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Research Article

Epidemiological Aspects and Antibiotics Susceptibility Patterns of Streptococcus pyogenes Isolated from Subjects with Tonsillitis, Sudan

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Abstract

Background: Globally, *Streptococcus pharyngitis* is a major public health challenge. The current study investigates the prevalence of *Streptococcal pyogenes* among children under 17 years old in ENT Kosti Teaching Hospital and examines the susceptibility of isolated *S. pyogenes* strains to commonly used antibiotics.

Methods: A total of 384 throat swabs were obtained from children under the age of 17 who attended the Kosti Teaching Hospital between 2019 and 2021. *Streptococcus pyogenes* was isolated by conventional microbiology procedures. Each *S. pyogenes* strain was subjected to antibiotic susceptibility testing according to the CLSI guidelines.

Results: Most participants of this study were females 219 (57%) and aged between 5 and 10 years 259 (67.4%). Out of the 384 participants, 134 (34.9%) and 255 (66.4%) suffered from lymphadenopathy and tonsil hyperplasia, respectively. Interestingly, lymphadenopathy and tonsil hyperplasia were more (*P* ⊠ 0.05) in the 5–10 age group than those aged 11–16 years. Moreover, 41.4% of the participants were infected by a GAS sore throat. GAS sore throat is significantly associated with lymphadenopathy (AOR: 2.375, 95% CI: 1.479–3.815, *P* ⊠ 0.000) and tonsil hyperplasia (AOR: 3.374, 95% CI: 1.939–5.874, *P* ⊠ 0.000). Notably, males (AOR: 0.853, 95% CI: 0.549–1.325, *P* 0.479) and individuals aged 5–10 years (AOR: 0.867, 95% CI: 0.464–1.618, *P* 0.654) were less likely to have a GAS sore throat. In our study, all isolated strains were sensitive to penicillin. Clindamycin, azithromycin, and erythromycin resistance were observed in 7 (4.4%), 44 (27.7%), and 47 (29.6%) isolates, respectively.

Conclusion: The study displayed the current situation of GAS sore throat in the White Nile state. Penicillin was found to be the effective drug to cure *S. tonsillitis* but a high rate of resistance to macrolides was noticed which is an alarming sign.

Keywords: azithromycin, clindamycin, erythromycin, GAS, *Streptococcus pyogenes*

1. Introduction

Pharyngitis or tonsillitis (sore throat) is defined as an inflammatory process involving the mucous membranes of the oropharynx and tonsils [1]. Tonsillitis is a major problem that threatens the health and socioeconomic lives of many people [1, 2]. Viruses are a common cause of pharyngitis; however, >15–30% of this condition is associated with group A streptococcus (GAS) infection [3, 4]. Streptococcal pharyngitis is a highly important disease, and its ultimate frequency arises among children aged 5–15 years [5]. The common signs of illness are usually abrupt and include painful throat, rapid onset fever, discomfort swallowing, enlarged tonsils, and tender cervical lymph nodes [6]. Transmission of *S. pyogene* mainly occurs with direct contact, contaminated objects, or nasal secretions from infected persons or carriers [7]. The occurrence of the disease is varied according to seasonal and environmental conditions [8]. *Streptococcus pyogenes (S. pyogene)*, also identified as Lancefield GAS, is a significant pathogenic bacteria associated with a wide range of human diseases. Much data collection and assessment of the global burden of GAS infection indicated that about 616 million suffer from pharyngitis, with a minimum of 111 million cases of skin diseases (pyoderma). More seriously, 18.1 million people complained of invasive diseases and not less than 517,000 deaths occurred due to serious invasive diseases and disease sequelae [9–13]. This data reflects the important rank of GAS among pathogenic bacteria and express the effect of GAS on worldwide mortality and morbidity [10, 12, 14]. GAS is an exceptional causative agent of diseases that require an etiologic identification and specific treatment [12]. The diagnosis of pharyngitis based on the history of disease with clinical remakes is useful, however, accurate diagnosis requires laboratory analysis [15, 16]. In children, the McIsaac scoring system is the most common clinical prediction procedure used for the identification of streptococcal pharyngitis. Culturing throat swab on sheep blood remains the perfect technique for the identification of GAS infections [5]. Rapid Antigen detection tests and serodiagnosis, including anti-deoxyribonuclease B (ADNase B) and antistreptolysin O (ASO), are additional diagnostic tools for GAS diseases [17]. Penicillin and its products are still the drugs of choice, however, in patients who are allergic to it, macrolide is the alternative drug prescribed to treat *S. pyogenes* infections [18]. Growing macrolide resistance has been stated. Furthermore, the fastest developing problem of antibiotic resistance of *S. pyogenes* is raised. Evidence about increasing minimum inhibitory concentration or reduced susceptibility to penicillin has been documented [19]. Various resistance rates have been reported according to geographical location and researcher [20, 21]. Unfortunately, little data on GAS pharyngitis were available regarding low-income countries [22]. Sudan is a poor country with poor health resources, researches concerning *S. pharyngitis* among children remains an ignored problem with few data available on the topic [23–27]. Moreover, trial treatment of microbial infections including tonsillitis without culture to recognize the causative pathogens is current practice in our study area and all over Sudan. Furthermore, data on prevalence, antibiotic susceptibility testing, and features related to *S. pharyngitis* among children in our state were least studied. Thus, this study intended to investigate the prevalence of GAS, antibiotics susceptibility patterns, and related aspects of *S. pyogenes* among children with pharyngitis in White Nile State, Sudan.

