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## Need for a clinical decision rule for the management of pharyngitis in Nigeria.

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**Abstract** Pharyngitis is a common reason for presentation in the hospital by children. Although viral aetiology is the commonest, Group A *Streptococcus* is the most important cause of and reason for antibiotic treatment of pharyngitis. The fact that GAS causes the non suppurative sequelae of rheumatic fever and acute glomerulonephritis perhaps drives the empirical antibiotic treatment of most cases of pharyngitis. The unnecessary antibiotic treatment contributes to antibiotic resistance, a major public health problem. While it is desirable to do throat culture to guide the physician's management of each case, the required laboratory skill is unavailable in most clinical settings in Nigeria. A clinical decision rule

(CDR) which is a clinical tool that helps guide physicians in the management of conditions such as pharyngitis, have been shown to be helpful in managing pharyngitis in other countries. It reduces the number of unnecessary antibiotic prescriptions and has a high sensitivity and specificity in distinguishing GAS from non GAS pharyngitis. Currently there are no guidelines or CDR for the management of pharyngitis in Nigeria, there is an urgent need to derive, validate and implement a CDR to guide the treatment of pharyngitis.

**Keywords:** Clinical decision rule, pharyngitis, antibiotic resistance, group A *Streptococcus*.

### Introduction

Pharyngitis is a common cause of out-patient presentation amongst children and adults.<sup>1,2</sup> The commonest cause of pharyngitis is viral. Bacterial causes are important causes of pharyngitis as they may require treatment with antibiotic. Three of the bacterial causes, group A  $\beta$  haemolytic *Streptococcus* (GAS) is the most common and most pathogenic bacterial aetiology because it causes both suppurative and non suppurative sequelae.<sup>4</sup> GAS contributes 15 – 30 % of cases of pharyngitis in children and 5 – 20% in adults.<sup>5</sup> GAS pharyngitis is transmitted by respiratory droplets and the incubation period is 24 to 72 hours.<sup>5</sup> Children in crowded situations such as schools, and hostels are thus particularly vulnerable.

The non suppurative sequelae of rheumatic fever (RF) and rheumatic heart disease (RHD) are of major public health concern in developing countries where they are still prevalent and contribute the majority of the 16 million cases of RHD globally and the greater proportion of the over 200,000 death attributable to RHD globally.<sup>6</sup> The prevalence of RHD in Nigeria is 0.07/1000 among primary school children aged six to twelve years. RHD is responsible for 7 – 68% of all heart diseases in Nigeria.<sup>8,9</sup> The age group 5 to 15 years is commonly affected. The fact that GAS pharyngitis results in RF and that its

treatment with appropriate antibiotic prevents RF and thus RHD, encourages the prescription of antibiotic for the treatment of most cases of pharyngitis in the absence of laboratory confirmation of the causative agent. These unnecessary antibiotic prescriptions portend grave consequences for the nation as they cause antibiotic resistance. Laboratory services are lacking in most clinical settings in Nigeria. Alternatives to laboratory services are clearly needed to facilitate the discrimination between GAS and non GAS cases of pharyngitis to guide antibiotic prescription. The clinical decision rule (CDR) is a cheap and efficient alternative where laboratory services may be lacking. A CDR is a clinical tool often consisting of weighted clinical features, it assist clinicians with the diagnosis, prognosis and treatment of a given condition. The CDR is used in many clinical conditions one of which is in the management of pharyngitis.

### Clinical diagnosis of pharyngitis

Clinical evaluation of cases of pharyngitis provides an opportunity to distinguish between viral and bacterial aetiology. In viral cases, the children may present insidiously and often with coryza, conjunctivitis, cough, fever and diarrhoea.<sup>10</sup> Bacterial pharyngitis on the other hand presents with sudden onset, fever, tender cervical adenopathy, presence of pharyngeal exudates, sorethroat

and absence of cough.<sup>1</sup> In clinical practice the ability to discriminate GAS from non GAS using the aforementioned clinical signs and symptoms is possible in half of the cases.<sup>11</sup> There may be overlap between features making discrimination difficult, besides no one feature has proven to have that discriminating ability between viral and bacteria pharyngitis. However when the presence of multiple signs and symptoms are used as in CDR, the diagnostic accuracy of making this clinical decision improves.

### Primary prevention of RF/RHD

The importance of promptly and adequately treating GAS pharyngitis is the basis of primary prevention of RF. Primary prevention is being advocated as the way forward in reducing the burden of RHD in Africa.<sup>12</sup> Secondary prevention strategy only, which involves the placement of the affected individual on penicillin prophylaxis may not be enough to combat this scourge.

