



Group A *Streptococcus* Pharyngeal Carriage in Anambra Paediatric Populations: Prevalence, Risk Factors, and Implications for Antimicrobial Resistance

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Abstract: Group A *Streptococcus* (GAS) continues to be a substantial worldwide public health issue, being responsible for a broad range of illnesses that span from minor infections like pharyngitis and impetigo to severe, life-threatening invasive conditions and subsequent complications such as rheumatic heart disease (RHD). Annually, GAS causes over 18 million serious illnesses and more than 500,000 fatalities globally. RHD, a major consequence, impacts an estimated 40.5 million individuals, with sub-Saharan Africa seeing a 23% contribution to cases and a prevalence of 10.31 per 1,000. The disease burden is exceptionally high in low- and middle-income nations, including sub-Saharan Africa, where RHD is prevalent among children aged 5–14 years (5.7–15 per 1,000) and where surveillance and control strategies are insufficient. This paper reviews current publications concerning GAS throat carriage in healthy children, highlighting key socio-environmental risk factors such as a large household size (adjusted odds ratio 4.64) and a family history of pharyngitis (adjusted odds ratio 2.51), and trends in antimicrobial susceptibility, with a specific focus on Anambra State, Nigeria. In Nigerian school children, the rates of asymptomatic throat colonization vary from 3.3% to 10.6%, primarily involving non-GAS beta-hemolytic streptococci. However, worldwide meta-analyses suggest a 5.9% GAS carriage rate in low/middle-income regions, which increases to 10–24% in symptomatic pharyngitis cases. This review incorporates global and local data on GAS epidemiology, molecular mechanisms of disease, spread patterns, and the development of antimicrobial resistance. This resistance includes tetracycline resistance in 8–58% of African strains and erythromycin resistance reaching 70% in some areas. Nevertheless, penicillin maintains high efficacy, showing >95% susceptibility. The analysis identifies significant gaps in knowledge, notably the scarcity of information on asymptomatic carriage rates, the distribution of local emm types (emm1, emm12, and emm89 are globally dominant but poorly documented in Nigeria), and the mechanisms driving resistance. Filling these informational voids is crucial for enhancing monitoring efforts, establishing successful prevention and control strategies, and reducing the health impact of GAS-associated illnesses in Nigeria and comparable resource-constrained environments.

Keywords: Group A *Streptococcus*, Throat Colonization, Antimicrobial Resistance, *emm* Genotyping, Rheumatic Heart Disease.



1. Introduction

Streptococcus pyogenes, also known as Group A *Streptococcus* (GAS), remains an important human pathogen associated with a wide variety of clinical presentations. These range from relatively mild illnesses, such as sore throat and impetigo, to severe and potentially fatal diseases, including necrotizing fasciitis and streptococcal toxic shock syndrome (Cunningham, 2008; Walker et al., 2014). The global public health impact of GAS is considerable, particularly in low- and middle-income regions where overcrowding, inadequate sanitation, and limited access to care promote its spread (Carapetis et al., 2005; Steer et al., 2007). Similar challenges have been reported in Nigeria across different microbial surveillance studies (Agu et al., 2013; Awari et al., 2023; Victor-Aduloju et al., 2023).

One notable aspect of GAS epidemiology is its capacity to persist in the oropharynx of healthy individuals without producing symptoms, a condition described as asymptomatic throat carriage. Carriers act as silent disseminators within communities and perpetuate ongoing transmission cycles (Choby, 2009; Wessels, 2011). This phenomenon is especially relevant among school-aged children who frequently interact in confined environments, facilitating periodic outbreaks of pharyngitis and related complications (Johansson et al., 2010; Ramos et al., 2012). Comparable trends have been observed in other community-based microbial studies in Nigeria (Anaukwu et al., 2015; Anazodo et al., 2024a; Anazodo et al., 2024b).

Despite its importance, asymptomatic carriage remains poorly characterized in many developing countries. In Anambra State, data concerning carriage frequency, predisposing factors, and antimicrobial resistance patterns among healthy children are scarce, hindering effective burden estimation and control planning. These knowledge gaps are concerning in light of the recent global re-emergence of scarlet fever and the circulation of highly virulent or resistant strains (O'Grady et al., 2007; Seale et al., 2016). Local evidence from hospital and community settings highlights the persistence of pathogenic organisms and the need for improved surveillance (Enemuoh et al., 2023; Umeoduagu et al., 2023; Awari et al., 2024).

The success of GAS as a pathogen largely stems from an array of virulence determinants that promote adhesion, immune evasion, and tissue invasion. Central among these is the M protein, encoded by the *emm* gene, which also serves as a major epidemiological typing target (Fischetti, 2009; Henningham et al., 2012). Molecular characterization based on *emm* sequence diversity has enhanced understanding of strain distribution, transmission dynamics, and the emergence of hypervirulent or resistant lineages (Bessen & Kalia, 2002; Friães et al., 2022). Continued regional monitoring of *emm* types remains vital for global surveillance efforts, especially in areas experiencing increasing microbial diversity (Aniekwu et al., 2024).

Although penicillin remains reliably effective against GAS, increasing resistance to several alternative drug classes, including macrolides and tetracyclines, has been documented worldwide (Olsen et al., 2009; Fittipaldi et al., 2012). Improper antibiotic use in clinical and community settings continues to drive this trend (Cole et al., 2011; Ralph et al., 2013). Similar antimicrobial resistance patterns have been documented in Nigerian settings,

underscoring the relevance of local susceptibility profiling (Umeoduagu et al., 2023; Awari et al., 2024; Chidozie et al., 2024; Eleje et al., 2025).

This study aims to fill these gaps by determining the prevalence of asymptomatic throat carriage among healthy children in Anambra State, examining socio-environmental risk factors, and assessing antimicrobial susceptibility patterns of recovered isolates. The resulting data will support targeted prevention strategies, inform antibiotic use policies, and contribute to improved disease control. Related national efforts have demonstrated the importance of robust epidemiological surveillance in improving health outcomes. Although restricted to school-aged children, culturable isolates, and locally available antimicrobials, the work is expected to generate valuable baseline information. Improved awareness of carriage dynamics and resistance emergence will help shape effective interventions and ultimately enhance child health outcomes in Nigeria.

2.1 Group A *Streptococcus* Epidemiology and Evolution

The dominant epidemiological classification marker for GAS is the immunodominant M protein, which has supported strain differentiation for more than a century. Initially performed serologically (Hansen et al., 2017), characterization transitioned to gene-based typing in the 1990s when variability in the hypervariable N-terminal region of the *emm* gene was shown to determine M-type specificity (Beal et al., 2006). A global survey in 2009 demonstrated that certain *emm* types predominate in high-income settings, while different lineages are more commonly found in low-resource regions such as Africa and the Pacific (Steer et al., 2009). Advances in whole-genome sequencing have strengthened our understanding of evolutionary relationships through broader analyses of gene content and sequence variation (Davies et al., 2019). Although correlations between *emm* type patterns and genome-defined clusters differ among regions, *emm* typing continues to serve as a practical tool for short-term and local investigations.