2. Materials and Methods

2.1. Study design and period

This cross-sectional study was conducted at the Kosti Teaching Hospital between 2019 and 2021.

2.2. Study area

Situated in southern Sudan and located between latitudes 12 to 13.30° North and longitude 31 to 33.30° East, White Nile state shares its border with Khartoum state in the North, North Kordofan state in the West, South Kordofan and Upper Nile states in the South-west, the state of Southern Sudan in the South, and the states of Al-Gazira and Sennar in the East. The state has a total area of 16,000 km^2. It has a population of 1.7 million according to the 2008 population census. Of this number, 85% live in rural areas and around 15% in urban areas. Agriculture is the main source of livelihood in the state, and 65% of the state population work either as farmers or as seasonal laborers. White Nile remains one of the least developed areas in the country. There are 3 teaching and 19 rural hospitals. The most important towns are Al-Dweim, Algabaleen, Al-Kawwa, Rabak the capital of the state, and Kosti which is the largest town housing the Kosti teaching hospital (the largest hospital in the state in which the current study was carried out).

2.3. Ethical considerations

The study approval was taken from Omdurman Islamic University (Khartoum). Authorities of Kosti Teaching Hospital granted permission to collect the specimens. Written consent was obtained from the investigated children's parents or guardians. A verbal agreement was obtained from all children.

2.4. Study participants, data, and sample size

The study participants were children with tonsillitis between the ages of 5 and 15 years who attended the Kosti Teaching Hospital ENT unit. Each participant underwent a general physical examination by an ENT consultant before being selected for the study. Patients with a history of respiratory surgery, autoimmune disease, radiotherapy, body abnormality, or chemotherapy were excluded. Children who were under antimicrobial use or those who had a history of antibiotic use at least seven days before the presentation were excluded. Data collection was done by using a pre-test questionnaire that covered the patients' demographical data (age, gender, and residence) and clinical information (sore throat, fever, tonsils hyperemia, and cervical lymphadenopathy). Figure **1** shows the study flow diagram.

The sample size was estimated using the following formula:

$n = Z^2 \times P\ (P{-}1)/d^2$,

where n is the sample size, Z is the standard normal variable (corresponding to the 95% level of significance = 1.96), P is the expected prevalence = 0.5% as determined by a preliminary study, and d is the precision corresponding to the effect size = 0.05.

Based on the above data, $n = (1.96)^2 \times P\ (P{-}1)/(0.05)^2 = 384$.

2.5. Samples collection and processing of specimens

Under good light and using the tongue depressor, the inside of the mouth was examined for signs of inflammation and the presence of pus and exudates. Using a sterile cotton swab, the two infected tonsils were swabbed and care was taken to avoid contamination of swabs with saliva or touching any part of the mouse. All swabs collected were labeled and immediately transferred to the laboratory.

