Title: The burden and risks of paediatric pneumonia in Nigeria: a desk-based review of existing literature and data

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Abstract

Background

Pneumonia is a leading killer of children under-five years, with a high burden in Nigeria. We aimed to quantify the regional burden and risks of paediatric pneumonia in Nigeria, and specifically the states of Lagos and Jigawa.

Methods

We conducted a scoping literature search for studies of pneumonia morbidity and mortality in under-five children in Nigeria from 10th December 2018 – 26th April 2019, searching: Cochrane, PubMed and Web of Science. We included grey literature from stakeholders' websites and information shared by organizations working in Nigeria. We conducted multivariable logistic regression using the Multiple Cluster Indicators Survey (MICS) 2016-17 dataset to explore factors associated with pneumonia. Descriptive analyses of datasets from 2010-2019 was done to estimate trends in mortality, morbidity and vaccination coverage.

Results

We identified 25 relevant papers (10 from Jigawa, 8 from Lagos and 14 national data). None included data on pneumonia or acute respiratory tract infection burden in the health system, inpatient case-fatality rates, severity, or age-specific pneumonia mortality rates at state-level. Secondary data analysis found that no household or caregiver socio-economic indicators were consistently associated with self-reported symptoms of cough and/or difficulty breathing, and seasonality was inconsistently associated, dependant on region.

Conclusion

There is a clear evidence gap around the burden of paediatric pneumonia in Nigeria, and challenges with the interpretation of existing household survey data. Improved survey approaches are needed to understand the risks of paediatric pneumonia in Nigeria, alongside the need for investment in reliable routine data systems to provide data on the clinical pneumonia burden in Nigeria.

Introduction

In 2017, approximately 5.4 million children under age 5 died worldwide. During this period the under-5 mortality rate in Nigeria was one of the highest globally, at 100 deaths per 1,000 live births, and second only to India in absolute numbers[1]. In Nigeria, community-acquired pneumonia is the single largest cause of under-5 deaths, accounting for 140,520 (19%) under-5 deaths in 2017[2]. Considerable progress will be needed to achieve the targets in Sustainable Development Goal (SDG) 3.2, reducing under-five deaths to 25/1,000 live births by 2030[3].

Three areas have been identified as key for interventions aimed at reducing pneumonia deaths: protection (ensuring the child receives appropriate nutrition from birth); prevention (including vaccines and HIV prevention); and treatment (improved care-seeking, case management, and provision of antibiotics and oxygen)[4,5]. To appropriately target these intervention approaches in Nigeria, a clear understanding of context-specific indicators from different states and local government authority areas are needed. This is particularly important to ensure gains made in reducing pneumonia also promote equity. To the best of our knowledge, a scoping review of the current pneumonia burden and risk factors has not been recently conducted in Nigeria, posing a critical evidence gap.

The aim of this study was to determine key indicators and outcomes for paediatric pneumonia in Nigeria as a whole, and specifically in Lagos (South-West), and Jigawa, (North-West) states. These two regions were selected as part of a wider programme of work (The INSPIRING Project) through discussion between project partners and the Ministry of Health, considering the potential for political support. Additionally, Nigeria is geographically diverse country, with unequal resource distribution. Jigawa is a poor, rural state, with 70% of the population living in severe poverty, while Lagos state is rich and densely populated[6]. These two states therefore also provide socio-economically diverse environments.

Materials and Methods

We conducted a literature review and secondary data analysis, from the 10th of December 2018 to the 26th of April 2019. The objectives of this desk review were: to determine the burden of pneumonia morbidity and mortality in children under-five in Lagos and Jigawa from 2010 to 2019; to estimate the coverage of key pneumonia prevention, diagnosis, treatment indicators; and establish the relationship between socio-demographic risk factors and pneumonia prevalence. While the primary interest was pneumonia, we also included data sources and papers which report on acute respiratory tract infections (ARI), as data on pneumonia was limited and these terms are often used interchangeably[7]. Data from the literature review and the secondary analysis were analyzed separately and then triangulated and presented together in the results section.