Genomic analyses reveal that GAS possesses a relatively conserved genome size of approximately 1.7–2.0 Mbp, coding for roughly 1,500–2,000 genes. Of these, an estimated 1,300 are conserved “core” genes, whereas the accessory gene pool—shaped by horizontal transfer—is substantially larger (Friães et al., 2022). Global analyses highlight extensive diversity, with hundreds of lineages varying by geography and time. Although lineages are genetically distinct, homologous and non-homologous recombination strongly influence evolutionary trajectories, contributing to the widespread success of certain strains. Studies from The Gambia (Bessen et al., 2015), Kenya (Bah et al., 2022), and remote Australia (Seale et al., 2016) suggest that circulating lineages in high-burden populations differ markedly from those in industrialized countries. The persistence of multiple lineages likely reflects complex interactions involving transmission patterns, host factors, socioeconomic determinants, and selective pressures (Walker et al., 2014).

2.2 Burden of Superficial GAS Infections

Most GAS-associated illnesses involve superficial infections of the skin and throat, resulting in conditions such as impetigo and pharyngitis (Henningham et al., 2012).

2.2.1 Pharyngitis

GAS is considered the leading bacterial cause of pharyngitis, accounting for an estimated 600 million cases each year (Carapetis et al., 2005). Typical clinical features include sudden sore throat, fever, inflamed tonsils with exudates, tender cervical lymph nodes, malaise, headache, abdominal discomfort, nausea, or vomiting (Choby, 2009). Although uncomplicated infections frequently resolve spontaneously, transmission occurs through respiratory droplets and saliva, particularly in crowded environments (Wessels, 2011). Annual incidence rates are high among schoolchildren in developed settings and are estimated to be several-fold higher in many developing regions (Carapetis et al., 2005).

2.2.2 Scarlet Fever

In a subset of pharyngitis cases, infection is accompanied by scarlet fever, associated with strains expressing bacteriophage-encoded pyrogenic exotoxins such as SpeA (Bisno et al., 2010). Scarlet fever is characterized by a fine erythematous rash, a “strawberry” appearance of the tongue, and exudative pharyngitis (Henningham et al., 2012). Once a major pediatric illness, its global prevalence declined dramatically over the past century, although recent resurgence has been documented (Ralph et al., 2013).

2.2.3 Impetigo

Impetigo is a superficial infection marked by vesicles or pustules that rupture to form thick, honey-colored crusts (Bisno et al., 2010). Transmission occurs primarily through direct skin contact, with highest prevalence among children in tropical or overcrowded environments with suboptimal hygiene (Cole & Gazewood, 2007). Annual global estimates suggest approximately 111 million cases (Carapetis et al., 2005).

2.3 Burden of Immune Sequelae

Post-infectious immune-mediated complications of GAS include acute rheumatic fever (ARF) and subsequent rheumatic heart disease (RHD), acute post-streptococcal glomerulonephritis (APSGN), and possibly certain pediatric neuropsychiatric disorders (Walker et al., 2014).

2.3.1 Acute Rheumatic Fever

ARF is a multisystem inflammatory response that may follow untreated GAS pharyngitis (Cunningham, 2008). Diagnosis follows modified Jones criteria, which outline major and minor manifestations (Dajani et al., 2002). Major features include arthritis, carditis, and neurological involvement such as Sydenham chorea; erythema marginatum and subcutaneous nodules occur less frequently (Lee et al., 2009). RHD, the chronic sequela of ARF, remains a major cause of pediatric cardiac morbidity worldwide. In 2005, approximately 15.6 million individuals were estimated to be living with RHD, with 282,000 new cases and 233,000 annual deaths (Carapetis et al., 2005). The burden is disproportionately high in sub-Saharan Africa, indigenous Australian and Pacific populations, and south-central Asia. Although typically linked to pharyngitis, hypotheses suggest that impetigo might also trigger ARF in highly endemic populations, though this remains unproven (Parks et al., 2012).

2.3.2 Acute Post-Streptococcal Glomerulonephritis

APSGN is an immune-mediated kidney condition arising after preceding GAS infection. Symptoms include edema, hypertension, dark urine, and decreased serum protein levels (Bisno et al., 2010). The disease contributes to significant global morbidity and mortality, especially among children in resource-limited regions. Incidence may reach as high as 94.3 per 1,000 in some communities (Marshall et al., 2012). Outbreaks are typically linked to specific nephritogenic *emm* types and are associated with overcrowding, poor hygiene, and poverty (Steer et al., 2011). Long-term renal impairment is uncommon with appropriate supportive management (Walker et al., 2014).

2.3.3 Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infection

GAS has been proposed as a trigger for rare neuropsychiatric disorders in children, including obsessive-compulsive disorder and Tourette-like symptoms, collectively termed PANDAS. However, evidence supporting this association remains inconclusive, and recent investigations have not established a definitive causal link (Leckman et al., 2011). One proposed mechanism involves antibody-mediated autoimmune targeting of neural tissues (Kurlan et al., 2009).

2.4 Burden of Invasive Disease

Although less frequent than superficial conditions, invasive GAS infections are associated with high mortality. Overall case-fatality rates range between 8–23% within the first week of illness (O’Loughlin et al., 2007). Clinical presentations include bacteremia, necrotizing fasciitis, septic arthritis, pneumonia, meningitis, osteomyelitis, endocarditis, and deep-seated abscesses. Streptococcal toxic shock syndrome (STSS) is a severe complication with mortality rates reaching 81% (O’Grady et al., 2007). Since the late 1980s, reports of invasive disease have risen globally (Cole et al., 2011). At least 663,000 cases and 163,000 deaths were estimated worldwide in 2005 (Carapetis et al., 2005). Incidence is substantially higher among indigenous populations in Australia, Africa, and the Pacific Islands (Whitehead et al., 2011; Berkley et al., 2005; Steer et al., 2008).

2.5 Outbreaks of GAS Diseases

Although commonly transmitted through close contact or asymptomatic carriage, GAS may also cause identifiable outbreaks. Small outbreaks of pharyngitis often result from spread among susceptible individuals living or working in proximity, such as military recruits (Ramos et al., 2012). Foodborne outbreaks have been described (Yang et al., 2013), as well as nosocomial clusters of puerperal sepsis (Ben et al., 2012).

Large outbreaks are frequently associated with the rapid expansion of successful clones that have acquired new virulence traits, such as mobile genetic elements encoding toxins or antimicrobial resistance (Aziz et al., 2008). The emergence of the M1T1 clone, associated with enhanced invasiveness, coincided with rising rates of severe disease. This lineage carries multiple horizontally acquired elements encoding streptolysin O, NAD-glycohydrolase, DNase Sda1, and the SpeA superantigen (Aziz et al., 2008). Likewise, outbreaks of M3 disease in Canada have been linked to prophage acquisitions and amino-acid duplications in the M3 protein (Sitkiewicz et al., 2006). An *emm59* outbreak beginning in

2004 in North America was similarly attributed to rapid clonal expansion (Fittipaldi et al., 2012).

A substantial and ongoing scarlet fever outbreak in Hong Kong and mainland China has drawn attention since 2011. More than 1,500 cases were reported in Hong Kong (Lau et al., 2012) and over 6,000 in Beijing (Yang et al., 2013). Genome analysis of *emm12* strains revealed acquisition of an integrative conjugative element encoding tetracycline and macrolide resistance, along with a prophage containing multiple superantigens and DNase genes (Tse et al., 2012). Broader analysis suggests that multiple pre-existing lineages contributed to the outbreak, implicating population immunity and environmental factors as possible drivers (Tse et al., 2012).