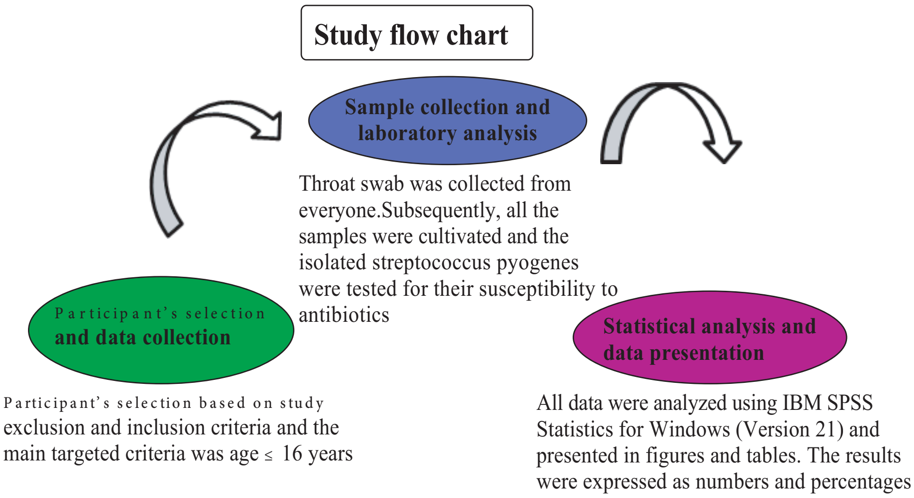

Figure 1: Study flow chart.

2.6. Inoculation of collected sample on culture media

5% sheep blood agar (Hi Media, India) was the growing medium used to isolate the organisms. Throat specimens were rolled firmly over one-sixth of the plate to deposit the specimen, the wire loop was used to streak the inoculum over the surface of the plate, and plates were incubated at 35°C overnight. A candle jar was used to provide an atmosphere of CO_2. After 24 hr of incubation, each plate was checked for colonies with β-hemolytic characteristics. Culture plates negative for β-hemolytic colonies were incubated for an additional 24 hr to allow for the recovery and detection of slow growers. Selected β-hemolytic colonies were subjected to another sub-culture using blood agar plates to obtain pure growth. After overnight incubation, the pure colonies were tested for their Gram reaction, catalase. All β-hemolytic and catalase-negative colonies were tested for Bacitracin susceptibility bacteria. The bacterial suspension was evenly spread onto a blood agar plate using a swab, and 0.05 U Bacitracin disc (Hi Media, India) was placed on the inoculated surface and incubated in a candle jar for 18–24 hr at 35°C. Any zone of inhibition surrounding the disc was indicative of a presumptive GAS.

2.7. Bacterial isolates

Three hundred eighty-four throat swabs were collected from subjects with tonsils infection (tonsillitis) from 2019 to 2021 in Kosti, Sudan. The specimens were collected from the main hospital of the state ENT unit. Only 159 *S. pyogenes* out of inoculated bacteria were reported as *S. pyogenes* based on colony morphology, beta-hemolysis on sheep blood agar, and sensitivity to bacitracin disc (0.05 U, Himedia, India).

2.8. Antibiotics susceptibility testing

The sensitivity testing was done after sub-culturing the bacteria onto a 5% blood agar medium (Hi-Media, India) overnight incubation at 37°C to yield a new growth of *S. pyogenes*. The test was performed according to the Clinical Laboratory Standards Institute (CLSI) [28]. About three to five well-defined colonies were picked using a sterile wire loop and emulsified into 3–5 ml sterile physiological saline to prepare a turbidity suspension equivalent to the 0.5 McFarland standards. Using a sterile cotton swab, the suspension of the test organism was inoculated into Mueller–Hinton sensitivity medium-based blood agar (Hi-Media, India). Next, sterile forceps were used to transfer the antimicrobial discs (erythromycin 15 mg, azithromycin15 mg, penicillin 10 mg, clindamycin 2 mg) onto the inoculated plate (all antibiotics were from Hi-Media, India). The inoculated plates were incubated overnight at 37°C and in the presence of 5% CO_2 provided by using a candle jar. Following the incubation, the zones of inhibition were measured by using a ruler and reported in mm. Compared with the manufacturer's reference chart results, the generated results were provided (Hi-Media, India). The susceptibility of isolates to each antibiotic was recorded as sensitive, resistant, or intermediated. *Streptococcus pyogenes* ATCC1916 was used as a control.

