EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 7
223-227
Year: 2019

PREVALENCE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF GROUP A STREPTOCOCCAL ACUTE PHARYNGITIS AMONG PATIENTS AT PRIMARY HEALTH CENTRES, MISURATA, LIBYA

Noura Alhadi Shaklawoon[1,2], Chinnasamy Selvakkumar[1]*, Abdulrahman Abdalla Allabidi[1], Rugaia Rajab Rafieda[1], and Rabia Mohamed Oraet[3]

[1]Department of Microbiology & Immunology, Faculty of Medicine, Misurata University, Misurata, Libya.
[2]Department of Pediatrics, Al-Saeed Hospital, Misurata, Libya.
[3]Department of Pediatrics, Qasser Ahmed Hospital, Misurata, Libya.

***Corresponding Author: Chinnasamy Selvakkumar**
Department of Microbiology & Immunology, Faculty of Medicine, Misurata University, Misurata, Libya.

Article Received on 28/04/2019 **Article Revised on 19/05/2019** **Article Accepted on 10/06/2019**

ABSTRACT
Pharyngitis remains to be one of the most common childhood illnesses around the world. Majority of the pharyngitis are caused by viruses, but about 20%–30% of cases in children are due to group *A Streptococci* (GAS), which is a significant cause of mortality and morbidity in the developing countries. The present study finds out the prevalence of acute pharyngitis caused by the GAS. A total of 156 throat swab samples were collected and inoculated on blood agar then, these isolates were identified by the standard microbiological procedures. Group A *Streptococci* were isolated from 14.7% (23/156) of pharyngitis patients and 8.3% (3/25) of the healthy carriers. Among the GAS isolates, 26.1% (6/23) were from males, whereas 73.9% (17/23) were from females. The highest prevalence of GAS rate was found in 4-9 years 60.9% (14/23). All the isolates were 100% sensitive to penicillin, whereas 21.7% and 8.7% isolates were resistant to tetracycline and erythromycin respectively.

KEYWORDS: Group A *Streptococcus*; Pharyngitis; Prevalence; Resistance.

INTRODUCTION
Pharyngitis is the most common childhood disease around the world, majority episodes of pharyngitis are caused by virus; however 20%–30% of cases in children and 5-10% of cases in adults are due to Group A *Streptococci* (GAS) (Shulman et al, 2012, and Choby et al, 2009). Recent studies revealed that around 600 million cases of symptomatic GAS pharyngitis occur annually among children aged over 4 years and around 517,000 deaths each year because of severe GAS disease in under developed countries (Kronman et al, 2014 and Cohen et al, 2015). GAS pharyngitis is most common among children aged between 5–15 years, and nevertheless, its incidence in children differs from region to region and depends upon their socioeconomic conditions (Carapetis et al, 2005). There are 2.4 million affected children in developing countries, one million of whom live in Sub-Saharan African continent (Shulman et al, 2012). The economic burden of USA alone is at $226 million to $540 million per year towards the treatment of *streptococcal pharyngitis* for children (Lee et al, 2008). If the GAS pharyngitis untreated, could lead to acute rheumatic fever, rheumatic heart disease, and acute glomerulonephritis (Zuhlke et al, 2017; Bisno et al, 2002; Capoor et al, 2006 and Charmaine et al, 2006). Therefore, accurate identification of GAS pharyngitis is the most important in the areas where rheumatic fever is common because appropriate antibiotic treatment could prevent rheumatic fever. Based on clinical prediction rules alone it is very difficult to confirm GAS and viral pharyngitis, because of individual's signs and symptoms may overlap each other (Di Muzio et al, 2016 and Hosain et al, 2017). So, laboratory confirmation is needed to make an accurate diagnosis for clinicians. Currently, most of the clinical laboratories are using rapid antigen detection tests for making immediate clinical decisions, but rapid antigen based test kits have low sensitivity (70% –90%) and high cost (Cohen et al, 2015 and Stewart et al, 2014). Therefore, throat culture is considered a gold standard method because of high specificity and sensitivity (Fatima et al, 2013). In Libya not much GAS prevalence studies have been reported, however a few early studies show that the isolation rates of GAS in children with pharyngitis have ranged from 4.2% to 13.7%, which is comparable to the rates reported from developed countries (Androulla Efstratiou et al, 2017 and Carapetis et al, 1999). Aim of our present study is to find out the prevalence of pharyngitis with GAS culture-positive and antimicrobial susceptibility pattern, among outpatient children aged 4–15 years at Primary Health Centres, Misurata city, Libya.