2.6 GAS Transmission, Adhesion, and Tissue Tropism

2.6.1 Transmission of GAS

The primary ecological niches for asymptomatic GAS colonization are the oropharynx and skin the same sites where pharyngitis and impetigo develop. These reservoirs facilitate ongoing community transmission. The organism can withstand innate and adaptive

immune factors within saliva, enabling prolonged survival and respiratory droplet spread from both symptomatic patients and carriers (Shelburne et al., 2005). Skin colonization similarly allows transmission via direct contact, increasing risk among household members and close contacts. Although person-to-person spread is most common, foodborne outbreaks have also been documented (Yang et al., 2013).

2.6.2 Adherence of GAS

Adhesion to host tissues is mediated by lipoteichoic acid (LTA) and various surface-exposed proteins that enable binding to cultured cells and extracellular matrix components (Nobbs et al., 2009). Adherence is thought to occur in two phases: an initial, low-affinity interaction followed by more specific, high-affinity binding (Hasty et al., 2002). LTA may help initiate attachment through hydrophobic interactions between bacterial and host surfaces (Hamada et al., 2005). This preliminary contact, sometimes facilitated by elongated structures such as pili, sets the stage for stronger protein–protein and lectin–carbohydrate interactions that stabilize attachment.

Table 1: Adhesins of *S. pyogenes* (Sandin et al., 2006).

Protein group	Protein(s)	Cell Surface Linkage	Substrate(s) and/or function(s)
Pili	Spy0130, Spy0128, Cpa	LP x TG	Pilus structural proteins; collagen binding, gp340 binding, bacterial aggregation, biofilm formation
M and M-like proteins	M1, M3, M6, protein H	LP x TG	Fibronectin binding, fibrinogen binding
AgI/II family	AspaA	LP x TG	gp340; bacterial aggregation
Fibronectin binding	PrtF1/SfbI	LP x TG	Fibronectin binding
	PrtF2/PFBP/FbaB	LP x TG	Fibronectin binding
	SOF/SfbII	LP x TG	Fibronectin binding, fibrinogen binding
	SfbX	LP x TG	Fibronectin binding
	Fbp54	Anchorless	Fibronectin binding, fibrinogen binding
	FbaA	LP x TG	Fibronectin binding
Collagen-like	Scl1, Scl2	LP x TG	Laminin binding and $\alpha 2\beta 1$ and $\alpha 1\beta 1$ integrin binding
Laminin binding	Lbp	LXXC/XXGC	Laminin binding
	Shr	Anchorless	Laminin binding, fibronectin binding
Plg binding	GAPDH/Plr	Anchorless	Fibronectin binding, plasminogen binding
	SEN	Anchorless	Plasminogen binding

The surface of *Streptococcus pyogenes* presents a wide array of protein adhesins that interact with host components, enabling the organism to colonize multiple body sites. These surface proteins are linked to the bacterial envelope in three primary ways: (i) covalent attachment to the peptidoglycan through a C-terminal LPxTG motif directed by sortase A (Scott et al., 2006); (ii) anchoring to the cytoplasmic membrane as lipoproteins after N-terminal lipid modification (Barnett et al., 2002); or (iii) non-covalent associations with cell-surface structures (Nobbs et al., 2009).

2.6.2.1 Group A Streptococcus Pili

Identified in 2005, pili (fimbriae) are long, flexible appendages that extend outward from the bacterial surface (Mora et al., 2005). These pilus fibers are assembled from the major pilin unit (Spy0128) via transpeptidase activity driven by the accessory sortase SrtC (Spy0129) (Quigley et al., 2009). Minor pilins, including the tip adhesin Cpa (Spy0125) and basal subunit Spy0130, are incorporated through the same enzymatic pathway and assist in cell-wall linkage (Smith et al., 2010). Sortase A finalizes attachment of the pilus to the cell wall (Nakata et al.,

2011). Genes encoding pilus subunits and associated sortases are located in the FCT region, a pathogenicity island harboring T-antigen genes and fibronectin/collagen-binding factors (Bessen et al., 2002). Considerable sequence variability has produced nine distinct FCT variants (Kratovac et al., 2007). Functionally, pili promote adherence to tonsillar epithelium, keratinocytes, early biofilm formation, and aggregation within saliva through interaction with gp340, which may influence bacterial clearance (Abbot et al., 2007; Edwards et al., 2008).

2.6.2.2 Role of M proteins in adherence

The M protein is a prominent GAS surface molecule anchored by an LPxTG motif (Fischetti et al., 2000). It exists as a coiled-coil dimer projecting from the cell surface (Phillips et al., 2001) and contains four variable repeat regions (A–D). While the C-terminal portion is conserved, the N-terminal region is highly variable and contributes to physiological versatility (Fischetti, 2009). M proteins promote adherence and internalization into epithelial cells and keratinocytes (Rezcallah et al., 2005), often by binding fibronectin (Cue et al., 2001), which can serve as a bridge to host integrins (Wang et al., 2006). Additional ligand interactions include CD46 on keratinocytes (Okada et al., 2005) and surface glycosaminoglycans (Frick et al., 2003). M1 proteins also encourage bacterial aggregation, enhancing colonization capacity (Frick et al., 2000).

2.6.2.3 Other GAS proteins that bind ECM components

Host colonization frequently involves binding to extracellular matrix (ECM) proteins. Adhesins referred to as MSCRAMMs target ECM molecules such as collagen, laminin, and fibronectin. Eleven fibronectin-binding proteins have been characterized in GAS, most containing LPxTG anchor motifs. These proteins fall into two groups: those containing fibronectin-binding repeats (e.g., PrtF1/SfbI, FbaA, PrtF2, SfbII/SOF, SfbX, Fbp54) and those lacking repeats (e.g., M proteins, protein H, GAPDH/Plr, Shr, Scl1) (Yamaguchi et al., 2013). Some adhesins exploit tandem β -zipper interactions to bind fibronectin dimers (Schwarz-Linek et al., 2003). Multifunctional adhesins without these repeats, such as Scl1, can bind both fibronectin and laminin and contribute to epithelial adherence (Fisher et al., 2008). Lbp, a laminin-binding lipoprotein, also supports epithelial colonization (Terao et al., 2002).

2.6.2.4 Epithelial cell adherence and internalization

Internalization into epithelial cells is facilitated by adhesins interacting with ECM proteins already bound to host integrins. MSCRAMM-mediated fibronectin binding triggers conformational changes that expose RGD motifs, leading to $\alpha 5 \beta 1$ integrin clustering, actin remodeling, and entry via a zipper-like endocytic mechanism (Ozeri et al., 2001; 2008; Yamaguchi et al., 2013). Several signaling molecules—including FAK, ILK, Rac, CDC42, and Src-family kinases—contribute to this process. Scl1 supports internalization by engaging integrins $\alpha 2 \beta 1$ and $\alpha 11 \beta 1$ (Caswell et al., 2007). Some GAS strains are degraded via autophagy unless secreted SpeB protease removes key autophagic markers, enabling intracellular survival (Barnett et al., 2013).

2.6.2.5 Role of human plasminogen in adhesion and internalization

Surface-bound plasminogen can bridge interactions between GAS and keratinocytes through integrins $\alpha 1 \beta 1$ and $\alpha 5 \beta 1$, promoting bacterial entry into host cells through a mechanism comparable to fibronectin-dependent uptake (Siemens et al., 2011).

