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# Bacteria etiological agents causing respiratory tract infections in children and their resistance patterns to a panel of ten antibiotics

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ABSTRACT

**Objective:** To study the bacteria etiological agents of respiratory tract infection among 280 school children in South East Nigeria, and to determine their antimicrobial resistance patterns to a panel of ten antibiotics. **Methods:** Throat swabs (280) were collected from students in four boarding schools located in Enugu and Onitsha metropolis. Standard microbiological procedures were used to screen these swabs to determine the prevalence of respiratory pathogens while the disc diffusion test was used to determine the antimicrobial resistance patterns of the recovered isolates. **Results:** Of the 280 samples screened, 57.1% were positive. *Haemophilus influenzae* was the most prevalent (16.1%), followed by *Streptococcus pyogenes* (13.9%), *Klebsiella pneumoniae* (12.5%), *Streptococcus pneumoniae* (6.8%), *Staphylococcus aureus* (5.4%) and *Corynebacterium diphtheriae* (2.5%). More isolates were recovered in the two male schools investigated. However, there was no significant difference in the overall prevalence of isolates according to sex or school location of the subjects. Greater number of isolates (56%) was recovered from those aged 11-14 years. This was statistically significant ($P<0.05$), compared to the other two age groups (15-18 years and 19-23 years). The pattern of resistance varied according to the bacteria species. There were multi-resistant isolates. Since these students stand the risk of contracting respiratory tract infection particularly from reservoirs among them, there is need to increase surveillance and develop better strategies to curb the increasing prevalence of respiratory tract infection in this and other similar regions of Africa. **Conclusions:** The spectrum of bacteria causing respiratory tract infection is still wide in Nigeria. Many isolates showed appreciable levels of antibiotic resistance apparently due to antibiotic abuse. Development of new strategies to curb this increasing prevalence of respiratory tract infection is warranted.

## 1. Introduction

Respiratory tract infections are common and perhaps the most frequently reported of all human infections. They are traditionally divided into two: upper respiratory tract infection and lower respiratory tract infections. Some of these infections are most times mild, transient lasting and sometimes self -limiting. Due to this, many infected persons tend to disregard them[1]. However, respiratory infections are a common and important cause of morbidity and mortality worldwide. For instance, in the USA alone, over sixty two million persons suffer from colds annually[2], while in the United Kingdom, about 8 million persons are infected by some forms of chronic lung diseases which now kills one in every five persons[3]. In Canada, respiratory disease is accountable for over 16% of deaths and 10% of hospitalizations[4]. Developing countries are no exception. For instance, in most African countries, the situation is more complicated and management is often difficult due to the problem associated with the identification of the etiological agents and administration of appropriate treatment in cases requiring antibiotic therapy[5]. This is perhahs the

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reason why the several pediatric deaths reported annually due to acute respiratory infection are from developing countries[6]. Respiratory tract infections are probably the most common acute illness encountered in outpatient setting ranging from self-limiting but mild catarrhal syndrome of the nasopharynx, often referred to as common cold to life threatening illnesses such as epiglottis. It involves all kinds of infections that include the sinuses, nasal passages, pharynx, and larynx, which serve as gateways to the trachea, bronchi, and pulmonary alveolar spaces. Some of the specific manifestations include: rhinitis, pharyngitis, sinusitis, epiglottis, laryngitis, and tracheitis.

Surveillance of respiratory tract infection especially acute cases in defined populations is required to monitor prevailing pathogens while the determination of population groups at risk is important for implementing preventive strategies[7,8]. Furthermore, monitoring of antimicrobial resistance patterns of the etiological agents is needed not only as a guide to the clinician when managing cases that require antibiotic therapy but also necessary to monitor the trend of these infections.

Although viruses account for most upper respiratory tract infections[9], bacteria are also known to cause primary infection or super infection and in most cases require targeted therapy. Cases of respiratory tract infections respond to antibiotics treatment, however, the abuse of antibiotics for respiratory tract infection is widespread particularly among children in developing countries and often might lead to resistance[10]. Antibiotic resistance patterns reported for respiratory tract bacteria in other countries including nearby countries to Nigeria are variable depending on the organism and the drug investigated[11]. Therefore, updated information on the etiological agents of upper respiratory tract infections and the determination of the antibiotic resistance patterns of recovered etiological agents are clearly needed for effective surveillance and monitoring since disease etiology are known to vary with time and geography[12]. Although some studies have been carried out on respiratory infections in Nigeria[13-18], not much has been done and no recent data exist on the etiology of respiratory tract infection in Nigeria children especially in the southeast flank.