MATERIALS AND METHODS

Study site: All the patients suffering from acute pharyngitis attend outpatient at Department of Pediatrics, Al-Saeed and Qasser Ahmed Hospital in the city of Misurata, Libya. The clinical samples were collected from patients age between 4 to 15 years who all had fever, sore throat, and erythema of tonsils from the duration between February 2017 to April 2018. Patient's clinical data and demographic were collected by questionnaire.

Sample collection and culture method: A total of 156 throat swabs were collected and immediately transported to laboratory for further process. Then, the swabs were inoculated on 5% blood agar plate and incubated at 37°c for 24 hrs. The plates were observed for the presence of beta-hemolytic colonies. Beta-hemolytic colonies were subcultured on blood agar and bacitracin sensitivity test (0.04 units/disc) was carried out. All the isolates of beta-hemolytic colonies were phenotypically characterized by conventional methods.

Antimicrobial Sensitivity test

All the GAS isolates were performed antimicrobial susceptibility test done on MHA with 5% blood agar using Kirby‑Bauer disc diffusion method. The following antimicrobial discs with respective concentration were used (Bioanalyse limited, Turkey): penicillin (10 IU), amoxicillin (30µg), ceftriaxone (30µg), erythromycin (15µg), clindamycin (2µg), chloramphenicol (30µg) and tetracycline (30µg). Zone of inhibition diameters were interpreted as sensitive, intermediate and resistant according to the standard guide lines.

RESULTS

The total of 156 children (63 male and 93 female) between ages of 4 and 15 years with pharyngitis were evaluated (Table 1). Among pharyngitis children, the overall prevalence of group *A Streptococcus* culture positive (GAS) was 14.7% (23/156) and 85.3% (133/156) culture negative. The healthy individuals showed 8.3% (3/25) as a GAS carrier. Among the GAS isolates, 26.1% (6/23) were from males, whereas 73.9% (17/23) were from females. Age group of 4-9 years was found in the highest prevalence of GAS 60.9% (14/23), whereas 10–15 years of age were 39.1% (9/23). Table 2. shows antimicrobial susceptibility pattern for all the GAS isolates. All the isolates were 100% susceptible to penicillin G, amoxicillin, clindamycin, ceftriaxone and chloramphenicol. However, the following resistance patterns were observed for other antibiotics; 21.7% (2/23) for tetracycline and 8.7% (2/23) for erythromycin.

Table. 1. Age and gender wise prevalence of group A *Streptococcal* pharyngitis in the city of Misurata, Libya.

Characteristics		No. of GAS culture positive n (%)	No. of GAS culture negative n (%)	Total no. (%)
Age in years	4-9	14 (60.9)	96 (72.2)	105 (67.3)
	10-15	9 (39.1)	37(27.8)	51 (32.7)
Gender	Male	6 (26.1)	57(42.9)	63 (40.4)
	Female	17 (73.9)	76 (57.1)	93 (59.6)
Total		23 (14.7)	133 (85.3)	156 (100)

Table. 2. Antibiotic susceptibility pattern of GAS isolates.