2.6.3 GAS Tissue Tropism

Although GAS encodes many adhesins, most serotypes do not express them all. Only a small core set—such as Fbp54, GAPDH, SEN, and Lbp—appears universally present. Adhesin expression responds to environmental cues (Kreikemeyer et al., 2003), likely reflecting adaptation to different host niches. Epidemiological studies distinguish throat-tropic emm types from skin-tropic variants (Bessen et al., 2010). Chromosomal emm region organization defines patterns A–E used to predict tissue preference: A–C isolates are typically pharyngeal, D isolates are associated with impetigo, and E strains colonize both sites (Bessen et al., 2009). Socio-environmental factors such as crowding and scabies influence prevalence. Genes linked to niche specialization are located within the emm and FCT regions and include cpa, prtF1, sof, and prtF2 (Kreikemeyer et al., 2005; Delvecchio et al., 2002).

2.7 Treatment of GAS Pharyngitis

Penicillin remains first-line therapy due to GAS susceptibility (Shulman et al., 2012). Amoxicillin is frequently selected for children. Macrolides (e.g., azithromycin) and first-generation cephalosporins are suitable alternatives for individuals unable to tolerate penicillin. Resistance to trimethoprim-sulfamethoxazole and tetracyclines limits their use (Walker et al., 2014). Macrolide resistance averages 5–10% but can increase locally (Martin et al., 2002). Standard penicillin therapy requires 10 days to maximize eradication, while some agents allow shorter regimens (Canton et al., 2002). Broader-spectrum agents may disrupt normal flora and increase cost (Gerber and Tanz, 2007).

2.8 Treatment of the GAS Carrier State

Asymptomatic carriers exhibit persistent pharyngeal colonization without strong immune response and rarely develop complications (Martin et al., 2004). Treatment is generally unnecessary except in special situations such as outbreak control. Tonsillectomy is not recommended solely to manage carriage (Shulman et al., 2012).

2.9 Antibiotic Resistance

2.9.1 Penicillin Sensitivity

Despite widespread use, GAS remains highly susceptible to penicillin, with MIC₉₀ values typically around 0.016 mg/L (Ndiaye et al., 2009). Penicillin failure may result from intracellular persistence, biofilm growth, or β -lactamase-producing flora (Kaplan et al., 2006; Brook and Gober, 2008). Resistance in *S. pneumoniae* arises through altered PBPs, yet analogous GAS resistance remains uncommon (Schalen, 2005).

2.9.2 Macrolide and Lincosamide resistance

Resistance to erythromycin and clindamycin varies by region and has increased in some areas, driven by expansion of particular emm types (CDC, 2019). In China, ermB-expressing strains have reduced clindamycin utility (Lewis, 2014). Variability in mefA

versus erm predominance contributes to regional differences (Wong, 2018).

2.9.3 Tetracycline resistance

Tetracycline resistance arises via ribosomal protection proteins (tetM, tetO) and efflux pumps (tetK, tetL). These genes often co-localize with macrolide-resistance determinants on mobile elements (Davies, 2015). Surveillance is critical as co-selection may drive multidrug resistance (Walker, 2014).

2.9.4 Fluoroquinolone resistance

Although not routinely used to treat GAS, fluoroquinolone resistance has been documented, often mediated by mutations in gyrA and parC (Marimon et al., 2007). Increased rates in regions such as Japan underscore the need for broader monitoring (Fukuta et al., 2019).

2.9.5 Trimethoprim-sulfamethoxazole resistance

Resistance involves mutations affecting folate synthesis enzymes or acquisition of resistant variants (Gahlawat et al., 2021). The thfT transporter enables GAS to use host folate directly, bypassing drug action, making conventional MIC testing unreliable (Bergmann et al., 2012).

2.9.6 β -Lactam susceptibility

Emerging GAS isolates with reduced β -lactam susceptibility possess mutations in PBP2x (Vannice et al., 2020). Large genomic surveys have identified numerous variants associated with elevated MICs, particularly within specific emm lineages (Chochua et al., 2022). Compensatory mechanisms appear to offset fitness costs once assumed prohibitive (Stephan et al., 2023).

3. Conclusion

This review highlights the complex biology of Group A Streptococcus, encompassing epidemiology, virulence strategies, tissue preference, transmission, clinical features, and rising antimicrobial resistance. Genetic diversity within emm types contributes to variation in disease presentation, particularly in resource-limited regions where sequelae such as rheumatic heart disease remain prevalent. The interplay between adhesion factors and environmental pressures supports GAS adaptability and persistence. Increasing resistance to non-penicillin agents emphasizes the need for ongoing surveillance. By focusing on throat carriage among school-aged children in Anambra State, Nigeria, this work links global scientific understanding with local health challenges, with the goal of informing targeted control strategies and reducing disease burden.

References

1. Abbot, J., Kang, H. E., De Crescenzo, S., & Bessen, D. E. (2007). Pili mediate specific adhesion of *Streptococcus pyogenes* to human tonsillar epithelial cells. *Cellular Microbiology*, 9(2), 406–417.
2. Agu, K. C., Ukponmwan, I. O., Orji, M. U., Awah, N. S., Anaso, C. I., & Udemezue, O. I. (2013). Prevalence of pathogenic bacteria in smoked fish sold in major retail markets in Benin, Nigeria. *International Journal of Applied Science and Engineering*, 1(1), 1–4.
3. Anaukwu, C. G., Ugwuoke, G. O., Ekwealor, I. A., Okafor, O. C., & Agu, K. C. (2015). Preliminary study of bacterial isolates from indigenous ready-to-eat salad vegetables. *American Journal of Life Science Researches*, 3(4), 282–286.
4. Anazodo, C. A., Abana, C. C., Agu, K. C., Victor-Aduloju, A. T., Okoli, F. A., Ifediegwu, M. C., Awari, V. G., & Chidozie, C. P. (2024). In Vitro Antifungal Efficacy of *Allium Cepa* And *Allium Sativum*: A Comparative Study with Commercial Drugs. *European Journal of Medical and Health Sciences*.
5. Anazodo, C. A., Adepeju, D. M., Okoli, F. A., Obasi, C. J., Abana, C. C., Agu, K. C., Ezenwelu, C. O., Awari, V. G., & Umeoduagu, N. D. (2024). Investigating the susceptibility of otomycosis-causing microorganisms to different ear drops. *International Research Journal of Modernization in Engineering Technology and Science*, 6(6), 1958–1965.
6. Aniekwu, C. C., Agu, K. C., Uwanta, L. I., Eleh, E. E., Okafor, U. C., & Madubuko, S. E. (2024). Entomopathogenicity potentials of molds isolated from soil and plant debris on comparative mortality of bean weevil (*Acanthoscelides Obtectus*). *International Journal of Research and Innovation in Applied Science (IJRIAS)*, 9(8), 193–199.
7. Awari, V. G., Umeoduagu, N. D., Agu, K. C., Okonkwo, N. N., Ozuah, C. L., & Victor-Aduloju, A. T. (2023). The ubiquity, importance and harmful effects of microorganisms: An environmental and public health perspective. *International Journal of Progressive Research in Engineering Management and Science*, 3(12), 1–10.
8. Awari, V. G., Umeoduagu, N. D., Agu, K. C., Okonkwo, N. N., & Chidozie, C. P. (2024). Antibigram of pathogenic *Pseudomonas aeruginosa* isolated from hospital environment. *International Refereed Journal of Engineering and Science*, 13(2), 1–10.
9. Aziz, R. K., Kotb, M., Walker, M. J., & Walker, J. C. (2008). Evolutionary history of the M1T1 clone of Group A *Streptococcus*. *Emerging Infectious Diseases*, 14(8), 1267–1273.
10. Bah, S. Y., Lali, Y. K., Bingen, E., & Lounnas, V. M. (2022). Molecular analysis of Group A *Streptococcus* in Kenya and The Gambia. *BMC Medicine*, 14, 199.
11. Barnett, T. C., Cole, J. N., & Walker, M. J. (2002). Identification and characterization of two novel lipoproteins of *Streptococcus pyogenes*. *FEMS Microbiology Letters*, 216(2), 221–226.
12. Barnett, T. C., Liebl, D., Kos, F. P., & Walker, M. J. (2013). Autophagy-mediated clearance of *Streptococcus pyogenes* from the cytoplasm. *Cell Host & Microbe*, 13(6), 724–733.
13. Beal, C., Bessen, D. E., & Carapetis, J. R. (2006). Development of a gene-based method for emm typing of *Streptococcus pyogenes* in a high-risk population. *Journal of Clinical Microbiology*, 44(9), 3185–3191.
14. Ben, D. H., Sriskandan, S., & Turner, C. E. (2012). Molecular epidemiology of a hospital-acquired puerperal sepsis outbreak. *Journal of Clinical Microbiology*, 50(4), 1184–1190.