The aim of our study was therefore to determine the etiology of respiratory tract infections amongst children in southeast Nigeria and the antimicrobial resistance patterns of the recovered bacteria pathogens to some antibiotics.

## 2. Materials and methods

### 2.1. Study background and subjects

The study involved two important cities in Southeast Nigeria: Enugu and Onitsha. Two secondary schools (one for each sex) with boarding facilities were selected in each city. The population of the schools and the boarding facilities allowed students to have very close relationships compared to non-boarding facilities. Overall, 280 students made up of 160 females and 120 males were investigated. The students' age ranged between 11-23 years with a mean age range of 15 years. The study aim and objectives were explained to all the participating students through their teachers and it was assured that all the information obtained with reference to their identities will be kept confidential. Based on this, consent and cooperation were solicited and obtained and verbal approval granted. Similarly, the administrative heads of these schools preferred to have the names of their respective schools remain confidential. We therefore identified the schools using the letters A and B for female and male boarding schools within Enugu and C and D for the corresponding schools within Onitsha. The numbers of students investigated in these schools were 75, 85, 57, 63 corresponding to A, B, C and D schools respectively.

Enrollment criteria used for the study were as follows: participant must be suffering from a respiratory tract infection and should not have been taking antibiotic(s) for 15 days prior to the actual collection of specimen used in the study.

The students presented varying kinds of respiratory infection(s) such as catarrh/running nose, sore throat, cough, cold, pneumonia, sinusitis, otitis media etc. The first two were more common (82%). The symptoms lasted for between 1 to 3 weeks depending on the individual. The study was undertaken between May 2007 to October, 2008. This period spans through dry and wet seasons in the study areas.

### 2.2. Sample collection and processing

Throat swabs were collected and sent to the laboratory for processing and analyses. They were processed following standard guidelines. Briefly, a loopful of each specimen was taken from the throat swab and inoculated on chocolate, blood and methylene blue agar. The plates were incubated under aerobic conditions in 5-10% carbon dioxide atmosphere at 37 ℃ for 24-48 h. Microscopic and macroscopic examinations of the growing colonies on the plates were performed. Suspicious colonies were then subcultured on a suitable solid culture media for purification and thereafter preserved on appropriate agar slants and stored in the refrigerator (4 ℃) for subsequent analysis. Preliminary identification was performed based on morphology and cultural characteristics of the pure cultures on selective and differential media as described by Cheesbrough[19]. The API 20E kit (Biomerieux, France) was then used for the final confirmation of the isolates following the instruction by the manufacturers.

### 2.3. Antibiotic susceptibility testing

Antibacterial susceptibility testing was performed using the Kirby-Bauer disc diffusion method as described by Bauer and co-workers[20]. Briefly, for each isolate, a small inoculum was emulsified in 3 mL sterile normal saline in Bijou bottles. The density was then compared with a barium chloride standard (0.5 McFarland). A sterile cotton swab was dipped into the standardized solution of bacterial cultures and used for evenly inoculating Mueller-Hinton agar plates (Oxoid, USA) and allowed to dry. Next, antibiotic discs with the following drug contents- ampicillin (10 μg), chloramphenicol (10 μg), cefuroxime (30 μg), ceftriaxone (30 μg), co-trimoxazole (25 μg), erythromycin (10 μg), gentamicin (10 μg), tetracycline (30 μg) and penicillin (10 IU) (Oxoid, England) were placed on the plates, spacing them well to prevent the overlapping of inhibition zones. The plates were incubated at 37 ℃ for 24 h, and the diameters of zone of inhibition were compared with recorded diameters of the reference isolate (*Escherichia coli* ATCC 25922) in order to determine susceptibility or resistance.

### 2.4. Statistical analysis

Data obtained were analyzed using the SPSS software for windows version 15. Comparison of data in respect of schools, sex, and age-groups were performed by *Chi*-square. *P* values of <0.05 were considered to be statistically significant.

