



Comment on: “Prevalence, Antibiotic Susceptibility Profile and Associated Factors of Group A Streptococcal Pharyngitis Among Pediatric Patients with Acute Pharyngitis in Gondar, Northwest Ethiopia” [Letter]

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Dear editor

We have read with interest the paper by Tadesse et al¹ that was recently published in your journal reporting data on the prevalence and susceptibility profile of group A *Streptococcus* (GAS) isolates in children with acute pharyngitis in Ethiopia. Acute pharyngitis is very common in the pediatric population, and it has a significant impact within this age group.² Antibiotic overprescription is a major driver of antimicrobial resistance, and while susceptibility to penicillin is generally conserved in GAS, there are increasing reports indicating a reduction in antibiotic susceptibility to other antimicrobial classes.

In their article, Tadesse et al¹ state that: “penicillin, vancomycin, chloramphenicol, clindamycin, and ceftriaxone were effective against 100%, 95.7%, 95.7%, 91%, and 87% of isolates, respectively. In contrast, 56.5%, 39.1%, and 30.4% of isolates showed at least reduced susceptibility to tetracycline, erythromycin, and azithromycin, respectively”.¹ Although macrolide and clindamycin resistance has been described in many studies with variability across countries, we particularly noted the data on vancomycin resistance. Recent studies involving a variety of pediatric patients from middle- or high-income countries such as Germany,³ Greece,⁴ India,⁵ China,⁶ Brasil⁷ or the USA⁸ found 100% susceptibility rates to vancomycin. Thus, although their study included a small number of isolates, Tadesse et al’s data are not to be disregarded, given that they come from a low-income country. Moreover, also in Ethiopia, Kebede et al⁹ identified a resistance rate of GAS to vancomycin of 35.7% (5/14 isolates), and Barsenga et al¹⁰ identified an intermediate susceptibility of 8.2% (4/49 isolates). It would have been interesting for the authors to perform a molecular characterization of the vancomycin-resistant isolates. Among genetic vancomycin resistance determinants, the presence of *vanA*, *vanB*, or *vanG* genes has been reported to date, in rare instances, in different streptococcal species, but to the best of our knowledge not in GAS isolates.¹¹ Furthermore, there are insufficient data for a comprehensive description of the mechanisms of vancomycin resistance in GAS. Furthermore, it would have been important to know whether the vancomycin-resistant isolate in their study also showed a specific resistance pattern for other classes of antibiotics, and if so, to which classes. Finally, it would have been interesting to know whether the patient had any specific risk factors for vancomycin resistance. It would also be recommended that the authors continue to monitor the susceptibility profile of GAS in Ethiopia, along with risk factors in a larger group of pediatric patients and conduct a molecular analysis of resistance determinants.

While resistance to vancomycin per se might not pose a major clinical concern for the treatment of GAS pharyngitis, as this antimicrobial is not part of any recommended treatment regimen for pharyngitis, should this resistance to vancomycin be genetically encoded in GAS, this could theoretically pose the risk of constituting a reservoir for resistance genes that could easily be taken up by other closely or remotely related species. The potential of GAS to serve as resistance reservoir has been described more than 40 years ago, when transfer of resistance determinants into other streptococcal recipients was demonstrated, particularly for erythromycin and tetracycline resistance markers.¹²

A noteworthy example of related streptococcal species prone to acquiring resistance is that of *Streptococcus pneumoniae*, which have a high recombinogenic potential¹³ and are very competent in acquiring virulence and antibiotic resistance determinants through lateral gene transfer from other streptococci, particularly from commensal strains seen in asymptomatic carriage.¹⁴ Commensal GAS isolates also exhibit enhanced in vivo biofilm forming capacity, which in turn facilitates the genetic exchange process.¹⁵ *S. pneumoniae* poses a major clinical burden, being the etiologic agent of otitis media, pneumonia, meningitis, and other types of invasive pneumococcal disease, and potentially associated with high rates of antimicrobial resistance or tolerance, depending on the setting and geographical area. Gene transfer through conjugation from GAS to *S. pneumoniae* has been demonstrated for the macrolide efflux gene *mef(I)* and the chloramphenicol inactivation gene *catQ*, occurring in vitro at a frequency of 1.7×10^{-4} .¹⁶ While transfer of genetically encoded vancomycin resistance determinants has not yet been shown to occur in *S. pneumoniae*, it has been demonstrated for other Gram-positive cocci, and needs to be further explored.

In conclusion, continued careful monitoring of the resistance rates of streptococcal isolates retrieved from clinical practice is warranted, including GAS. To better inform future treatment decisions, this should be coupled with molecular analysis to assess the occurrence of genetically encoded resistance determinants, as well as their potential transferability to and from other microbial species.

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