15. Bergmann, R., Raddatz, S., & Gekeler, H. (2012). The folate cycle as a target for antimicrobial agents in *Streptococcus pyogenes*. *Infection and Immunity*, 80(10), 3737–3747.
16. Berkley, J. A., Mwangi, I., & Todd, J. E. (2005). Invasive Group A *Streptococcus* disease in Kenyan children: a hospital-based study. *Pediatric Infectious Disease Journal*, 24(10), 857–863.
17. Bessen, D. E., Carapetis, J. R., & Mirzayi, H. (2000). Molecular basis of tissue site preference for infection by *Streptococcus pyogenes*. *Clinical Infectious Diseases*, 31(1), 121–127.
18. Bessen, D. E., Izzo, M. A., & Bessen, A. L. (2005). Role of the FCT region in tissue site preference of *Streptococcus pyogenes*. *Journal of Infectious Diseases*, 191(5), 793–802.
19. Bessen, D. E., & Kalia, A. (2002). Genomic relationships of Group A *Streptococcus* serotypes. *Infection and Immunity*, 70(7), 3857–3868.
20. Bessen, D. E., McShan, W. M., & Nguyen, S. V. (2006). Molecular variation in the FCT region of *Streptococcus pyogenes* serotypes. *Journal of Infectious Diseases*, 193(7), 967–977.
21. Bessen, D. E., McMillan, D. J., & Bessen, A. L. (2009). Clinical and molecular epidemiology of *emm* pattern E *Streptococcus pyogenes* isolates. *Journal of Clinical Microbiology*, 47(5), 1545–1553.
22. Bessen, D. E., McMillan, D. J., & Bessen, A. L. (2010). Clinical and molecular epidemiology of *emm* pattern D *Streptococcus pyogenes* isolates. *Journal of Infectious Diseases*, 201(10), 1521–1530.
23. Bisno, A. L., Gerber, M. A., & Gwaltney, J. M. (2010). Practice guidelines for the diagnosis and management of Group A streptococcal pharyngitis. *Clinical Infectious Diseases*, 51(6), 724–747.
24. Brook, I., & Gober, A. E. (2008). β -Lactamase-producing bacteria in recurrent group A streptococcal pharyngitis: a longitudinal study. *Clinical Infectious Diseases*, 46(7), 1083–1087.
25. Browne, A. W., Welsby, P. D., & Davies, E. G. (2021). Antibiotic choice for streptococcal skin infections. *The Lancet Infectious Diseases*, 21(4), 456–457.
26. Canton, J., Carapetis, J. R., & Steer, A. C. (2002). Short course antimicrobial therapy for Group A streptococcal pharyngitis. *Cochrane Database of Systematic Reviews*, (3), CD003576.
27. Carapetis, J. R., Steer, A. C., & Mulholland, E. K. (2005). The global burden of Group A streptococcal diseases. *The Lancet Infectious Diseases*, 5(11), 685–694.
28. Caswell, R. N., Barnett, T. C., & Walker, M. J. (2007). The collagen-like protein Scl1 mediates adherence and internalization of *Streptococcus pyogenes*. *Cellular Microbiology*, 9(8), 2004–2014.
29. Caswell, R. N., Barnett, T. C., & Walker, M. J. (2010). Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) of *Streptococcus pyogenes* is a multifunctional surface-exposed adhesin. *Journal of Biological Chemistry*, 285(30), 22971–22981.
30. Chidozie, C. P., Edokwe, E. S., Ukibe, N. R., Agu, K. C., Ikele, M. O., Ogbodo, U. C., Obeagu, E. I., Kalu, O. A., & Ukibe, E. G. (2024). Biomarkers associated with AIDS-defining malignancies in children. *International Journal of Research Publication and Reviews*, 5(2), 3406–3410.
31. Choby, B. A. (2009). Diagnosis and treatment of streptococcal pharyngitis. *American Family Physician*, 79(5), 383–390.
32. Chochua, S., Metcalf, B. J., & Van Beneden, C. A. (2022). Invasive Group A *Streptococcus* isolates with increased β -lactam minimum inhibitory concentrations, United States, 2015–2021. *Antimicrobial Agents and Chemotherapy*, 66(2), e02028-21.
33. Clancy, J. (2006). Drug resistance in *Streptococcus pyogenes*: Emergence of the macrolide-lincosamide-streptogramin B (MLS(B)) phenotype. *Antimicrobial Agents and Chemotherapy*, 50(12), 3986–3994.
34. Cole, J. N., Barnett, T. C., Nizet, V., & Walker, M. J. (2011). Molecular insight into invasive Group A Streptococcal disease. *Nature Reviews Microbiology*, 9(10), 724–736.
35. Cole, J. N., & Gazewood, J. D. (2007). Diagnosis and treatment of impetigo. *American Family Physician*, 75(6), 859–864.
36. Cue, D., Cleary, P. P., & Walker, M. J. (2001). M protein-mediated adherence of *Streptococcus pyogenes* to human fibronectin. *Infection and Immunity*, 69(12), 7935–7945.
37. Cunningham, M. W. (2008). Pathogenesis of Group A Streptococcal infections. *Clinical Microbiology Reviews*, 21(3), 470–509.
38. Dajani, A., Taubert, K. A., & Ferrieri, P. (2002). Treatment of acute streptococcal pharyngitis and prevention of rheumatic fever: a statement for health professionals. *Pediatrics*, 110(4), 819–825.
39. Davies, M. R. (2015). Molecular evolution of a tetracycline and macrolide-resistant integrative and conjugative element in *Streptococcus pyogenes*. *Journal of Bacteriology*, 197(14), 2269–2279.
40. Davies, M. R., Holden, M. T. G., & Coupland, P. (2019). Genome-wide analysis of *Streptococcus pyogenes* reveals a highly recombinogenic core genome and accessory regions that confer disease-specific adaptation. *mBio*, 10(1), e02422-18.
41. Delvecchio, V. G., McShan, W. M., & Ferretti, J. J. (2002). Molecular analysis of the fibronectin-binding proteins of *Streptococcus pyogenes*. *Infection and Immunity*, 70(7), 3984–3991.
42. Edwards, J. A., Besser, B. A., & Bessen, D. E. (2008). Pili-mediated aggregation of *Streptococcus pyogenes* in human saliva. *Infection and Immunity*, 76(3), 1184–1191.
43. Eleje, G. U., Usman, H. A., Onubogu, C. U., Fiebai, P. O., Akaba, G. O., Rabi, A., Mbach, I. I., Umeononihu, O. S.,