2.9. Statistical analysis

All data were analyzed using IBM SPSS Statistics for Windows (Version 21). The results were expressed as numbers and percentages. The statistical differences were evaluated using the Chi-squared and Fisher's Exact tests. Multinomials and binary were involved in investigating the associations of dependent variables with the independent factors. A *P*-value ≤ 0.05 was considered significant.

3. Results

3.1. Sociodemographic and clinical features of the study participants

Three hundred and eighty-four participants were enrolled in this research – 219 (57%) females and 165 (43%) males. The age of the studied participants ranged from 5 to 15 years with a mean age of 9.0 and a standard deviation (SD) of 3.0. The vast majority of study participants 259 (67.4%) were between the ages of 5 and 10 years. Moreover, about 296 (77.1%) participants were from urban and 88 (22.9%) were from rural areas.

Furthermore, 268 (69.8%) participants were in primary school, 59 (15.4%) in secondary school, and <57 (14.8) in kindergarten (Table 1).

Out of the 384 participants, only 34.9% had lymphadenopathy and 66.4% suffered from tonsil hyperplasia. Fever and sore throat were found in all patients. Interestingly, there was a significant dissimilarity (P ⊠ 0.05) in the occurrence of lymphadenopathy and tonsil hyperplasia, which were more in the 5–10 years age group compared to individuals of 11–16 years (Table 2).

Table 1: Characteristics of the study participants.

Variable		**Frequency: N (%)**
Gender	Male	165 (43)
	Female	219 (57)
Age (yr)	5–10	259 (67.4)
	11–16	125 (33.6)
Residence	Urban	296 (77.1)
	Rural	88 (22.9)
Education level	Kindergarten	57 (14.8)
	Primary school	268 (69.8)
	Secondary school	59 (15.4)

N, Number.

3.2. Prevalence of GAS sore throat

The overall prevalence of GAS associated with tonsillitis (sore throat) in this research was 159 (41.4%) and 225 (58.6%) due to non-GAS sore throat (Figure **2**). There was no significant variation in the frequency of GAS sore throat among gender, age groups, education levels, and residence, P ⊠ 0.05. Regarding the link of GAS sore throat with the clinical features, we found that the frequency of GAS sore throat was significantly higher in individuals with lymphadenopathy or tonsil hyperplasia, P ⊠ 0.05. The findings of logistic regression analysis also revealed that GAS sore throat is significantly associated with lymphadenopathy (AOR: 2.375, 95% CI: 1.479–3.815, P ⊠ 0.000) and tonsil hyperplasia (OR: 3.374, 95% CI: 1.939–5.874, P ⊠ 0.000). Notably, males (OR: 0.853, 95% CI: 0.549–1.325, P 0.479) and individuals aged 5–10 years (OR: 0.867, 95% CI: 0.464–1.618, P 0.654) were less likely to be infected by a GAS sore throat, but it is not significant. Consequently, lymphadenopathy and tonsil hyperplasia ($P < 0.05$) were independent predictors of *S. pyogenes* pharyngitis in children (Table 3).

Table 2: Clinical features of the study subjects.