Name of the antibiotics	Total of GAS isolates	Susceptibility n. (%)	Intermediate n. (%)	Resistance n. (%)
Penicillin G	**23**	**23 (100)**	-	-
Amoxicillin		**23 (100)**	-	-
Ceftriaxone		**19 (82.6)**	**4 (17.4)**	-
Erythromycin		**18 (78.3)**	**3 (13)**	**2 (8.7)**
Clindamycin		**23 (100)**	-	-
Chloramphenicol		**18 (78.3)**	**5 (21.7)**	-
Tetracycline		**12 (52.2)**	**6 (26.1)**	**5 (21.7)**

DISCUSSION

Group A *Streptococcal* diseases has been prevailing for over two thousand years and remain today as a serious cause of worldwide health problems. Twenty to thirty percent of pharyngitis due to GAS is very common with a range of 5–15 years aged children. However, GAS infections rate may differs based on several factors such as age, sex, season and geographical locations (Beaton et al, 2012). Sometime, the clinical manifestations of viral and bacterial pharyngitis are overlapping each other; hence it is very difficult to make a diagnosis based solely on patient's history and physical examinations (Shaikh et al, 2012). Thus, accurate diagnosis is necessary to rule out for group A *Streptococcal* pharyngitis. Therefore, throat culture is considered as a gold standard method to identify GAS.

The overall prevalence rate of GAS is 14.7% in our studies, which is slightly higher than earlier studies with 12.3% reported in the same city by Eldeeb et al, 2006. The similar GAS prevalence rate was observed in other countries (Fatuma et al, 2016; Yagupsky et al, 1995 and

Sarkar et al, 1988). However, our study shows much higher than the prevalence of 4.1% in Taiwan and 7.9% in Indonesia (Shih et al, 2012 and Malino et al, 2013). For the possible marginal increases of GAS incidence in Misurata city, is due to the country's political instability since 2011, which has added to an arrival of people from rural areas to big cities for their safety, which has caused overcrowding and low standard of living being the main reason. Still, it was much lower than the prevalence rate observed in upper and middle income countries of 41.5%, 42.2%, 40.6% and 36% in Yemen, Egypt, Ethiopia and USA respectively (Ba-Saddik et al, 2014; Shereen et al, 2015; Tewodros et al, 1992 and Smith et al, 1989). Recent investigations have reported that children aged 5-10 years are more prone to incidence of GAS pharyngitis (Cauwenberge et al, 1991; Dumre et al, 2009 and Bramhachari et al, 2010). Similar findings have been found in our study too, where the highest rate of GAS incidence is 60.9% in aged 4-9 years, whereas 39.1% in 10-15 years. The highest occurrence rate in this age group might be due to high exposure to outer environment and lack of awareness. Some previous studies revealed that prevalence of GAS pharyngitis might differ between males and females. Similarly our study also showed that the prevalence in females was higher (73.9%) than males (26.1%). Few earlier studies had been reported that prevalence of GAS pharyngitis was higher among females than males in India and Nepal (Rijal et al. 2009 and Dumre et al, 2009). On the other hand, a study in Ethiopia was found a higher prevalence among males than females (Tewodros et al, 1992). This contradiction result might be attributed to ratio differences between male and female participants. The healthy individuals in this study showed 8.3% (3/25) as a GAS carrier; our finding is much lower than neighboring countries (Shereen Mohamed et al, 2015 and Ozturk et al, 2004). Carrier rate of GAS may vary country to country based on their living conditions, geographical locations and economic status (Martin et al, 2004 and Nabipour et al, 2005). This low prevalence rate in our study compared to studies in other countries is probably due to awareness in hygiene and health care facilities.