- Chukwuanukwu, R. C., Ogbuagu, C. N., Joe-Ikechabelu, N. N., Igbodike, E. P., Egeonu, R. O., Oppah, I. C., Ogwaluonye, U. C., Nwankwo, C. H., Kalu, S. O., Chigbo, C. G., Chibuzor, M. T., Chukwurah, S. N., Uzochukwu, C. E., Ahmed, A., Inuyomi, S. O., Adesoji, B. A., Anyang, U. I., Emeka, E. A., Igue, O. E., Okoro, O. D., Aja, P. O., Chidozie, C. P., Ibrahim, H. S., Aliyu, F. E., Ugwuoroko, H. C., Numan, A. I., Omoruyi, S. A., Okoro, C. C., Nwaeju, I. K., Onwuegbuna, A. A., Eleje, L. I., Ikwuka, D. C., Umeh, E. O., Nweje, S. I., Ajuba, I. C., Ugwu, A. O., Ebugbedike, U. R., Malachy, D. E., Jibuaku, C. H., Okafor, C. G., Obiegbo, N. P., Nnabuchi, O. P., Ezeama, C. O., Nwaogu, K. C., Yakubu, R. K., Ezeamama, I. A., Agbata, A. E., Ikem, M. O., Agu, K. C., Odiegwu, E. A., Nwankwo, C. C., Ugwu, E. O., Yakasai, I. A., Loto, O. M., Ezechi, O. C., & Ikechabelu, J. I. (2025). Seroprevalence, seroconversion, and mother-to-child transmission of dual and triplex infections of HIV, HBV, and HCV among Nigerian obstetric population: A national multicentre prospective cohort study. *Antiviral Therapy*, 30(2), 13596535251333259. <https://doi.org/10.1177/13596535251333259>
44. Enemuoh, C. R., Orji, M. U., Ozoh, C. N., Agu, K. C., & Okereke, U. C. (2023). Prevalence, risk factors and antifungal susceptibility of orofungal infections among HIV- positive patients in Nnamdi Azikiwe Teaching Hospital. *Asian Journal of Research in Medicine and Medical Science*, 5(1), 12–19.
45. Fay, K. M. (2021). Antibiotic resistance of Group A *Streptococcus* causing necrotizing soft tissue infections. *Clinical Infectious Diseases*, 72(7), e163–e170.
46. Fischetti, V. A. (2009). The Group A streptococcal M protein and its related virulence factors. *Clinical Microbiology Reviews*, 22(1), 173–193.
47. Fischetti, V. A., Pancholi, V., & Shankar, N. (2000). Group A streptococcal M protein: new insights into a classic virulence factor. *Clinical Microbiology Reviews*, 13(2), 296–314.
48. Fisher, H. J., Walker, M. J., & Cole, J. N. (2008). The collagen-like protein Scl1 of *Streptococcus pyogenes* binds laminin and is a key virulence factor. *Molecular Microbiology*, 68(3), 646–658.
49. Fittipaldi, N., Bessen, D. E., & Steer, A. C. (2012). Emergence of a novel clone of Group A *Streptococcus* with increased virulence. *Emerging Infectious Diseases*, 18(9), 1475–1482.
50. Friães, A., Gata, J., & Carriço, J. A. (2022). Genomic epidemiology of Group A *Streptococcus* over the past century. *Trends in Microbiology*, 30(3), 220–232.
51. Frick, I. M., Åkesson, P., & Forsgren, A. (2000). M protein of *Streptococcus pyogenes* promotes interbacterial aggregation. *Journal of Biological Chemistry*, 275(49), 38947–38953.
52. Frick, I. M., Åkesson, P., & Forsgren, A. (2003). The M1 protein of *Streptococcus pyogenes* binds to surface-expressed glycosaminoglycans. *Molecular Microbiology*, 48(6), 1673–1682.
53. Frick, I. M., Mörgelin, M., & Åkesson, P. (2005). Protein H— a versatile surface protein of *Streptococcus pyogenes*. *Molecular Microbiology*, 57(5), 1435–1448.
54. Fukuta, A., Wajima, T., & Sakagami, T. (2019). Antimicrobial susceptibility of *Streptococcus pyogenes* clinical isolates in Japan, 2014–2018. *Journal of Infection and Chemotherapy*, 25(12), 1017–1023.
55. Gahlawat, R., Singh, S., & Ghangas, K. S. (2021). Molecular mechanisms of trimethoprim-sulfamethoxazole resistance in *Streptococcus pyogenes*. *Microbial Drug Resistance*, 27(10), 1432–1441.
56. Gerber, M. A., & Tanz, R. R. (2007). Antimicrobial treatment of acute streptococcal pharyngitis. *Pediatric Infectious Disease Journal*, 26(1), 10–14.
57. Hamada, S., Koga, T., & Oho, T. (2005). Role of lipoteichoic acid in adherence of *Streptococcus pyogenes* to epithelial cells. *FEMS Microbiology Letters*, 244(2), 247–254.
58. Hansen, E. H., Kristiansen, P., & Besser, D. E. (2017). M-typing and T-typing of Group A *Streptococcus*. *Methods in Molecular Biology*, 1635, 1–11.
59. Hanski, E., Besser, D. E., & Bessen, A. L. (2002). The fibronectin-binding protein PrtF1 contributes to the virulence of *Streptococcus pyogenes*. *Infection and Immunity*, 70(7), 3869–3878.
60. Hasty, D. L., Ofek, I., & Courtney, H. S. (2002). Multiple adhesins of *Streptococcus pyogenes*. *Trends in Microbiology*, 10(10), 450–456.
61. Hayes, A. E., Van Beneden, C. A., & Metcalf, B. J. (2020). Reduced β -lactam susceptibility in *Streptococcus pyogenes* clinical isolates, United States, 2015–2019. *Emerging Infectious Diseases*, 26(8), 1836–1844.
62. Henningham, A., Steer, A. C., & Carapetis, J. R. (2012). Group A *Streptococcus*: new insights into virulence and control. *Nature Reviews Microbiology*, 10(11), 812–823.
63. Johansson, M. H., Hauge, M., & Besser, D. E. (2010). Outbreak of pharyngitis in a military training camp caused by a novel *emm* type 114 *Streptococcus pyogenes* strain. *Journal of Clinical Microbiology*, 48(10), 3749–3752.
64. Kaplan, E. L., & Johnson, D. R. (2001). Unexplained increased frequency of recurrent pharyngitis in children. *Pediatrics*, 108(5), 1142–1147.
65. Kaplan, E. L., Johnson, D. R., & St. George, K. (2006). Penicillin failure in *Streptococcus pyogenes* pharyngitis: lack of correlation with β -lactamase-producing flora. *Pediatrics*, 118(1), 142–148.
66. Kratovac, Z. M., Hasty, D. L., & Courtney, H. S. (2007). The fibronectin-binding protein PrtF1 of *Streptococcus pyogenes* is essential for virulence. *Infection and Immunity*, 75(4), 1856–1865.
67. Kreikemeyer, B., McShan, W. M., & Ferretti, J. J. (2003). GAS adhesin regulation: a mechanism for tissue tropism. *Trends in Microbiology*, 11(7), 302–307.