## 3. Results

Out of the overall number of 280 boarding students analyzed, 57.1% had positive cultures for respiratory tract pathogens. The detailed prevalence for each bacteria isolate from the throat swabs of students in Southeast Nigeria is shown in Table 1. Six different types of bacteria were recovered: *Haemophilus influenzae* (*H. influenzae*), *Klebsiella pneumoniae* (*K. pneumoniae*), *Streptococcus pyogenes* (*S. pyogenes*) and *Staphylococcus aureus* (*S. aureus*). Others were *Streptococcus pneumoniae* (*S. pneumoniae*) and *Corynebacterium diphtheriae* (*C. diphtheriae*).

The number of students in the age range, 11-14, 15-18 and 19-23 are respectively 171, 89, 20. Of the recovered isolates, *H. influenzae* had the highest prevalence of 16.1% followed by *S. pyogenes* (13.9%) and *K. pneumoniae* (12.5%). Others were *S. pneumoniae* (6.8%), *S. aureus* (5.4%) and *C. diphtheriae* (2.5%). More bacteria isolates were recovered separately in schools D (72.1%) located at Onitsha and B (66.7%) located in Enugu, followed by schools A (49.3%) and C (47.5%) located in Enugu and Onitsha respectively. Prevalence was generally higher in male schools (B and D) compared to female schools (A and C) as more isolates were recovered from male schools compared to female schools. However, there was no significant difference in the overall number of isolates recovered in the study based on sex in both schools ($P>0.05$).

*H. influenzae* was the most predominant isolate recovered in each school except in school C where *S. pneumoniae* was the most prevalent. However, *C. diphtheriae* was the least bacteria isolate recovered in individual schools (Table 1).

The overall occurrence of isolates was significantly higher ($P<0.05$) in the age group 11-14 years compared to the other two age groups (15-18 and 19-23) studied respectively.

Table 2 shows the number of isolates from upper respiratory bacteria pathogens in different schools investigated. The total number examined in school A, B, C and D are respectively 75, 85, 57 and 63.

Table 3 shows the antibiotic resistance patterns of the isolates recovered from the students to a panel of ten antibiotics.

**Table 1**

Distribution of upper respiratory tract isolates recovered from different age groups of school children investigated.

| Species | Age group (yrs) | | | |
|---|---|---|---|---|
| | 11-14 | 15-18 | 19-23 | Total |
| | No (%) | No (%) | No (%) | No (%) |
| *H. influenzae* | 33 (19.3) | 5 (5.6) | 7 (35.0) | 45 (16.1) |
| *K. pneumoniae* | 21 (12.3) | 9 (10.1) | 6 (30.0) | 35 (12.5) |
| *S. pyogenes* | 17 (9.9) | 12 (13.5) | 10 (50.0) | 39 (13.9) |
| *S. aureus* | 8 (4.7) | 4 (4.5) | 3 (15.0) | 15 (5.4) |
| *S. pneumoniae* | 8 (4.7) | 6 (6.7) | 5 (25.0) | 19 (6.8) |
| *C. Diphtheriae* | 4 (2.3) | 3 (3.4) | - | 7 (2.5) |
| Total | 91 (56.9)* | 39 (24.4) | 31 (19.4) | 160 (57.1) |

$P<0.05$ when compered with 15-18, 19-23 age groups respectively.

**Table 2**

The number of isolates of the upper respiratory bacteria pathogens in different schools investigated.

| Sex | Schools | | | | Total |
|---|---|---|---|---|---|
| | A (Female) | B (Male) | C (Female) | D (Male) | |
| *H .influenzae* | 13 | 12 | 9 | 11 | 45 |
| *K. pneumoniae* | 9 | 11 | 8 | 7 | 35 |
| *S. pyogenes* | 4 | 6 | 4 | 5 | 39 |
| *S. aureus* | 3 | 2 | 4 | 6 | 15 |
| *S. pneumoniae* | 8 | 5 | 14 | 12 | 19 |
| *C. diphtheriae* | - | 2 | 1 | 4 | 7 |
| Total (%) | 37 (49.3) | 38 (66.7) | 40 (47.5) | 45 (72.1) | 160 |

The total number examined in the schools: A, B, C and D are respectively 75, 85,57 and 63.