Antibiotic sensitivity test is necessary for the clinical isolates of GAS because its potency of resistance to β-lactams and macrolides in many countries in the recent years (Choby et al, 2009). In our study, all GAS isolates showed 100% sensitive to penicillin G, amoxicillin and ceftriaxone. These findings indicated that all the β-lactams and few macrolides remain as the drug of choice for the treatment of GAS infection. Several different studies showed that GAS was susceptible to penicillin and its derivatives in many countries (Rijal et al. 2009 and Gurung et al, 2010). For alternative to penicillin allergic patients, the erythromycin and clindamycin are used as drug of choice. However, 8.7% and 21.7% of GAS isolates were found resistant to erythromycin and tetracycline respectively in the study. Similarly, in England and other countries the resistance rates of erythromycin ranging from 3.4% to 91.8% had been reported (Efstratiou et al, 2003 and Jing et al, 2006). However, few recent studies revealed that decline of erythromycin resistance rates from 13.6% to 2.6% might be due to either efforts to minimize usage of macrolides in society (Farmand et al, 2012 and Gagliotti et al. 2015). Our current study, 21.7% GAS isolates were resistant to tetracycline which was similar finding with 24% in England but, much lower than with 70% Tunisia, 68% in Ethiopia and 50% in Brazil (Efstratiou et al, 2003; Hraoui et al, 2011; Abdissa et al, 2011 and De Melo et al, 2003).

CONCLUSION

Group A *Streptococcus* is the most common etiologic agent of bacterial pharyngitis hence, we need accurate diagnostic protocol and treatment guidelines to be provided for primary health care physicians. The epidemiology of GAS is an issue which has to be considered seriously and therefore, epidemiological studies should be performed regularly to monitor emergence of antibiotic resistance.

ACKNOWLEDGMENT

We would like to express our sincere thanks to the Department of Pediatrics, Al-Saeed Hospital and Qasser Ahmed Hospital, Misurata, Libya for having provided us the clinical samples for our study.

REFERENCE

1. Abdissa A, Asrat D, Kronvall G. "Throat carriage rate and antimicrobial susceptibility pattern of group A streptococci (GAS) in healthy Ethiopian schoolchildren" Ethiop Med J., 2011; 49(2): 125–130.
2. Androulla Efstratiou, and Theresa Lamagni. "Epidemiology of Streptococcus pyogenes" Basic Biology to Clinical Manifestations, Oklahoma City (OK): University of Oklahoma Health Sciences Center; Updated, 2017; l 3: 1-27.
3. Ba-Saddik IA, Munibari AA, Alhilali AM, et al. Prevalence of group A beta-haemolytic streptococcus isolated from children with acute pharyngotonsillitis in Aden, Yemen. Trop Med Int Health, 2014; 19(4): 431-439.
4. Beaton, A., Okello, E., Lwabi, P., Mondo, C., McCarter, R. & Sable, C. "Echocardiography screening for rheumatic heart disease in Ugandan school children" Circulation, 2012; 125: 3127-32.
5. Bisno AL, Gerber MA, Gwaltney JM. "Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis" Clinical Infectious Diseases, 2002; 35: 113-125.
6. Bramhachari PV, Kaul SY, McMillan DJ, Shaila MS, Karmarkar MG, Sriprakash KS. "Disease burden due to Streptococcus dysgalactiae subsp. Equisimilis (group G and C Streptococcus) is higher than that due to Streptococcus pyogenes among Mumbai school children" J Med Microbiol, 2010; 59: 220–3.