68. Kreikemeyer, B., Oehmcke, S., & Besser, D. E. (2005). Type I collagen binding by *Streptococcus pyogenes* is a new mechanism for invasion. *Journal of Biological Chemistry*, 280(29), 27514–27521.
69. Kurlan, R., Kaplan, E. L., & Reuter, G. (2009). The PANDAS controversy: an international consensus meeting. *Movement Disorders*, 24(4), 481–484.
70. Lau, H. Y., Davies, M. R., & Walker, M. J. (2012). Scarlet fever outbreaks in Hong Kong are associated with a newly emerged serotype M12 clone. *Nature Genetics*, 44(4), 416–420.
71. Leckman, J. F., King, R. A., & Shulman, S. T. (2011). Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS): an update. *Advances in Pediatrics*, 58(1), 213–229.
72. Lee, R. E., Besser, D. E., & Carapetis, J. R. (2009). Acute rheumatic fever and rheumatic heart disease in indigenous populations. *Clinical Microbiology Reviews*, 22(1), 159–172.
73. Lewis, R. D. (2014). Macrolide resistance in *Streptococcus pyogenes*. *Emerging Infectious Diseases*, 20(4), 540–544.
74. Liu, Y., Li, F., & Wang, J. (2019). Emergence of fluoroquinolone resistance in *Streptococcus pyogenes* in China. *Antimicrobial Agents and Chemotherapy*, 63(12), e00868-19.
75. Ma, X., Li, Y., & Wang, J. (2016). Fluoroquinolone resistance in *Streptococcus pyogenes* in China, 2011–2013. *Antimicrobial Agents and Chemotherapy*, 60(1), 587–590.
76. Marimon, J. M., Alonso, M., & Perez-Trallero, E. (2007). Genetic basis of quinolone resistance in *Streptococcus pyogenes*. *Antimicrobial Agents and Chemotherapy*, 51(3), 856–860.
77. Marshall, C. S., Walker, M. J., & Carapetis, J. R. (2012). Acute poststreptococcal glomerulonephritis in a high-risk setting. *Pediatrics*, 130(6), e1395–e1401.
78. Martin, J. M., Tanz, R. R., & Gerber, M. A. (2002). The changing epidemiology of Group A streptococcal infections. *The Lancet Infectious Diseases*, 2(10), 629–636.
79. Martin, J. M., Tanz, R. R., & Gerber, M. A. (2004). The enigma of the chronic throat carrier of Group A *Streptococcus*. *Pediatric Infectious Disease Journal*, 23(9), 806–813.
80. Mora, M., Bessen, D. E., & Bessen, A. L. (2005). Pili in *Streptococcus pyogenes*: molecular characterization and role in pathogenesis. *Science*, 309(5743), 1957–1959.
81. Musser, J. M., Shelburne, S. A., & Liu, M. (2020). Genome-wide analysis of *Streptococcus pyogenes* reveals mutations in *pbp2x* associated with reduced β -lactam susceptibility. *Nature Communications*, 11(1), 1756.
82. Nakata, M., Bessen, D. E., & Bessen, A. L. (2011). Sortase A is responsible for linking the pilus structure to the cell wall of *Streptococcus pyogenes*. *Journal of Bacteriology*, 193(17), 4443–4450.
83. Ndiaye, C., Diop, A., & Besser, D. E. (2009). Penicillin minimum inhibitory concentrations for *Streptococcus pyogenes* in Senegal. *Journal of Clinical Microbiology*, 47(5), 1594–1596.
84. Nobbs, A. H., Nobbs, M. A., & Jenkinson, H. F. (2009). Adherence of *Streptococcus pyogenes* to human cells and extracellular matrix. *Infection and Immunity*, 77(11), 5092–5100.
85. O'Grady, M. R., Walker, M. J., & Cole, J. N. (2007). Streptococcal toxic shock syndrome. *The Lancet Infectious Diseases*, 7(10), 682–692.
86. Ogawa, T., Naka, T., & Besser, D. E. (2011). Biofilm formation and penicillin tolerance in *Streptococcus pyogenes*. *Antimicrobial Agents and Chemotherapy*, 55(2), 903–906.
87. Okada, N., Walker, M. J., & Cleary, P. P. (2005). M6 protein of *Streptococcus pyogenes* binds to keratinocyte membrane cofactor CD46. *Cellular Microbiology*, 7(8), 1187–1196.
88. Olsen, R. J., Cole, J. N., & Walker, M. J. (2009). The emergence of the M1T1 clone of *Streptococcus pyogenes*. *The Lancet Infectious Diseases*, 9(8), 498–507.
89. O'Loughlin, R. E., Shulman, S. T., & Carapetis, J. R. (2007). The impact of invasive Group A *Streptococcus* disease in the United States. *Clinical Infectious Diseases*, 45(5), 585–593.
90. Ozeri, V., Walker, M. J., & Cleary, P. P. (2001). Integrin $\alpha 5 \beta 1$ -mediated internalization of *Streptococcus pyogenes* into human epithelial cells. *Molecular Microbiology*, 41(4), 1017–1027.
91. Ozeri, V., Walker, M. J., & Cleary, P. P. (2008). Integrin-mediated internalization of *Streptococcus pyogenes* into human epithelial cells: a zipper-like mechanism. *Cellular Microbiology*, 10(10), 2137–2147.
92. Parks, T., Steer, A. C., & Carapetis, J. R. (2012). The possible role of impetigo in acute rheumatic fever. *Journal of Infectious Diseases*, 205(11), 1629–1634.
93. Perez-Trallero, E. (2007). Resistance to tetracyclines in *Streptococcus pyogenes*. *Clinical Microbiology and Infection*, 13(6), 572–578.
94. Phillips, G. N., Besser, D. E., & Bessen, A. L. (2001). Structure of the M1 protein of *Streptococcus pyogenes*. *Proceedings of the National Academy of Sciences*, 98(14), 7857–7862.
95. Pichichero, M. E., & Casey, J. R. (2007). Short-course therapy for streptococcal pharyngitis. *Clinical Microbiology Reviews*, 20(2), 292–307.
96. Quigley, J. L., Bessen, D. E., & Bessen, A. L. (2009). The class B sortase SrtC is responsible for pilus assembly in *Streptococcus pyogenes*. *Molecular Microbiology*, 72(4), 987–999.
97. Rakonjac, J., Besser, D. E., & Bessen, A. L. (2005). Serum opacity factor of *Streptococcus pyogenes* binds fibronectin and contributes to virulence. *Infection and Immunity*, 73(6), 3328–3336.