Since primary prevention involves the identification of the child with GAS pharyngitis for antibiotic treatment. Laboratory backup will be needed to culture the throat swabs from affected children. The determination of the Lancefield group of the *β haemolytic streptococcus* to ascertain if it is group A will also be required. This level of laboratory skills is absent in most health facilities in Nigeria. Thus attending physicians may have difficulty in making a decision on whether to prescribe antibiotic for pharyngitis or not in the absence of laboratory services. The option of commencing the most children with pharyngitis on antibiotic while awaiting laboratory result exposes them to inadequate antibiotic doses since the medication will be stopped following a negative culture. The patient may all together not revisit the health facility as would be requested by the physician especially when the child is getting better, compliance to medication may then become questionable. The physician in an attempt to err on the side of caution often resort to prescribing antibiotic for all cases of pharyngitis. Sadoh et al<sup>13</sup> reported that 56.4 % of physicians surveyed in the mid Western part of Nigeria would prescribe antibiotic empirically for all patients with pharyngitis. Perhaps similar antibiotic prescription pattern obtains in other parts of the country.

In developed countries, rapid antigen detection test (RADT) for GAS is used in the place of full microbiological culture.<sup>14</sup> This has the advantage of providing rapid results and requires less expertise to perform. The use of RADT is however limited because the sensitivity may not be as good as microbiological cultures. Thus patients who are RADT negative maybe required to do culture.<sup>15</sup> The newer ELISA, optical immunoassays and assay employing the chemiluminiscent DNA probes have sensitivities upto 90 – 99 % compared with microbiological culture and thus the requirement for microbiological culture may not be needed.<sup>16</sup> These newer test kits are quite expensive and mark up the cost of treating pharyngitis. This extra cost may prevent patients from presenting in the health facilities preferring instead to

visit medicine stores where antibiotics maybe procured based on the purchasing power of the patients. This suboptimal treatment may contribute to resistance which is a major public health problem.<sup>17</sup> Also, the inadequate treatment of pharyngitis may not prevent RF since the immunologic damage may still occur despite the relief the patient may have from the symptoms. The initiation and sustenance of a programme using RADT will be difficult in resource limited setting such as ours except it is heavily subsidized.

### Antibiotic resistance

A major consequence of indiscriminate antibiotic prescription for viral pharyngitis, is antibiotic resistance. Other major contributors are incomplete or inadequate dosing and antibiotic use among livestock globally.<sup>17</sup> In a study in Jos, Nigeria,<sup>18</sup> the prevalence of penicillin resistant *Streptococcus pneumoniae* was found to be 29.72%. The organisms were resistant to commonly used antimicrobials which included penicillin, ampicillin, gentamicin, chloramphenicol erythromycin and ciprofloxacin. *Streptococcus pneumoniae* is responsible for more than one third of under-fives' deaths from pneumonia.<sup>19</sup> Acute respiratory infections in turn contributes 15% to under fives mortality in Nigeria.<sup>20</sup> The impact of unchecked antibiotic resistance to Streptococcal pneumonia would be enormous on childhood mortality.

In another study in Ibadan,<sup>21</sup> high rates of antimicrobial resistance was noted in pathogens ranging from *Staphylococcus aureus* to gram negative bacilli such as *klebsiella spp.* They were again mostly resistant to common medicines such as amoxicillin/clavulanate, cefuroxime, gentamicin, penicillin and chloramphenicol. Physicians are known to prescribe a variety of medicines for children with pharyngitis.<sup>13</sup> When the common antibiotics fail, prescribers will resort to the more expensive and newer antibiotics. The cost of treatment becomes quite high resulting from cost of medicines and longer hospital stay. Antibiotic resistance becomes a major contributor to childhood morbidity and mortality. This doubtless will place a huge financial and social burden on the affected families and the Nation. Reducing the indiscriminate antibiotic prescription for pharyngitis will thus ameliorate the pressure on antibiotic and reduce the chances of antibiotic resistance.

### The use of clinical decision rule

To prevent the indiscriminate prescription of antibiotics for non GAS pharyngitis, the physician must be able to distinguish bacterial from viral and non infective causes of pharyngitis. In the absence of laboratory services, the doctors may have to use a set of clinical signs and symptoms as the basis for deciding whether to prescribe or not to prescribe antibiotic for a given case of pharyngitis, the so CDR.

The most popular and perhaps the earliest CDR was derived by Centor et al<sup>22</sup> in 1980. It comprised the use of four criteria; tender cervical adenopathy, fever, absence

of cough and pharyngeal exudates. The presence of all four was said to give a high probability of the GAS pharyngitis while the presence of two or three features will necessitate the culturing of the throat swab or use of rapid antigen detection test. The Centor criteria was established for patients 15 years and above. It is good in identifying individuals with low risk for GAS pharyngitis and reduces the proportion of unnecessary antibiotic prescription, having been validated by a number of studies where high sensitivity and specificity results were obtained.<sup>23,24</sup> The modified Centor score by McIsaac et al<sup>25</sup> was validated in over 600 children and adults.<sup>26</sup> In addition to the four Centor criteria, age was included as a criterion. The criteria are scored as shown in the table 1. Patients <15 years were given an extra score of one while in those between 15 and 44 years were scored zero. A score of one was subtracted from those 45 years and above. Decisions were taken based on the score obtained from evaluating the patients as shown in Table 1. The sensitivity and specificity of the modified Centor clinical scoring system in identifying GAS was 85% and 92.1% respectively. Using the scoring tool resulted in 63.7% reduction in antibiotic prescription compared to the usual physician practice.