Variable		Frequency: N (%)							
		Fever		Sore throat		Lymphadenopathy		Tonsil hyperemia	
		Yes	No	Yes	No	Yes	No	Yes	No
Overall		384 (100)	0 (0)	384 (100)	0 (0)	134 (34.9)	250 (65.1)	255 (66.4)	129 (33.6)
Gender	Male	165 (100)	0 (0)	165 (100)	0 (0)	62 (37.6)	103 (62.4)	106 (64.2)	59 (35.8)
	Female	219 (100)	0 (0)	219 (100)	0 (0)	72 (32.9)	147 (67.1)	149 (68)	70 (32)
X^2		–				0.915		0.607	
P-value		–				0.339		0.436	
Age (yr)	5–10	259 (100)	0 (0)	259 (100)	0 (0)	110 (42.5)	149 (57.5)	206 (79.5)	53 (20.5)
	11–16	125 (100)	0 (0)	125 (100)	0 (0)	24 (19.2)	101 (80.8)	49 (39.2)	76 (60.8)
X^2			–	–		20.097		61.491	
P-value			–	–		<0.000		<0.000	
Residence	Urban	296 (100)	0 (0)	296 (100)	0 (0)	94 (31.8)	202 (68.2)	193 (65.2)	103 (34.8)
	Rural	88 (100)	0 (0)	88 (100)	0 (0)	40 (45.5)	48 (54.5)	62 (70.5)	26 (29.5)
X^2			–	–		5.602		0.839	
P-value			–	–		0.018		0.36	
Education level	Kindergarten	57 (100)	0 (0)	57 (100)	0 (0)	29 (50.9)	28 (49.1)	48 (84.2)	9 (15.8)
	Primary school	268 (100)	0 (0)	268 (100)	0 (0)	95 (35.4)	173(64.6)	185 (69)	83 (31)
	Secondary school	59 (100)	0 (0)	59 (100)	0 (0)	10 (16.9)	49 (83.1)	22 (37.3)	37 (62.7)
X^2			–	–		14.808		31.35	
P-value			–	–		0.001		<0.000	

Data assessed by Pearson Chi-Square.N, Number; X^2, Chi-Square.

3.3. Antibiotics susceptibility findings

159 GAS isolates were tested for their susceptibility to erythromycin (15 μg), clindamycin (2 μg), penicillin (10 U), and azithromycin (15 μg). We found that all the isolated strains were sensitive to penicillin. However, the frequency of antibiotic resistance to clindamycin, azithromycin, and erythromycin resistance was observed in 7 (4.4%), 44 (27.7%), and 47 (29.6%) of isolates, respectively (Figure **3**). Additionally, the rate of clindamycin, erythromycin, and azithromycin resistance was more in individuals suffering from lymphadenopathy ($P < 0.05$) or tonsil hyperplasia ($P < 0.05$). Furthermore, the rate of clindamycin and azithromycin resistance was also more in males than females but it was not significant (Table 4).

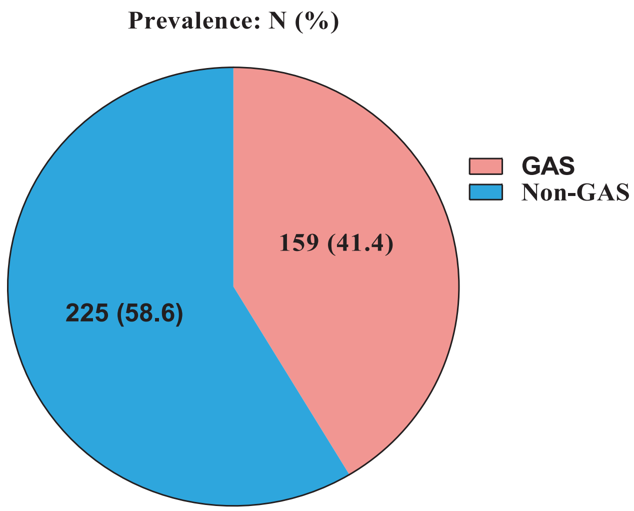

Figure 2: Overall prevalence of streptococcal sore throat. GAS, Group A streptococci; Non-GAS, Non-group A streptococci; N, Number.