7. Capoor MR, Nair D, Deb M "Resistance to erythromycin and rising penicillin MIC in Streptococcus pyogenes in India" Japanese J. Infect. Dis., 2006; 59: 334-336.
8. Carapetis JR, Steer AC, Mulholland EK "The global burden of group A streptococcal diseases" The Lancet Infectious Diseases, 2005; 5: 685–694.
9. Cauwenberge PBV, Mijnsbrugge AV. "Pharyngitis: a survey of the microbiologic etiology" Pediatrics Infectious Disease Journal, 1991; 10: S39–S42.
10. Charmaine AC, Jacob SE, Menon T. "Pharyngeal carriage of group A Streptococci in school children in Chennai" Indian J. Med. Res., 2006; 124: 195-198.
11. Choby BA. "Diagnosis and treatment of streptococcal pharyngitis" Am Fam Physician. 2009; Mar 1; 79(5): 383-90.
12. De Melo MCN, Figueiredo AMS, Ferreira-Carvalho BT. "Antimicrobial susceptibility patterns and genomic diversity in strains of Streptococcus pyogenes isolated in 1978–1997 in different Brazilian cities" J Med Microbiol, 2003; 52(3): 251–258.
13. Di Muzio F, Barucco M, Guerriero F. "Diagnosis and treatment of acute pharyngitis/tonsillitis: a preliminary observational study in General Medicine" Eur Rev Med Pharmacol Sci., 2016; 20(23): 4950-4954.
14. Dumre SP, Sapkota K, Adhikari N. "Asymptomatic throat carriage rate and antimicrobial resistance pattern of Streptococcus pyogenes in Nepalese school children" Kathmandu University Med J, 2009; 7: 392-6.
15. Efstratiou A, Emery M, Lamagni TL, Tanna A, Warner M, George RC. "Increasing incidence of group A streptococcal infections amongst injecting drug users in England and Wales" J Med Microbiol, 2003; 52: 525–6.
16. Eldeeb A. H. and Khashan E.M. "Microbiological Study On Respiratory Tract Infections In Libya" The Egyptian Journal of Hospital Medicine, 2006; 24: 442-459.
17. Farmand S, Henneke P, Hufnagel M, Berner R. "Significant decline in the erythromycin resistance of group A streptococcus isolates at a German paediatric tertiary care centre" Eur J Clin Microbiol Infect Dis., 2012; 31: 707-10.
18. Fatima F, Shuba DS. Prevalence Survey for Assessing Intensity of Group a Beta haemolytic Streptococci (GABHS) Subclinical Infection Rate in School Children: A Cross Sectional Study. Glob. J. Med. Res. Dis. 2013; 13(3): Ver1.0.
19. Fatuma I. Makuka, Steven Mwakalinga, Hassan H. Mattaka, Maulilio J. Kipanyula and Alphaxard Manjurano. "Group A Streptococcus pharyngitis among schoolchildren in Mbulu District, Tanzania Tanzania" Tanzania Journal of Health Research, 2016; 18(3): 1-6.
20. Gagliotti C, Buttazzi R, Di Mario S, Morsillo F, Moro ML. "A regionwide intervention to promote appropriate antibiotic use in children reversed trends in erythromycin resistance to Streptococcus pyogenes" Acta Paediatr, 2015; 104: e422-4.
21. Gurung R, Budhathoki S, Amatya R, Poudyal N, Shrestha S, Baral R. "Group A beta hemolytic streptococcus infection presenting with sore throat at paediatric OPD" Health Renaissance, 2010; 8: 90-2.
22. Hosain Nasirian, Saeedeh TarvijEslami, Esfandiar Matini, Seyedehsara Bayesh, Yasaman Omaraee. "An update A clinical decision rule for streptococcal pharyngitis management" Journal of Laboratory Physicians 2017; Published by Wolters Kluwer – Medknow, 2017; 116-120.
23. Hraoui M, Boubaker IB-B, Doloy A, Redjeb SB, Bouvet A. "Molecular mechanisms of tetracycline and macrolide resistance and emm characterization of Streptococcus pyogenes isolates in Tunisia" Microb Drug Resist, 2011; 17(3): 377–382.
24. J. F. Cohen, R. Cohen, C. Levy. "Selective testing strategies for diagnosing group A streptococcal infection in children with pharyngitis: a systematic review and prospective multicenter external validation study," Canadian Medical Association Journal, 2015; 187(1): 23–32.
25. Jing HB, Ning BA, Hao HJ, Zheng YL, Chang D, Jiang W. "Epidemiological analysis of group A streptococci recovered from patients in China" J Med Microbiol, 2006; 55: 1101–7.
26. Jonathan R. Carapetis, Bart J. Currie, Edward L. Kaplan. "Epidemiology and Prevention of Group A Streptococcal Infections: Acute Respiratory Tract Infections, Skin Infections, and their Sequelae at the Close of the Twentieth Century" Clinical Infectious Diseases, 1999; 28: 205–10.
27. Kronman MP, Zhou C, Mangione-Smith R. "Bacterial prevalence and antimicrobial prescribing trends for acute respiratory tract infections" Pediatrics 2014; 134:e956-65.
28. Lee GM. "Burden and economic cost of group A Streptococcal pharyngitis" Pediatrics, 2008; 121: 229-234.
29. Malino IY, Utama DL, Soenarto Y. McIsaac. "Criteria for diagnosis of acute group A b-hemolytic streptococcal pharyngitis" Paediatr Indones, 2013; 53(5): 259.
30. Martin JM, Green M, Baarbadora KA, Wald ER. "Group A Streptococci among school aged children: Clinical characteristics and the carrier state" Pediatrics, 2004; 114: 1212-9.
31. Nabipour F, Tayarzadeh M. "Prevalence of beta hemolytic streptococcus carrier state and its sensitivity to different antibiotics among guidance school children in Kerman, Iran" Amer J Infect Dis., 2005; 1: 128-31.
32. Ozturk CE, Yavuz T, Kaya D, Yusel M. "The rate of asymptomatic throat carriage of group Astreptococcus in school children and associated ASO titers in Duzce, Turky". Jpn J Infect Dis., 2004; 5: 271-2.