**Table 3**

The resistance patterns of the recovered bacteria isolates from upper respiratory tract infections in Southeast Nigeria expressed in percentage to a panel of ten antibiotics.

| Antimicrobial agent (Concentration) | *H. influenzae* | *K. pneumoniae* | *S. pyogenes* | *S. aureus* | *S. pneumoniae* | *C. diphtheriae* |
|---|---|---|---|---|---|---|
| Ampicillin (10 μg) | 55.6 (25) | 51.4 (18) | 66.7 (26) | 60.0 (9) | 57.9 (11) | 57.1 (4) |
| Gentamycin (10 μg) | 11.1 (5) | 8.6 (3) | 10.3 (4) | 13.3 (2) | 10.5 (2) | 14.3 (1) |
| Cefuroxime (30 μg) | 8.9 (4) | 11.4 (4) | 5.1 (2) | 26.7 (4) | 15.8 (3) | 14.3 (1) |
| Chloramphenicol (10 μg) | 31.1 (14) | 51.4 (18) | 30.8 (12) | 26.7 (4) | 42.1 (8) | 42.9 (3) |
| Ciprofloxacin (5 μg) | 13.3 (6) | 20.0 (7) | 12.8 (5) | 13.3 (2) | 15.8 (3) | 14.3 (1) |
| Co-trimoxazole (25 μg) | 46.7 (21) | 60.0 (21) | 53.8 (21) | 80.0 (12) | 63.2 (12) | 71.4 (5) |
| Erythromycin (10 μg) | 22.2 (10) | 28.6 (10) | 35.9 (14) | 33.3 (5) | 30.0 (6) | 28.6 (2) |
| Ceftriaxone (30 μg) | 4.4 (2) | 8.6 (3) | 10.3 (4) | 13.3 (2) | 5.3 (1) | 14.3 (1) |
| Penicillin (10 IU) | 91.1 (41) | 88.6 (31) | 89.7 (35) | 93.3 (14) | 89.5 (17) | 85.7 (6) |
| Tetracycline (30 μg) | 40.0 (18) | 54.3 (19) | 46.2 (18) | 53.3 (8) | 52.6 (10) | 57.1 (4) |

Actual number of isolates is shown in the brackets.

## 4. Discussion

The primary goal of this study was to ascertain the current prevalence/trend of bacteria causing respiratory tract infection among young children in schools located in Enugu and Onitsha in southeastern Nigeria. The antibiogram of the recovered bacterial isolates were also determined in order to ascertain the resistance patterns of the recovered bacterial isolates to a panel of ten antibiotics.

*H. influenzae* was the most frequently recovered pathogen (16.1%), followed by *S. pyogenes* (13.9%) and *K. pneumoniae* (12.5%). The isolation rates for the others were *S. pneumonia* (6.8%), *S. aureus* (5.4%) and *C. diphtheriae* (2.5%).

Several authors have previously reported these isolates as major cause of respiratory tract infections in categories of human subjects including children of school age[1,21,23]. Although studies on respiratory tract infections are somewhat scanty especially in the southeast part of Nigeria, a few older studies carried out on other geographical area of the country also implicated these organisms as the major cause of respiratory tract infections. Interestingly, a group of researchers also found *H. influenzae* as the predominant cause of upper respiratory tract infection, with a prevalence of 20% in Cameroon, a West African country which shares a common border with Nigeria[1]. In Saudi Arabia, Al-Hadramy and his colleagues found *H. influenzae* as the most predominant organism responsible for 67.9% of respiratory tract infections in that country[24]. In Japan, similar observations were also reported by Shimada *et al*[21]. Garibaldi[25] also reported this organism as the second major cause of respiratory infection and the etiological agent responsible for 15% of community acquired pneumonias in the United States of America. This was before the introduction of infant *Haemophilus influenzae* type B (Hib) vaccination in the USA in 1991[26]. In recent times however, evidence following the post Hib vaccine era in these and other countries suggest a changing and indeed very reduced trend in the incidence of *H. influenza*[27]. For instance, in the USA, the overall incidence of all classical Hib manifestations has been lowered by 98% among children 4 years of age or younger and stood at 1.6 per 100 000 per annum about a decade ago[28]. In 2009, among children younger than 5 years of age, 35 cases of invasive disease due to Hib were reported in the United States according to the Center of Disease Control. In addition, another 178 cases caused by unknown *H. influenzae* serotypes were reported, so the actual number of Hib cases could be between 35 and 213. Most cases were among unvaccinated or incompletely vaccinated children[29]. In Chile, a 90% decline in Hib disease was observed while Costa Rica and Israel reported 57% and 95% decline respectively[28].