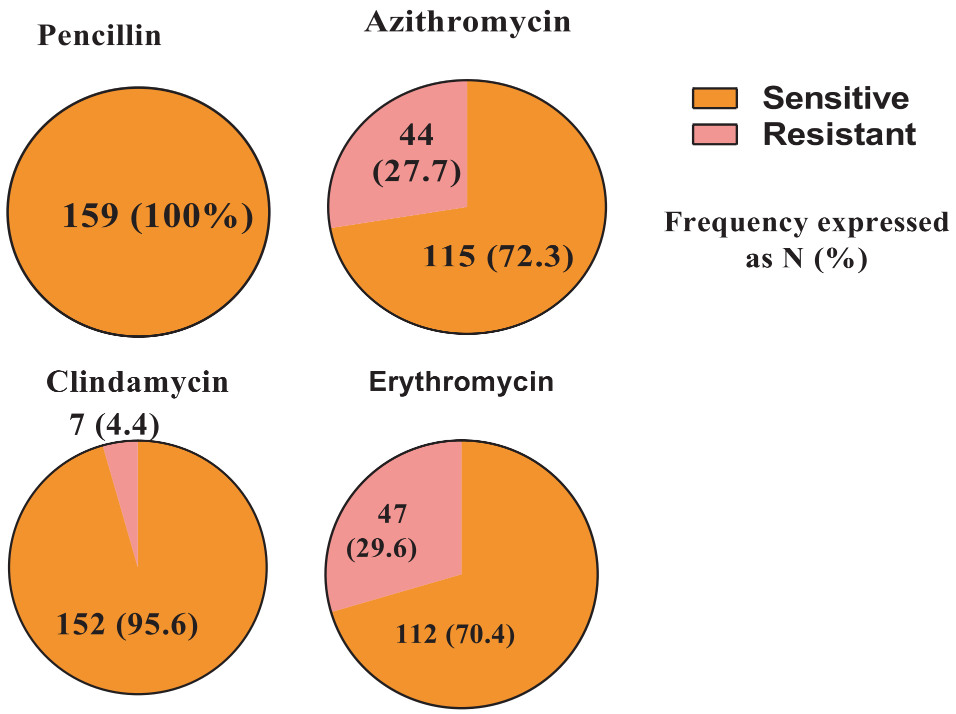

Figure 3: Susceptibility of the isolated GAS to antibiotics. GAS, Group A streptococci; N, Number.

4. Discussion

Human infections caused by *S. pyogenes* are a common reason for morbidity and mortality globally [29]. The prevalence of acute pharyngotonsillitis caused by *S. pyogenes* is approximately 15 to 30%. This percentage varies from region to region [30]. In the

Table 3: Association of streptococcal sore throat with gender, age groups, residence, and clinical features of participants.

Variable			Prevalence			Association			
						Unadjusted		Adjusted	
			N (%)	X^2	P-value	OR (95%CI)	P-value	AOR (95% CI)	P-value
Gender	Female		95 (43.4)			1		1	
	Male		64 (38.8)	0.818	0.366	0.853 (0.549–1.325)	0.479	0.853 (0.549–1.325)	0.479
Age (yr)	11–16		49 (39.2)			1		1	
	5–10		110 (42.5)	0.372	0.542	0.867 (0.464–1.618)	0.654	0.867 (0.464–1.618)	0.654
Residence	Rural		35 (39.8)			1		1	
	Urban		124 (41.9)	0.126	0.723	1.317 (0.783–2.217)	0.300	1.317 (0.783–0.217)	0.300
Education level	Secondary school		29 (49.2)			1		1	
	Primary school		104 (38.8)	2.622	0.27	1.016 (0.547–1.889)	0.959	0.398 (0.151–1.048)	0.062
	Kindergarten		26 (45.6)			0.398 (0.151–1.048)	0.062	0.391 (0.183–0.837)	0.016
Clinical features	Lymphadeno-pathy	No	83 (33.2)			1		1	
		Yes	76 (56.7)	19.886	0.000	2.375 (1.479–3.815)	0.000	2.375 (1.479–3.815)	0.000
	Tonsil hyperplasia	No	31(24)			1		1	
		Yes	128 (50.2)	24.173	0.000	3.374 (1.939–5.874)	0.000	3.374 (1.939–5.874)	0.000

Statistical analysis performed using Pearson Chi-square and binary and multinomial logistic regression.
N, Number; X^2, Chi-square; OR, Odd ratio; AOR, Adjusted odd ratio; CI, Confidence interval.