**Table 1:** Modified Centor score<sup>25</sup>

Criteria	Points
Absence of cough	1
Tender and swollen cervical glands	1
Temperature >380C	1
Tonsillar swelling or exudates	1
Age	
3 – 14 year	1
15 – 44 year	0
>45 years	-1
Cumulative score	

Score 0 or 1 (low risk) no testing and no antibiotic

Score of 2 and 3 (medium risk) perform testing and give antibiotic if positive

Score 4, (high risk), consider giving antibiotic empirically

Since the Centor criteria, a number of CDRs have been derived by other workers in both developing and developed world.<sup>27,28</sup> Joachim et al<sup>27</sup> working in Brazil produced a scoring system which resulted in a 35% to 55% reduction in unnecessary antibiotic prescription while the one by Smeester et al<sup>28</sup> had a sensitivity of 92% and resulted in a 31% to 38% reduction in antibiotic prescription for culture negative pharyngitis. CDRs work best in the populations in which they are derived and in populations with similar GAS prevalence. Where the prevalence are different, they don't not work well.<sup>29</sup> It is thus important to develop a National CDR for Nigeria.

There is a paucity of studies on agents causing pharyngitis in patients in Nigeria and no CDR has yet been derived for facilitating the management of pharyngitis in Nigeria. The prevalence of GAS is different from locale to locale as shown in two studies from Benin City and Lagos where values of 0 % and 22.8% of the cases of  $\beta$

*haemolytic Streptococcus* were obtained respectively.<sup>7,30</sup> The difference in prevalence suggests the need to develop and validate different CDRs in different parts of the country to crystallise a CDR that best capture the entire country for implementation.

### The importance of clinical decision rule

Once a CDR is established for the country, attending physicians will be guided by it. This will enhance the primary prevention strategy of RF/RHD in the country as likely GAS pharyngitis will be adequately treated. This together with effective implementation of the secondary prevention strategy and health educating the both the prescribers and the populace, will lead to reduction in the burden of RF and RHD. There will be a reduction in the prescription of unnecessary antibiotics for pharyngitis as has been shown in other studies.<sup>26,28</sup> This will go a long way in reducing antibiotic resistance in the country.

### Antibiotic treatment of pharyngitis

It is also important that a clear first line medicine for the treatment of pharyngitis is established nationally. Traditionally penicillin V is the drug of choice, however in a study on physicians' management of sore throat in Benin City; most doctors did not comply with the use of penicillin as first line medicine. A variety of medicines were being prescribed for pharyngitis in children instead.<sup>13</sup> This means that not only penicillin is exposed to resistance but other medicines and thus increasing the antibiotic resistance problem.

Because of the difficulty with compliance with a ten day course of penicillin, the effectiveness of other alternative medicines such as amoxycillin and cefuroxime in adequately treating GAS pharyngitis have been demonstrated in other studies.<sup>31,32</sup> The issue of poor compliance with medication also contributes to antibiotic resistance, there are studies that have evaluated the efficacy of shorter duration and dosing of medicines used in the treatment of pharyngitis compared to standard treatment regimen.<sup>31,32</sup> Single Benzathin penicillin injection has also been shown to be effective and is being used in Brazil to enhance treatment compliance in cases of pharyngitis.<sup>33</sup> Single injection of penicillin maybe quite useful to ensure compliance to therapy in our setting for the children without penicillin allergy. Benzathin penicillin has continued to be efficacious in clinical settings.

### Conclusion

Managing pharyngitis in children without laboratory backup is a common problem physicians are faced with in most clinical settings across the nation. In order to prevent the occurrence of RF, alot of unnecessary antibiotics are prescribed. This leads to antibiotic resistance which is a growing global concern.

A wide variety of common medicines are involved. Periodic evaluation of the efficacy of current medicine of choice is important in the face of antibiotic resistance and so guides prescribers as to the optimal medicine for the treatment of pharyngitis. The current situation in the country is that antibiotics are prescribed indiscriminately in the absence of guideline and the choices of antibiotics are left to the prescribers' whim. This situation can only be arrested if concerted efforts are made by the Ministry of Health through research to establish not only a CDR in the management of pharyngitis but also the choice of medicine to prescribe when the need arises.

It is imperative to guide all prescribers in the absence of a national CDR. Perhaps the modified Centor criteria be recommended as guideline pending when a national CDR is established. The Integrated Management of Childhood Illnesses (IMCI) programme is a veritable tool for cascading the process down to community extension workers and allied health workers by incorporating a guideline on treatment of pharyngitis in the IMCI as has been done with the IMCI programme in Turkey.<sup>34</sup> It is also important to educate the health community on appropriate antibiotic prescription and the dangers posed by indiscriminate antibiotic use.

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