared to Libyans of various age and sex.

AIM OF THE WORK

To determine if the commonest causative organisms in the studied patients, in comparison between Egypt and Libya, to determine the prevalent bacteria whether commensal or pathogenic among both children and adults.

REVIEW OF LITERATURE

Pathophysiology of Tonsillopharyngitis:

Pharyngitis is defined as an acute inflammation of pharynx, tonsils or both. It typically present as sore throat, particularly upon swallowing, and is often accompanied by fever and headache ***(Gerber, 2005).*** Acute pharyngitis is one of the most common reasons for children's visits to primary care physicians or paediatricians ***(Carapetis et al., 2005a).***

The etiology is usually infectious, with most cases being of viral origin. These cases are usually benign and self-limiting ***(Wessels, 2011).*** The most significant bacterial cause in children and adults is streptococcus Pyogenes (S.Pyogenes), also known as group A beta-hemolytic streptococcus (GABHS). It estimated to account for 20-40% of cases of acute pharyngitis in children ***(Shaikh et al., 2010).***

GABHS pharyngitis assumes a special significance because of the risk of suppurative complications or non suppurative post-streptococcal diseases.

Including acute rheumatic fever and rheumatic heart disease, acute glomerulonephritis, Scarlet fever, streptococcal toxic shock syndrome and pediatric autoimmune neuropsychiatric disorder (PANDASI) ***(Choby, 2009).*** In low-income countries, rheumatic heart disease remains the most commonly acquired

heart disease in children, adolescents and young adults ***(Carapetis et al., 2005b).***

I. Epidemiology:

The incidence of GABHS pharyngeal infections varies between countries and also within the same country depending on several factors including age group, season, socioeconomic conditions, environmental conditions and level of primary health care ***(Ralph and Carapetis, 2013)***.

The disease is predominantly of school age children, with incidence peaking between 5-15 years of age (37%) compared to children < 5 years (24%). The prevalence of GABHS pharyngitis is significantly lower for children <3 years of age, ranging from (10-14%) ***(Chiappini et al., 2011)***. The disease is rare in infants, due to transplacental maternal immunity ***(Stevens and Kaplan, 2002)***.

The incidence peaks during the late winter and early spring seasons, and is more common in cooler and temperate climates ***(Bessen, 2009)***.

GABHS pharyngitis is everywhere but is more frequent in low-income countries. Crowding and poor hygiene increase the chance of an outbreak of GABHS infections ***(Cunningham, 2008)***. So, close interpersonal contact in schools, military quarters, dormitories, and families with several children appears to be a risk factor for the disease ***(Lindbaek et al.,***

2004). Asymptomatic pharyngeal carriage of GABHS occurs in (3-26%) of healthy children, and (3-17%) of children younger than 5 years of age ***(Shaikh et al., 2010)***. The pathogen can be found in its carrier state without causing illness in the pharynx for weeks or months and can spread the infection ***(Bessen, 2009)***.

II. Mode of transmission:

Transmission of GABHS is believed to occur by direct person-to-person contact, most likely through droplets of saliva or nasal secretions ***(Ryan and Ray, 2004)***. It has been found that dried bacteria in dust are not infectious, presumably due to a reduction in infectivity after desiccation. However, since *S. pyogenes* may survive on the inanimate objects for up to 4 weeks, environmental hygiene and disinfection should be strictly observed especially within institutions and families ***(Wagenvoort et al., 2005)***.

Food borne streptococcal pharyngitis has long been recognized ***(Bisno and Stevens, 2000)***. Unpasteurized milk used to be a common food vehicle, which was often derived from cows with clinical mastitis**,** also other food items can still be contaminated by asymptomatically colonized food handlers (through hands or respiratory secretions) resulting in outbreaks with high attack rates ***(Levy et al., 2003)***. In contrast to pharyngitis resulting from droplet transmission, food borne cases tend to have a high attack rate (50-90%) and shorter incubation periods ***(Yang et al., 2013)***.

After the bacteria are first taken into the body, there is an incubation period of between 1-5 days. During incubation, the bacteria are very capable of infecting others ***(Choby, 2009)***.

