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Commentary

Rethink Respiratory Rate for Diagnosing Childhood Pneumonia

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Commentary

One in six childhood deaths is caused by pneumonia, making it the largest infectious cause of death for children worldwide [1], particularly in low and middle-income countries (LMIC) where timely pneumonia diagnosis is a much greater challenge because of limited resources [2]. The World Health Organization (WHO) defines pneumonia as the presence of fast breathing and/or chest indrawing in children who present with cough or cold and/or difficulty breathing. If diagnosed early, antibiotic therapy can be initiated to effectively treat pneumonia [3]. Fast breathing had long been considered a sensitive clinical sign of pneumonia in a child with cough or difficulty breathing [4], particularly in LMIC. The WHO has recommended that community health workers (CHWs) use the respiratory rate (RR) for diagnosis and that they treat pneumonia in children according to specific case-management algorithms [5]. There are numerous technologies for measuring RR by detecting changes in selected parameters, such as exhaled carbon dioxide, air temperature, humidity and chest wall movement [6,7]. Each method has strengths and limitations, and most of them are not suitable for LMIC [8].

In this journal, Baker et al. [9] report the outcome of a clinical study that assessed the performance of four non-contact relatively simple manual RR counters for use by CHWs in screening for pneumonia among 454 sick children in LMIC settings. Those methods included the Mark Two ARI timer (MK2 ARI), counting beads with an ARI timer, the Rrate Android phone, and the Respirometer feature phone applications. The development of the protocol and methods are nicely described in a video produced by the authors (https://www.malariaconsortium.org/

resources/video-library/927/protocol-film-implementing-a-trial-to-evaluate-pneumonia-diagnostic-devices).

All four devices were compared to an automated RR counter using Masimo capnography reference measurements. The results showed that while CHWs were able to obtain RRs from children in the majority of cases, the agreement of their measurements with the reference standard was low for all devices tested. Counting RRs using the four devices, albeit simple, was also associated with a huge inter-observer variability, thus characterizing "human counting" as being subjective and unreliable. Accurate and reliable counting in young infants was especially difficult, with only 8–20% of the assessments being in agreement with the reference standard, regardless of the RR device used. Though this was the first large, multicenter evaluation of the use of RR counting aids to diagnose pneumonia by CHW in children <5 y, the results of this study agree with previous studies. For example, CHWs correctly diagnosed and treated only 40% of all cases of childhood pneumonia by counting the RR in two Ugandan studies [10,11]. In our more recent study in the Democratic Republic of Congo [12], we observed that movement, crying, and stranger anxiety, particularly in children <3 y, were significant impediments to accurate assessment of RR. Ginsburg et al.'s systematic review provided an overview of the RR measurement tools that have undergone clinical evaluations of accuracy against a reference standard among spontaneously breathing children <5 y [13]. Unfortunately, most of those accuracy studies were not done and/or validated in LMIC. There are also concerns about the validity of the various reference standards used in such studies, including the one used by Baker et al. An editorial by Ansermino et al. [14] suggested that the tolerance level should be an order of magnitude greater than the random variation observed with the reference device when comparing reference and investigational medical devices. Thus, they argue that "*RR measurement studies would benefit from an uncertainty (probabilistic) approach to the reference standard, including procedures to measure and reduce this uncertainty*".

The reference issue notwithstanding, the measurement of RR in children remains challenging. Non-contact devices, such as those employed in the Baker et al. study, are thought to cause less distress to the child and therefore are less likely to alter the child's RR. However, they still rely on the CHW to count the RR or to tap the screen of a phone, and both CHW-based methods are prone to error and lead to overdiagnosis and/or underdiagnosis and inappropriate treatment.

Baker et al. state that "*counting RR manually, with breaths being difficult to see and count being hard to maintain without interruptions that require the count to be repeated, is a difficult procedure to do accurately and*

more is required of a device than simply supporting the health workers to keep count of the number of breaths a patient takes over 60 seconds." We agree entirely. We believe that there is an urgent need to re-think our existing dogmas about using RR as a stand-alone or sole diagnostic criterion for diagnosing pneumonia. Detecting work of breathing (WOB), for example, has recently emerged as being useful and even superior to breath counting in the diagnosis of pneumonia, particularly in severe cases [15–17], and it warrants further investigation.

Accumulating literature suggests that the use of a *combination* of signs and symptoms and potential point of care (POC) markers may be better than RR as a stand-alone tool. A systematic review by Rambaud-Althaus et al. concluded that any decision tree based solely on a single clinical sign is unlikely to increase diagnostic precision of childhood pneumonia [15]. In accordance with that review, a set of carefully designed machine learning tools combining four quantifiable vital signs (RR, heart rate, O_2 saturation, and temperature) was shown to support multi-faceted diagnoses of childhood pneumonia [16]. Similar conclusions were reached by another systematic review by Shah et al. in 2017 [17]. The latter review suggested that WOB is a better predictor than RR for diagnosing pneumonia. This year, a study from Tanzania suggested an interesting combination of clinical signs (RR and WOB) coupled with POC (e.g., C-reactive protein levels) to increase diagnostic yield of pneumonia and reduce antibiotic prescription [18].

Finally, a large study from Malawi challenged the role of RR in the management of nonsevere fast-breathing pneumonia [19]. This was a double-blind, 2-arm, randomized clinical noninferiority trial on 1343 children aged 2 to 59 months with pneumonia with a follow-up of 14 days. There was no significant difference in outcome between children who received antibiotics or placebo by day 14. The authors cite a 2016 Cochrane review that found that there is insufficient evidence for antibiotic use as a means of preventing suppurative complications, such as pneumonia [20].

In line with previous studies [21], the 2019 study from Malawi suggest that the diagnostic yield of fast breathing among children with true bacterial pneumonia appeared to have been low, implying that fast breathing might be neither an appropriately sensitive nor a specific sign of bacterial pneumonia, thus challenging the role of RR in the diagnosis of pneumonia.

In summary, the Baker et al. study as well as emerging literature calls for a radically different approach to better diagnose pneumonia in children. We need to think out of the box as we approach the 3rd decade of the 21st century.

Author Contributions

Conception, design, and drafting of the manuscript: I.A., M.L.

Declaration of Competing Interest

None declared.

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