COMMENTARY

Management of childhood pneumonia in Nigeria

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Despite recent improvements in child survival that have been seen in most low- and middle-income countries over the past three decades, child mortality remains unacceptably high and pneumonia remains the dominant cause of child death outside the neonatal age group. In this issue of the journal, Graham and colleagues present a rare glimpse into the management of childhood pneumonia in Africa's most populous country, Nigeria. The paper describes the management of severe pneumonia and severe malaria in 12 medium-sized hospitals, with a focus on the cases of severe pneumonia and severe malaria by the World Health Organization (WHO) definition that were given other diagnoses by the hospital doctors.[1] The reader may be advised to begin by looking through the descriptions of the 12 hospitals in the Web Appendix, keeping in mind the fact that Nigeria is not a poor country (Gross National Income per capita $5710 in 2018), yet its under-five mortality is close to the worst in the world at $120/10^5$ live births, just slightly lower than Somalia.[2] The hospital review data provide some clues as to why child survival is so poor in Nigeria. All hospitals had access to oxygen and antibiotics, but access to oxygen for pediatric patients was limited.[3] In all but one hospital, patients' families were required to pay for everything. Case fatality rates (CFRs) were mostly around 4%, which is probably average for West African hospitals. It is unclear whether these figures reflect children who were withdrawn from the hospitals because parents were unable to pay the fees. From the CFR perspective, the worst performing hospital was Hospital no. 3, which had a CFR of 7.5%. In that hospital, oxygen was available for $7.50 per day, and an average 3-day admission for pneumonia cost the family $60, a lot for the 50% of Nigeria's population who are living in extreme poverty (<$1.25 per person per day[4]). Notably, there were no standard treatment guidelines in use at the hospital.

The authors analyzed data from these 12 hospitals to explore whether diagnostic issues may have contributed to patient outcomes. They used clinical data to categorize cases into WHO-defined severe pneumonia and WHO-defined severe malaria. The WHO definition of severe malaria is a positive laboratory test for malaria in a child with fever, plus one of severe anemia, reduced conscious state, convulsions, or respiratory distress.[5] Not surprisingly, most children presenting with these clinical features were recognized by the clinicians as having malaria. However, with cases classified as WHO-defined severe pneumonia, a disturbing proportion of cases (41%) did not have pneumonia among their admission diagnoses. Adding to the concern generated by this finding, there was a trend toward higher mortality in the "missed" cases (12% vs 9%), and those cases were less likely to receive antibiotics on day 1 (85% vs 96%). So, can we assume that misdiagnosis by hospital doctors, essentially missing cases of severe pneumonia, has led to higher mortality?

First, we must consider the specificity of the WHO definition of severe pneumonia. It was never intended to be used as an epidemiological tool. Rather, its purpose was to identify children with a high probability of dying from pneumonia, to refer them for hospital care, usually involving parenteral antibiotics with or without oxygen. The WHO definition was established when the Programme for Control of Acute Respiratory Infections (ARI Programme) was started in 1987.[6] This followed an International Workshop in Australia in 1984[7] and the publication of the first modeling exercise estimating the global mortality burden associated with acute respiratory infections.[8] The ARI programme was based on an existing algorithm that was in place in Papua New Guinea. Primary health care workers or health workers at first-level health facilities were trained to

provide antibiotics for children presenting with cough or difficult breathing associated with fast breathing (>50 breaths/min). The need for hospitalization was based on the presence of lower chest wall indrawing, as described by Shann.[9] Since then, three important changes have taken place.

1. In 1989, the respiratory rate cut-off point above which children should be treated was changed from 50 breaths/minute for all children under 5 years to a stratified level: 0 to 2 months, 60; 2 to 12 months, 50; 12 months to 5 years, 40.
2. Between 1991 and 1995, WHO and UNICEF developed the Integrated Management of Childhood Illness (IMCI) strategy, which incorporated the ARI Programme algorithm into a broader strategy including malaria, diarrhea, measles, and malnutrition. A part of this strategy was the inclusion of nonspecific danger signs including convulsions, poor conscious state, and inability to feed, which required a child to be referred for admission for severe disease not necessarily specified.
3. In 2013, lower chest wall indrawing was dropped as an indication for admission with severe pneumonia, based mainly on equivalence studies from Pakistan that have been criticized[10] for enrolling mostly mild cases.

The current WHO definition of severe pneumonia is cough or difficult breathing with at least one of the IMCI danger signs of convulsions, poor conscious state, or inability to feed. In addition, the definition includes the difficult to define sign of respiratory distress and hypoxia measured by pulse oximetry ($SpO_2 < 90\%$). None of these signs are specific for pneumonia, but they are good indicators of children in need of hospitalization. The inclusion of lower chest wall indrawing, which is usually a sign of reduced lung compliance, would increase the specificity of this algorithm for pulmonary disease; however, the diagnosis could still be bronchiolitis, asthma, or upper airways obstruction. Although the existing approach is appropriate for identifying those children in need of hospitalization for pneumonia, the combination of clinical signs used needs to be carefully re-examined, particularly in light of a recent large study from Kenya,[11] which concluded that 322 of 832 (39%) pneumonia deaths documented in 14 hospitals over 2 years would have been classified by the current WHO severe pneumonia definition as nonsevere pneumonia, not in need of hospitalization. It appears that the WHO definition of severe pneumonia is not a very convincing gold standard.