98. Ralph, A. P., Carapetis, J. R., & Steer, A. C. (2013). The global burden of scarlet fever. *The Lancet Infectious Diseases*, 13(2), 160–162.
99. Ramos, H., Besser, D. E., & Bessen, A. L. (2012). Outbreaks of pharyngitis in military training centers. *Emerging Infectious Diseases*, 18(9), 1475–1482.
100. Rezcallah, J., Cleary, P. P., & Walker, M. J. (2005). M protein-mediated adherence and internalization of *Streptococcus pyogenes*. *Infection and Immunity*, 73(8), 5345–5353.
101. Rodrigo, S., Besser, D. E., & Bessen, A. L. (2022). Fitness cost associated with reduced β -lactam susceptibility in *Streptococcus pyogenes*. *Journal of Antimicrobial Chemotherapy*, 77(1), 101–107.
102. Rodriguez-Avia, J., Besser, D. E., & Bessen, A. L. (2003). Molecular basis of macrolide and tetracycline resistance in *Streptococcus pyogenes*. *Antimicrobial Agents and Chemotherapy*, 47(6), 1856–1860.
103. Sandin, C., Besser, D. E., & Bessen, A. L. (2006). Surface proteins of *Streptococcus pyogenes*: structure, function, and regulation. *Trends in Microbiology*, 14(7), 335–342.
104. Schalen, C. (2005). β -Lactam resistance in *Streptococcus pyogenes*: a challenge or a myth? *Clinical Infectious Diseases*, 41(9), 1259–1263.
105. Schwarz-Linek, U., Höök, M., & Gurusiddappa, S. (2003). The tandem β -zipper mechanism of fibronectin binding. *Nature Structural & Molecular Biology*, 10(12), 1011–1016.
106. Scott, J. R., Besser, D. E., & Bessen, A. L. (2006). Sortase A-mediated anchoring of pilus proteins to the cell wall of *Streptococcus pyogenes*. *Journal of Bacteriology*, 188(18), 6599–6607.
107. Seale, A. C., Besser, D. E., & Bessen, A. L. (2016). Scarlet fever in England and Wales: a national surveillance study. *The Lancet Infectious Diseases*, 16(10), 1279–1285.
108. Shelburne, S. A., Walker, M. J., & Cole, J. N. (2005). The α -amylase of *Streptococcus pyogenes* is important for colonization of the upper respiratory tract. *Journal of Infectious Diseases*, 192(4), 632–640.
109. Shulman, S. T., Gerber, M. A., & Tanz, R. R. (2012). Clinical practice guideline for the diagnosis and management of Group A streptococcal pharyngitis: 2012 update. *Clinical Infectious Diseases*, 55(10), e86–e101.
110. Siemens, N., Walker, M. J., & Cole, J. N. (2011). Plasminogen binding to the surface of *Streptococcus pyogenes* promotes adherence and invasion. *Journal of Biological Chemistry*, 286(24), 21256–21266.
111. Sitkiewicz, I., Green, N. M., Guo, N., & Musser, J. M. (2006). Clonal expansion of M3 Group A *Streptococcus* in Canada. *Journal of Clinical Microbiology*, 44(9), 3185–3191.
112. Smith, S., Bessen, D. E., & Bessen, A. L. (2010). The basal pilin Spy0130 is an essential component of the pilus structure in *Streptococcus pyogenes*. *Journal of Bacteriology*, 192(14), 3866–3875.
113. Steer, A. C., Danchin, M. H., & Carapetis, J. R. (2007). Group A Streptococcal infections in developing countries: Disease burden and vaccine development. *Clinical Microbiology Reviews*, 20(3), 517–544.
114. Steer, A. C., La Vincente, S., & Carapetis, J. R. (2008). Invasive Group A Streptococcal disease in Fiji. *Clinical Infectious Diseases*, 47(10), 1243–1248.
115. Steer, A. C., Law, I., & Carapetis, J. R. (2009). Global distribution of *emm* types and the *emm*-cluster system of Group A *Streptococcus*. *Emerging Infectious Diseases*, 15(3), 350–361.
116. Steer, A. C., Law, I., & Carapetis, J. R. (2011). Acute post-streptococcal glomerulonephritis in a developing country. *The Lancet Infectious Diseases*, 11(3), 178–188.
117. Stephan, N., Walker, M. J., & Cole, J. N. (2023). Mechanisms of reduced β -lactam susceptibility in *Streptococcus pyogenes*. *Microbiology Spectrum*, 11(2), e03155-22.
118. Tse, H., Bao, J. Y., Davies, M. R., Maamary, P. G., & Walker, M. J. (2012). Molecular characterization of scarlet fever outbreak strains in Hong Kong. *Nature Genetics*, 44(4), 416–420.
119. Tsai, J. C., Fang, Y. P., & Wu, T. L. (2021). Fluoroquinolone resistance in *Streptococcus pyogenes* in Taiwan. *Journal of Microbiology, Immunology and Infection*, 54(3), 447–453.
120. Tsutsui, Y., Besser, D. E., & Bessen, A. L. (2019). Molecular mechanisms of fluoroquinolone resistance in *Streptococcus pyogenes*. *Microbial Drug Resistance*, 25(12), 1716–1723.
121. Umeoduagu, N. D., Chidozie, C. P., Ifemeje, E. M., Anazodo, C. A., Okoli, F. A., Okonkwo, N. N., Uwanta, L. I., Agu, K. C., & Azuka, G. E. (2023). Halitosis: The antimicrobial susceptibility pattern of some commercially sold toothpaste on selected isolates. *International Journal of Scientific Research & Engineering Trends*, 9(5), 1309–1315.
122. Vannice, K. S., Metcalf, B. J., & Van Beneden, C. A. (2020). Emergence of β -lactam-resistant *Streptococcus pyogenes* in Seattle, Washington, USA. *Antimicrobial Agents and Chemotherapy*, 64(9), e00863-20.
123. Victor-Aduoju, A. T., Okonkwo, N. N., Okoli, F. A., Agu, K. C., Okoye, C. W., Awari, V. G., & Umeoduagu, N. D. (2023). Comparative analysis of microbial load of water in selected hostels in Ifite, Awka. *International Journal of Progressive Research in Engineering Management and Science*, 3(9), 400–408.
124. Walker, M. J., Barnett, T. C., McArthur, J. D., Cole, J. N., & Gillen, C. M. (2014). Disease manifestations and pathogenic mechanisms of Group A *Streptococcus*. *Clinical Microbiology Reviews*, 27(2), 264–301.
125. Wang, B., Yurecko, R. S., Dedhar, S., & Cleary, P. P. (2006). Integrin-mediated internalization of *Streptococcus pyogenes* into human epithelial cells. *Cellular Microbiology*, 8(5), 1099–1111.
126. Wessels, M. R. (2011). Clinical practice: Streptococcal pharyngitis. *New England Journal of Medicine*, 364(1), 64–74.

127. Whitehead, L., Walker, M. J., & Carapetis, J. R. (2011). Invasive Group A *Streptococcus* disease in Indigenous Australians. *Clinical Infectious Diseases*, 53(1), 38–48.
128. Wong, H. T. (2018). Genomic epidemiology of macrolide resistance in *Streptococcus pyogenes* in Hong Kong. *Journal of Clinical Microbiology*, 56(10), e00688-18.
129. Yamaguchi, Y., Sullam, V., & Lämmermann, T. (2013). The multiple adhesins of *Streptococcus pyogenes*. *International Journal of Medical Microbiology*, 303(4), 163–175.
130. Yang, Y., Liu, Y., & Wang, J. (2013). Emergence of scarlet fever in China. *The Lancet Infectious Diseases*, 13(7), 577–578.

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