The risk of contagion most likely depends upon the inoculum size and the virulence of the infecting strain, individuals are most infectious during the acute phase of the illness. After antibiotic treatment, the infective period is reduced to 24 hours and most physicians will allow affected children to return to school 36-48 hours after antimicrobial therapy is started ***(Vincent et al., 2004)***.

III. Pathogenesis:

It is thought there are 3 stages in the pathogenesis of GABHS pharyngitis as seen in **(Fig 1)** ***(Fieber and Kovarik, 2014)***.

i. Adherence to the host pharyngeal epithelial tissue, often followed by invasion into and persistence in host epithelial cells.

ii. Nutrient acquisition to enable proliferation in the host.

iii. Evasion (avoidance) of the host immune response.

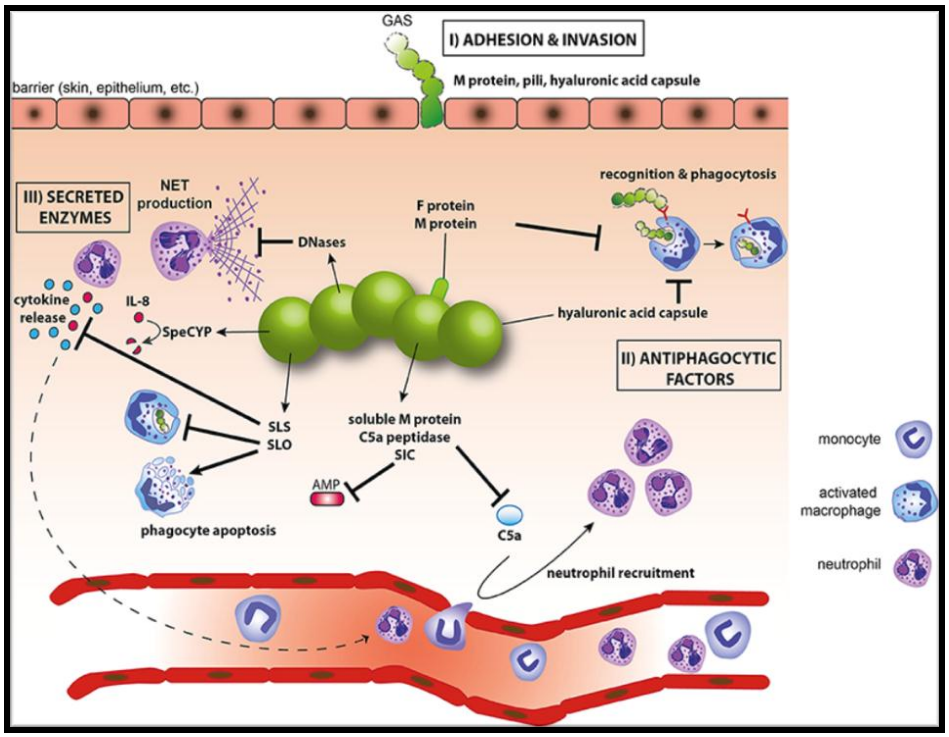


Figure (1): Stages of GABHS pathogenesis ***(Fieber and Kovarik, 2014)*.**

Several adhesins and molecules have been implicated in GABHS adhesion to and invasion of host epithelial cells including Complement 5a (C5a) peptidase, Fibronectin-binding protein of group A streptococci type A (FbaA), Fibronectin-binding protein 54 (FBP54), hyaluronic acid capsule, Lipoteichoic acid (LTA), M protein, pili, Protein F1, Protein F2 and Serum opacity factor (SOF) ***(Shelburne et al., 2008)***. Intracellular persistence of GABHS has been linked to recurrent cases of pharyngitis and may potentially contribute to the failure of penicillin during treatment ***(Henningham et al., 2012)***.

In addition to the capacity to internalize into host cells, GABHS strains have evolved a number of other mechanisms to avoid the host immune response; hyaluronic acid capsule, M protein, Streptococcal inhibitor of complement (SIC), and Protein F1, each has been reported to confer resistance to phagocytosis ***(Hoe et al., 2002 and Hyland et al., 2007)***.