However, despite that Hib conjugate vaccine had a significant effect on decreasing disease incidence and carriage prevalence, some regions continue to have ongoing carriage despite relatively high vaccine rate[30].

It has been reported that *H. influenzae* is recoverable from the nasopharynx of about 80% of healthy persons and that children exposed to ampicillin within 6 months were more frequent carriers of this pathogen[24]. However, there is no data on the carriage rate of this organism in southeast Nigeria. Therefore, it will be difficult to interpret our data which shows that this organism is the most prevalent in our study with regards to the carriage rate of this organism.

The implication of the current finding would seem to suggest that students in the affected schools are likely prone to these respiratory tract infectious agents. This is because these students mingle together and share things in common as they live together in boarding facilities. Similarly, their teachers are also at the risk of contracting these pathogens. Although our data is consistent with previous reports, it might be difficult to state the reason for the relatively high prevalence of these respiratory pathogens. However, ecological and geographic/climatic factors may be responsible. Furthermore, young people are more prone to these respiratory pathogens perhaps because of their lower immunity levels. Malnourishment may also be a contributory factor as some students are not well fed and may be more prone to the etiological agents.

Some investigators also suggested that teachers could be carriers to these etiological agents[1], however, we were not able to investigate this as samples were not collected from teachers in the schools studied because they declined consent.

As earlier pointed out, the introduction of Hib vaccine has contributed greatly in reducing the high prevalence of *H. influenzae* in several countries and controlling spread of this pathogen. However, a study in rural Kenya shows that the introduction of Hib vaccine did not result in rapid elimination of Hib disease[31]. The effects of these remain to be seen in Nigeria as there are currently no data on this. Nigeria only applied to Global Alliance For Vaccines And Immunization (GAVI) for Hib and pneumococcal vaccine support in May 2009 after several visits and meetings with GAVI and Hib Initiative representatives[32]. *S. pyogenes* was the second most common respiratory pathogen recovered in our study with a prevalence of 24.4%. This finding is consistent with the report from previous investigators from Buea, Cameroon who found a prevalence of 20.1%[1]. Similar reports were observed in Yaounde[33]. In contrast, Ndip *et al*[1] could not recover this pathogen in another Cameroon study carried out recently and attributed this to antibiotic abuse which is common in that part of Cameroon according to the authors. There were no significant difference ($P>0.05$) in the occurrence of the pathogens with respect to the four schools investigated or according to sex. This means that respiratory infections are neither dependent on sex nor school in the areas investigated. However, there was a significant difference ($P<0.05$) according to the various age groups investigated. Those aged 11-14 had more respiratory infections (56.9%), followed by those aged 15-18 years (24.4%) and the least was those aged 19-23 years (19.4%). It therefore follows that younger children are more vulnerable to this kind of respiratory infections. This observation is similar to another report which showed that children of younger age are more disposed to dermatophytic infections than their older colleagues[34,35]. Researchers in Gambia also found that younger children were more vulnerable compared to older children[36].

There were two striking observations: in the two cities where the investigated schools were located, we observed that at least one of the schools showed higher prevalence of respiratory pathogens compared to the other. Secondly, there was generally higher prevalence of respiratory pathogens in male compared to female schools in both cities. We are not able to specifically explain these observations but it is possible that peculiar habits in each school may be the reason for the first observation. Other authors recovered more isolates from female (56%) compared to males (44%) but found no significant difference in these observations[1].

Our study shows that the bacterial isolates were most sensitive to ceftriaxone, followed by gentamycin and cefuroxime. These antibiotics were therefore the most susceptible in that order. Cefuroxime was the most effective against *H. influenzae* with only 2 isolates showing resistance. This was followed next by *S. pneumoniae* with also one isolate showing resistance. In Nigeria, the poverty level is high and majority of the illiterate population and major drug abusers are most probably in this class. Thus, for ceftriaxone, we presume that its higher cost relative to the other drugs tested might be the reason for its reduced abuse as the recovered pathogens showed higher sensitivity to it. The rate of antibiotic abuse in Nigeria is so high and such that in majority of the cases, people can walk-in in both licensed and non-licensed pharmacy outlets and obtain antibiotics without doctor's prescription. Gentamycin ranked second in terms of overall resistant rate. Perhaps the route/mode of administration of gentamycin reduces its abuse as previously suggested by researchers in Cameroon[1]. Since gentamycin is sold in Nigeria as injectables, its route of administration thus becomes a barrier to its abuse compared to other oral preparations. In a recent study which evaluated the use of antibiotics without prescription among young adults in Nigeria, Oyetunde *et al*[37] found that over 38% of respondents purchased antibiotics without prescription.