present study, we present the prevalence of *S. pyogenes* associated with tonsillitis among Sudanese children who attended the Kosti Teaching hospital. A total of 384 study participants were involved in this study, of which 165 (43%) were males and 219 (57%) were females. Our findings reveal that of the 384 patients, only 159 (41.4%) were infected by a GAS sore throat and 58.6% by a non-GAS sore throat. This was lower when compared with a previous study carried out in the study area [26]. It is also lesser than that found in Mohammed *et al*.' study (2016) (86%), which was conducted in Khartoum city, Sudan [25]. In contrast, it is higher than the results of Al Fadhil *et al*. (35.5%) and Abdelwahab *et al*.'s (2014) (6%) studies, which were also conducted in Khartoum city, Sudan [23, 24]. The prevalence of *S. pyogenes* associated with pharyngitis among children in African studies compared to the current study was higher (66.7%) in a Nigerian study by Uzodimma *et al*. and lower in an Egyptian study by Sultan *et al.* (28%), a Kenyan study by Osowicki *et al*. (23%), and an Ethiopian study by Tesfaw *et al*. (11.3%) [30–33].

Table 4: Relationship of antibiotics susceptibility patterns of the GAS isolates (N = 159) with gender, age groups, residence, and clinical features of study subjects.

Variable			Number	Clindamycin: N (%)		Erythromycin: N (%)		Azithromycin: N (%)	
				S	R	S	R	S	R
Gender	Male		64	61 (95.3)	3 (4.7)	47 (72.3)	18 (27.7)	46 (70.8)	19 (29.2)
	Female		95	91 (95.8)	4 (4.2)	65 (68.4)	30 (31.6)	69 (72.6)	26 (27.4)
	X^2			0.000		0.278		0.066	
	P-value			1.000^{C}		0.598		0.797	
Age (yr)	5–10		110	104 (94.5)	6 (5.5)	77 (70)	33 (30)	78 (70.9)	32 (29.1)
	11–16		49	48 (98)	1 (2)	35 (70)	15 (30)	37 (74)	13 (26)
	X^2			0.303		0.000		0.162	
	P-value			0.582^{C}		1.000		0.687	
Residence	Urban		124	118 (95.2)	6 (4.8)	85 (68.5)	39 (31.5)	88 (71)	36 (29)
	Rural		335	34 (97.1)	1 (2.9)	27 (77.1)	8 (22.9)	27 (77.1)	8 (22.9)
	X^2			–		–		–	
	P-value			1.000^{F}		0.404^{F}		0.528^{F}	
Education level	Kindergarten		26	24 (92.3)	2 (7.7)	17 (65.4)	9 (34.6)	17 (65.4)	9 (34.6)
	Primary school		104	99 (99.2)	5 (4.8)	75 (72.1)	29 (27.9)	77 (74)	27 (26)
	Secondary school		29	29 (100)	0 (0)	20 (69)	9 (31)	21 (72.4)	8 (27.6)
	X^2			1.864		0.603		0.881	
	P-value			0.367^{F}		0.766^{F}		0.704^{F}	
Clinical features	**Lymphadeno-pathy**	Yes	76	72 (94.7)	4 (5.3)	50 (65.8)	26 (34.2)	51 (67.1)	25 (32.9)
		No	83	80 (96.4)	3 (3.6)	62 (74.7)	21 (25.3)	64 (77.1)	19 (22.9)
	X^2			–		1.512		1.983	
	P-value			0.710^{F}		0.219		0.159	
	Tonsil hyperplasia	Yes	128	121 (94.5)	7 (5.5)	84 (65.6)	44 (34.4)	87 (68)	41 (32)
		No	31	31 (96.4)	0 (0)	28 (90.3)	3 (9.7)	28 (90.3)	3 (9.7)
	X^2			–		–		–	
	P-value			0.347^{F}		0.008^{F}		0.013^{F}	

Data analysis performed using Pearson's Chi-square and Fisher's Exact test^{F}.
N, Number; X^2, Chi-Square; S, Sensitive; R, Resistant; GAS, Group A streptococci.