GABHS can also evade the host immune response via streptodanase mediated degradation of Neutrophil extracellular traps (NETs) ***(Walker et al., 2007);*** the inhibition of antimicrobial peptides, mediated by SIC and Superantigens (SAgs) ***(Nyberg et al., 2004 and Fernie-King et al., 2007);*** the interference of complement activation due to the actions of SIC, Streptococcal C5a peptidase (SCP), M protein, Streptococcal collagen-like surface protein 1 (Scl1), and SAgs ***(Caswell et al., 2008 and Terao et al., 2008);*** and the inhibition of neutrophil chemotaxis, via the activity of Streptococcal chemokine protease C (ScpC) ***(Hidalgo-Grass et al., 2006)***.

Once GABHS has established a superficial infection (such as pharyngitis), the secretion of pyrogenic exotoxins contributes to the establishment of scarlet fever ***(Henningham et al., 2012)***.

Staphylococcus aureus is a complex pathogen with numerous classes of virulence factors. A broad array of virulence factors contribute to S. aureus pathogenesis include pore forming toxins (alpha-hemolysin, leucocidin), superantigens (enterotoxins,

toxic shock syndrome toxin-1), phagocytosis inhibitors (polysaccaharide capsule, protein A), and immune evasion molecules (chemotaxis inhibitory protein, staphylokinase, aureolysin). This necessary for protein secretion and establishment of infection. Microbial Surface Components Recognizing Adhesive Matrix Molecules (MSCRAMMs) are cell wall anchored proteins ***(Bartlett, 2010).***

MSCRAMMs are involved in attachment of S. aureus to host cells or extracellular matrix as first step in the development of infection. MSCRAMMs were identified by their ability to bind extracellular matrix proteins such as fibrinogen, fibronectin and collagen ***(Bartlett, 2010).***

IV. Clinical presentation:

The onset of symptoms in patients with bacterial pharyngitis is often abrupt ***(Wessels, 2011)***. Patients with bacterial pharyngitis commonly present with sore throat, severe pain on swallowing and fever with sudden onset (temperature ≥ 38°C). Other symptoms include headache, malaise and muscle pain may be present. Chills may be present but rigors are not typical**.** Gastrointestinal symptoms such as anorexia, nausea, vomiting and abdominal pain are frequent ***(Choby, 2009).***

Cough, coryza, conjunctivitis, hoarseness, runny nose, mouth ulcer and diarrhea are more common with viral pharyngitis ***(Shulman et al., 2012)***.

The severity of streptococcal infection varies greatly, in severe cases in (older children and adults), there is marked pharyngeal pain associated with difficulty in swallowing and high fever (≥ 39°C). These symptoms may be less focal and more gradual in younger children ***(Brook and Dohar, 2006)***. Throat pain may be severe, and it is often worse on one side. However, severe unilateral pain or an inability to swallow should raise concern about a local suppurative complication such as peritonsillar or retropharyngeal abscess, particularly if these symptoms arise or progress several days into the illness ***(Wessels, 2011)***.

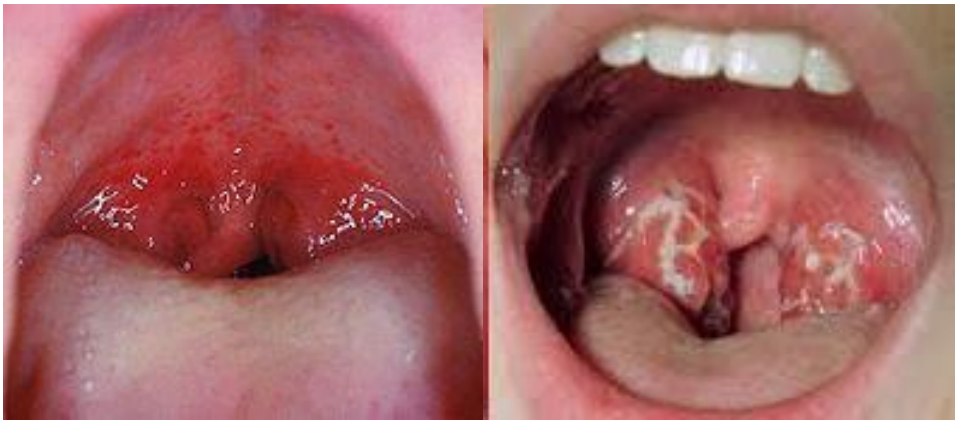
In most persons, fever resolves within 3 to 5 days, and throat pain resolves within 1 week, even without specific treatment ***(Linder et al., 2005)***.