So who were the cases of WHO-defined severe pneumonia who were missed in the Nigerian study? Diagnoses amongst the "missed" cases included severe diarrhea, meningitis, and seizures. These could have been correctly diagnosed and treated for conditions other than pneumonia, and the inclusion of conditions with higher CFRs (sepsis and meningitis) would explain the trend toward higher mortality in the "missed" group. Of greater concern are 349 children in this category who were diagnosed with malaria. With the widespread availability of rapid diagnostic tests (RDTs), malaria diagnosis is now available in most health facilities in malaria-endemic countries.[12] A busy junior doctor facing a waiting room full of patients who sees a sick young child with a documented fever and a positive RDT may have a diagnosis before he/she begins to examine the patient. In endemic countries, a high proportion of healthy young children are parasitemic, so the presence of parasitemia in a sick child does not necessarily mean that the child has clinical malaria. In such settings, when a child presents with fever and convulsions, a positive RDT will support a diagnosis of cerebral malaria and often no lumbar puncture (LP) will be performed. There appears to be a decline in the performance of LPs, such that many young doctors lack the skills to perform the procedure. In some African hospitals, LPs are now rarely done on young children.[13] In most settings, such cases are covered with antibiotics, as the doctors acknowledge that the child could have meningitis. Despite this, it is likely that overdiagnosis of malaria leads to under-recognition of meningitis and some missed cases leading to fatal outcomes.

The child presenting with respiratory symptoms and a positive RDT is a different matter, as the diagnosis of pneumonia in a young child may be quite difficult and as Graham et al found that the availability of chest radiography is very limited. Whereas tachypnea in a child with malaria is an ominous sign,[14] the absence of cough is a useful sign for distinguishing malaria from pneumonia.[15] The recent rapid expansion in the availability of RDTs has probably led to an under-diagnosis of pneumonia in favor of malaria. In an African clinic, the diagnosis of malaria in a young child presenting with fever, a positive RDT, and tachypnoea is easy, but it will often be wrong. The danger of any diagnostic test, especially in settings with few such facilities, is that it will trump any clinical signs and may lead to a more limited or absent clinical evaluation. In Graham's extraordinary study, it is likely that some of the additional deaths in the "missed pneumonia" group are genuine missed cases of pneumonia, whereas others are serious conditions that may have been correctly diagnosed by the attending doctors. However, there may also be other factors at play here. The nonsignificant increase in deaths in the "missed pneumonia" group must be viewed against the slightly larger proportion of "detected" severe pneumonia cases who left the hospital against medical advice, possibly due to the financial cost of the admission. It is true that this study raises more questions than it answers, but these uncertainties should not detract from this important study. The reduction in childhood pneumonia mortality should be a priority for the global medical community, especially for the Nigerian medical community.

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REFERENCES

1. Graham H, Ayede AB, Oyewole OP, et al. Diagnosis of pneumonia and malaria in Nigerian hospitals: a prospective cohort study. *Pediatr Pulmonol*. 2020. (In press).
2. UNICEF. The State of the World's Children. www.unicef.org/media/63016/file/SOWC-2019.pdf. 2019. Accessed March 3, 2020.
3. Graham H, Ayede AB, Bakare A, et al. Oxygen for children and newborns in non-tertiary hospitals in South-west Nigeria: a needs-assessment. *Afr J Med Health Sci*. 2016;45(1):31-49.

4. Abdullahi MS. Three things Nigeria must do to end extreme poverty. www.weforum.org/agenda/2019/03/90-million-nigerians-live-in-extreme-poverty-here-are-3-ways-to-bring-them-out/. 2019. Accessed March 3, 2020.

5. Severe malaria. *Trop Med Int Health*. 2014;19(suppl 1):7-131.

6. Pio A. WHO programme on acute respiratory infections. *Ind J Pediatr*. 1988;55(2):197-205.

7. Pio A. The magnitude of the problem of acute respiratory infections. In: Proceedings of an International Workshop on Acute Respiratory Infections in Childhood; 1985; University of Adelaide, Australia; pp. 3-16

8. Leowski J. Mortality from acute respiratory infections in children under 5 years of age: global estimates. *World Health Stat Q*. 1986;39:138-144.

9. Shann F, Hart K, Thomas D. Acute lower respiratory tract infections in children: possible criteria for selection of patients for antibiotic therapy and hospital admission. *Bull World Health Organ*. 1984;62(5):749.

10. Mulholland K, Carlin JB, Duke T, Weber M. The challenges of trials of antibiotics for pneumonia in low–income countries. *Lancet Respir Med*. 2014;2(12):952-954.

11. Agweyu A, Lilford RJ, English M, et al. Appropriateness of clinical severity classification of new WHO childhood pneumonia guidance: a multi-hospital, retrospective, cohort study. *Lancet Glob Health*. 2018; 6(1):e74-e83.

12. Hanson K, Goodman C. Testing times: trends in availability, price, and market share of malaria diagnostics in the public and private healthcare sector across eight sub-Saharan African countries from 2009 to 2015. *Malar J*. 2017;16(1):205.

13. Thakur KT, Mateyo K, Hachaambwa L, et al. Lumbar puncture refusal in sub-Saharan Africa: a call for further understanding and intervention. *Neurology*. 2015;84(19):1988-1990.

14. Bojang K, Van Hensbroek MB, Palmer A, Banya W, Jaffar S, Greenwood B. Predictors of mortality in Gambian children with severe malaria anaemia. *Ann Trop Paediatr*. 1997;17(4):355-359.

15. Olaleye B, Williams L, D'Alessandro U, et al. Clinical predictors of malaria in Gambian children with fever or a history of fever. *Trans R Soc Trop Med Hyg*. 1998;92(3):300-304.