Moreover, the occurrence of tonsils infection was predominant observed among urbanized patients 124 (41.9%), while the disease was found only in 35 (39.8) patients from rural areas. This could be due to the living conditions and personnel behavior or more likely due to the consumption of cold drinks and fast food, which are easily available in the urbanized area compared to rural areas. The result of this research revealed that GAS tonsillitis predominately occurred in children aged 5–10 years (68%) and the incidence among those aged 11–16 years is relatively low (32%). Similar observations were reported for the age group of 6–12 years (61%) [34]. However, contrary to the results of the current study, a previous study performed on this subject area showed a higher rate of streptococcal pharyngitis among those aged 16–20 (85.7%) than those who were 11–15 (70%) and 5–10 (56.2%) years old. The distribution of streptococcal pharyngitis was more in female patients (95 [43.4%]) than in male patients (64 [38.8%]). Similarly, Mohammed *et al*. and Ahmed *et al.'s* studies reported that the majority of those who complained of tonsillitis were females. This is probably because the number of female patients admitted was more than male patients. On the other hand, Singh *et al*. reported that the frequency of streptococcal pharyngitis was more in boys than girls [35].

Furthermore, it was noted that 64% of primary school students, 19% of secondary school students, and 17% from kindergarten were infected by GAS pharyngitis. Our finding was proportionally 19%, which is similar to the results of Sharma *et al*. who found a GAS frequency of 17.5% in children aged 11–15 years (secondary-school level) [59]. However, the current research showed a higher frequency of GAS in the age group 5–10 years. This may be due to cross-infection because of overloaded classrooms and poor air circulation in them, low immunity, and the nature of children's activity. Probably, the variation between studies could be due to the difference in sample size, study subjects, climates, seasons, and diagnostic procedures. According to the AST results, all isolates were sensitive to penicillin, which is similar to the findings of other previous studies [36–39]. In contrast to these results, a previous study carried out in Egypt found that four strains of *S. pyogene* were resistant to penicillin [40], which is different from our findings and the available literature. The efficiency of this drug could be due to the incapability of GAS to generate β-lactam enzymes. However, penicillin can be ineffective in treating *S. pyogenes* infections, as its action is evaded through the introduction into the epithelial cells, which is difficult for penicillin to reach inside cells [41]. Moreover, the development of the biofilm phenomenon [42] and the presence of other β-lactamase-producing bacteria act as protective tools for *S. pyogenes* [43, 44]. Many previous studies showed comparable findings. Indeed, the rate of resistance to erythromycin was 21.3%, Egypt [40], Lebanon 23%, [45], and Greece 22.8 % [46], which is lower than our result. Sayyahfar *et al.*'s study reported that 33.9% of GAS isolates were resistant to erythromycin [47]. The findings of these studies are considered more relevant to our study in which the resistance rate to erythromycin was 29.6%. Compared to this, several studies showed a low rate of resistance to erythromycin as reported in Norway (2.7%) [48], the United States (5.2%) [49], France (6.5%) [50], Italy (7.4%) [29], Spain (2.8%) [51], Tunis (5.2%) [52], and Taiwan (10.7%) [53]. Additionally, the clindamycin resistance rate of GAS in our study was 4.4%, however, many studies have shown higher results

– for instance, Iran (13.5%) and Korea (32.5%) [54, 55]. On the other hand, a low rate of clindamycin was reported in Italy (1.4%) and the USA (0.5%) [56, 57]. Our study showed an azithromycin resistance of 27.7% which is similar to the results of Sharma *et al.* (28.6%) and Rijal et *al.* (24%) [58, 59]. In contrast to these results, recently Khademi *et al*. reported that the resistance of azithromycin was 12%. The variation of reports outcomes may be due to the diversity of genotypic and phenotypic characters of circulating strains, or guidelines of antibiotic utilization rules between the different sites of the earth.

5. Conclusion

The high proportion of GAS was isolated from the throats of children suffering from tonsillitis in White Nile State. Regardless of the resistance of isolates to some antibiotics, penicillin still is the drug of choice for streptococcal tonsillitis with 100% sensitivity. GAS tonsillitis with lymphadenopathy or tonsil hyperplasia showed a significant frequency of macrolides resistance. The development of macrolides resistance among isolates of GAS reflects the need for alternative choices for the management of GAS tonsillitis in subjects with a penicillin allergy.

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Competing Interests

None declared.

Availability of Data and Material

The dataset generated during this study are available from the corresponding author on reasonable request.

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