Examination of the throat may reveal erythema and edema of the pharynx and uvula and diffuse erythema and hypertrophy of the lymphoid tissue in the posterior pharynx ***(Lin et al., 2003)***.

The posterior pharyngeal wall may be covered with a greyish-white membrane or exudate. The pharynx is often described as beefy or bright red, with the color ending abruptly at the soft palate. Petechiae may be present on the soft palate as seen in **(Fig 2a)** ***(Choby, 2009)***.

Tonsils are commonly swollen, erythematous, and covered with punctate or confluent greyish-white exudates as

seen in **(Fig 2b)**. The breath is characteristically foul. The anterior cervical lymph nodes are often quite tender and enlarged, especially at the angle of the jaw. This sign occurs early in the course of infection ***(Van Howe and Kusnier, 2006)***.



(a) (b)

Figure (2): Clinical examination of strep throat ***(Choby, 2009).***

(a): Petechiae; small red spots on the soft palate

(b): Large tonsils with exudates

Cervical lymphadenopathy and pharyngeal or tonsillar inflammation or exudates are common signs. Palatal petechiae and scarlatiniform rash are highly specific but uncommon ***(Dos Santos and Berezin, 2005)***.

Pharyngeal vesicles and ulcers are associated with viral upper respiratory tract infections; their presence reduces the likelihood that a sore throat is caused by GABHS ***(Ebell et al., 2000)***.

Chronic pharyngeal carriage is the persistent presence of pharyngeal GABHS without active infection or immune/inflammatory

response. Patients may carry GABHS for 1 year despite treatment. Chronic carriers are at little to no risk of immune-mediated post-streptococcal complications because no active immune response occurs. Moreover, it is not linked to invasive GABHS infections ***(Shulman et al., 2012)***.

Carriage of one GABHS serotype does not preclude infection by another; therefore, throat culture or rapid antigen test is appropriate when GABHS pharyngitis is suspected. Testing is unnecessary if clinical symptoms suggest viral upper respiratory infection ***(Tanz and Shulman, 2007)***.

V. Complications:

GAS pharyngitis can be associated with suppurative and non-suppurative complications ***(Wessels, 2005)***.

A. Suppurative complications:

- Cervical lymphadenitis
- Peritonsillar or retropharyngeal abscess
- Sinusitis
- Mastoiditis
- Otitis media
- Meningitis
- Bacteremia
- Endocarditis

B. Non-suppurative complications:

- Acute rheumatic fever (ARF)
- Post streptococcal acute glomerulonephritis (PSAGN)
- Post streptococcal reactive arthritis
- Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDASI)
- Scarlet fever

1. Acute rheumatic fever (ARF)

Acute rheumatic fever is a post-infectious, non-suppurative sequel of pharyngeal infection with *S. pyogenes*. The disease manifests as an inflammation of the joints (arthritis), heart (carditis), central nervous system (chorea), skin (erythema marginatum), and/or subcutaneous nodules. Of the associated symptoms, only damage to the valve tissue within the heart, or rheumatic heart disease (RHD), can become a chronic condition leading to congestive heart failure, strokes, endocarditis and death ***(Marijon et al., 2012)***.

The cross-reactivity is believed to occur through molecular mimicry, where all or part of a M protein resembles at least some portion of host tissue ***(Cunningham, 2003)***. In ARF and RHD, the M-protein crosses react with cardiac myosin, which induces T-cell mediated attack of the heart tissue and valves ***(Guilherme et al., 2007 and Gorton et al., 2011)***. Once valve tissue is damaged and inflamed, proteins that are