The bacterial isolates showed lower resistance to cefuroxime, followed by gentamycin and ceftriaxone in that order. The relatively higher cost of cefuroxime similar to ceftriaxone is a major factor controlling its abuse. In addition to that, these drugs are relatively new in Nigeria compared to penicillin, ampicilin and co-trimoxazole which have been available in Nigeria for decades and are very cheap. This might be the major reason for the poor sensitivity of the recovered isolates in our study to some of these antibiotics.

Substantial number (55.5%) of *H. influenzae* isolates, the most prevalent isolate in the study, were resistant to ampicillin. This contradicts reports from the United Kingdom and Denmark[38] which showed that only 6.2% and 5.0% of *H. influenzae* were respectively resistant to ampicillin in these countries. Moreover, another report in Turkey found only about 20% to be resistant to ampicillin[39]. Nevertheless, our reports agree more closely to another West African study which found 60% of resistance[1]. Bhattacharya *et al*[40] also reported a resistance of 68% to ampicillin in India. The possible reason for the low prevalence in UK and Denmark may be due to the controlled use of these antibiotics in these countries which helps in controlling their abuse and the subsequent emergence of resistance as opposed to the situation in Africa and most other countries. Our data on the resistance pattern of ampicillin, which we suggest is related to its abuse, is consistent with the findings of Oyetunde *et al*[31]. They observed that 70% of respondents in Lagos, Nigeria abused Ampiclox® (a brand of ampicillin and cloxacillin), followed by 13.3% that abused ampicillin. These respondents bought these antibiotics without prescriptions. Moreover, 90% of these respondents used the drug for inadequate duration (< 5 days) or at wrong dosing intervals[37].

The resistance pattern shown by *H. influenzae* to tetracycline in our study also agrees with the pattern found in Cameroon and India[1,34]. *S. pneumoniae* ranked 5th in our study in terms of general prevalence rate and showed similar resistance patterns observed in India and Cameroon for second and third generation of cephalosporin (cefuroxime and ceftriaxone) when the number of isolates tested in each group is taken into consideration[1,40]. This data differs from a very recent report in India which implicated *S. pneumoniae* as both the most prevalent (30%) respiratory pathogen and most resistant among pediatric patients attending a regional hospital in that country[22]. This difference could be due to cultural or geographic reasons.

Ciprofloxacin is a relatively new quinolone in Nigeria and yet ranked 4th in our study in terms of the resistant rate. This is not surprising because of its abuse which has been made worse by the availability of cheap brands in the Nigerian market. This finding also correlates with a study in Lagos, Nigeria which listed ciprofloxacin among abused antibiotics[37].

In conclusion, there is need to address the increasing occurrence of respiratory tract infections in children in southeast Nigeria. There is also urgent need to avoid the dissemination of these pathogens to the vulnerable population of other school children. This is important as an outbreak is possible especially from those who may be reservoirs for these dangerous pathogens such as *H. influenzae*. The susceptibility data obtained in our study provides useful information to the clinicians when they make decisions on therapeutic options. Furthermore, this study reveals the spectrum of respiratory tract pathogens and is thus of great epidemiological importance. The rapid movement of persons from one country to another or even within the same country makes this information no less important. The purchase of antibiotics as if they were over-the-counter drugs which culminate in the administration of such drugs without prescription leading to wrong dosing need to be effectively curbed to forestall antibiotic abuse and possible development of resistance to these agents. Governments in Nigeria and many other African countries where these vaccines are not yet introduced should step up efforts aimed at introducing the required vaccines and effectively design good policy strategies to ensure its successful implementation. Watt *et al*[27] stated that the global burden of Hib disease is substantial and almost entirely vaccine preventable and concluded that Hib vaccine could reduce childhood pneumonia and meningitis and decrease child mortality.

## Conflict of interest statement

We declare that we have no conflict of interest.

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