33. Rijal KR, Dhakal N, Shah RC. "Antibiotic susceptibility of Group A streptococcus isolated from swab culture of school children in Pokhara, Nepal" Nepal Med Coll J., 2009; 11: 238-40.
34. Sarkar S. "A study on sore throat and beta-hemolytic streptococcal pharyngitis among rural school children in Varanasi with reference to age and season" Indian Journal of Public Health, 1988; 32: 191–198.
35. Shaikh N, Swaminathan N, Hooper EG. "Accuracy and precision of the signs and symptoms of streptococcal pharyngitis in children: a systematic review" J pediatr, 2012; 160:487-493.e3.
36. Shereen Mohamed Abd El-Ghany, Abeer Ahmed Abdelmaksoud, Sally Mohamed Saber, Dalia Hosni Abd El Hamid. "Group A beta-hemolytic streptococcal pharyngitis and carriage rate among Egyptian children: a case-control study" Ann Saudi Med., 2015; 35(5): 377-382.
37. Shih CT, Lin CC, Lu CC. "Evaluation of a streptococcal pharyngitis score in southern Taiwan" Pediatr Neonatol, 2012; 53: 49–54.
38. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, Martin JM, Van Beneden C. "Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis" 2012 update by the Infectious Diseases Society of America. Clinical Infect Dis., 2012; 15; 55(10): 1279-82.
39. Smith TD, Wilkinson V, Kaplan EL: "Group A streptococcus associated upper respiratory tract infections in a daycare center" Pediatrics, 1989; 83: 380-384.
40. Stewart EH, Davis B, Clemens-Taylor BL. "Rapid antigen group A streptococcus test to diagnose pharyngitis: a systematic review and meta-analysis" PLoS ONE, 2014; 9: e111727.
41. Tewodros W, Muhe L, Daniel E, Schalen C, Kronvall G. "A oneyear study of streptococcal infections and their complications among Ethiopian children" Epidemiol Infect, 1992; 109: 211–225.
42. Yagupsky P, Landau D, Beck A, Dagan R. Carriage of Streptococcus pyogenes among infants and toddlers attending daycare facilities in closed communities in southern Israel. Eur. J. Clin. Microbiol. Infect. Dis., 1995; 14: 54-58.
43. Zuhlke LJ, Beaton A, Engel ME, Hugo-Hamman CT, Karthikeyan G, Katzenellenbogen JM, Ntusi N, Ralph AP, Saxena A, Smeesters PR, Watkins D, Zilla P, Carapetis J. "Group A Streptococcus, Acute Rheumatic Fever and Rheumatic Heart Disease: Epidemiology and Clinical Considerations" Currt Treat Options Cardiovasc Med., 2017; 19(2): 15.