Literature review

Search criteria

A search was conducted using the following terms: ("pneumonia" OR "lung inflammation" OR "pulmonary inflammation" OR "pneumonitis" OR “ARI” OR “acute respiratory infection”) AND ("nigeria*" OR "lagos" OR "jigawa*") AND ("pediatric*" OR "paediatric*" OR "child*" OR "infan*" OR "toddler" OR "newborn" OR "neonate" OR "baby" OR "babies"). Searches were conducted in: Cochrane, PubMed and Web of Science. We also searched grey literature (Popline, SSRN, WorldCat, Turning Research into Practice, National Institute for health and Care Excellence, ResearchGate) and key stakeholder organizations' websites, including: World Health Organization (WHO), UNICEF, Save the Children, Clinton Health Access Initiative, Oxygen for Life Initiative, and Stop Pneumonia. We contacted 21 organizations working in Nigeria to enquire about on-going and unpublished works (Web-appendix 1).

Inclusion and Exclusion criteria

We used the following inclusion criteria:

- Study population included children aged between 0 and 59 months old
- Included data from Lagos or Jigawa states
- Any study design, including published and unpublished, original articles, literature reviews and reports
- Included data on any of: morbidity, mortality, barriers to accessing care, quality of care, health system burden, associations with social determinants of health
- Published from 1st Jan 2010 to 18th March 2019 for academic papers, and to 1st March 2019 for grey literature.

We did not implement a language restriction, but all the information retrieved was in English. Pre-2010 articles were deemed too old to be relevant for the current situation.

The primary outcomes of interest were: pneumonia/ARI mortality rates; inpatient case fatality rates (CFR); pneumonia/ARI cases presenting to primary, secondary and tertiary facilities; prevalence of different pneumonia severity; pneumonia/ARI treatment; comorbidities; care-seeking behavior; nutrition and feeding practices; and preventive behaviors (e.g. vaccine coverage and cooking fuel).

Article Selection

Articles were excluded based on the title, then abstract and full text screening for inclusion and exclusion criteria. Relevant data was extracted using a study-developed tool on the pre-specified outcomes of interest, and key paper characteristics such as the definition of pneumonia/ARI used.

Secondary data analysis

Data sourcing

Datasets with information on pneumonia or ARI prevalence and household, caregiver or child characteristics from 2010-2019, and including Lagos and Jigawa were included. Available datasets were: the 2016-2017 and 2011 Multiple Cluster Indicators Survey (MICS); the National Nutrition and Health Survey (NNHS) from 2015 and 2014; the Demographic and Health Survey (DHS) from 2013. A DHS was completed in 2018, but data were not yet available at the time of analysis.

These datasets all use household surveys, and include household and individual level data on socioeconomics, nutrition, and health. The three surveys share a similar design, selecting survey respondents with a stratified two-stage cluster design in which the 2006 population census enumeration areas are stratified by state, and into rural and urban areas in the case of DHS and NNHS. Enumeration areas are then sampled from each stratum, and households sampled from within these areas. Detailed methodologies for the surveys have been published[7-9].

Definitions

The household surveys all contain data on ARI, defined as a caregiver report of the child having a cough and fast and/or difficulty breathing, in the two weeks prior to the household survey[7].

Four groups of risk variables were analyzed: geographic environment (season, region); household environment (cooking fuel, crowding, wealth quintile, urban/rural residence); maternal characteristics (religion, marital status, education, age, ARI knowledge); and child characteristics (age, sex, nutritional status, vaccination uptake, report of fever/diarrhoea). Vaccine status was based on caregiver recall or documentation in a vaccination card, with complete vaccination defined by age-group, in-line with the Extended Programme of Immunisation (EPI) schedule. Wealth index was calculated using household ownership of key assets, and categorised into quintiles. We defined these variables *a priori*, with full details presented in Web-appendix 2.

<u>Statistical analysis</u>

We described the temporal trends in under-five mortality, ARI prevalence and vaccination uptake, using all data points between 2010-2019. We described ARI knowledge, reporting by caregivers, treatment seeking and vaccination uptake, by socio-economic indicators using MICS 2016-2017 data.

We determined associations between ARI and geographic, household, caregiver and child characteristics, using univariable and multivariable logistic regression. We conducted a national-level, and stratified analyses for Jigawa and Lagos states. Primary analysis used the MICS 2016-2017 dataset, as the most recent, with a sensitivity analysis conducted using the 2013 DHS data. Sample weights were applied to account for the survey design. Variables with more than 10% missing data were excluded from adjusted models. All analyses were done in Stata SE14.

Results

The searches returned 308 academic articles, and 436 grey literature documents, of which 25 met inclusion criteria (Figure 1, Web-appendix 3). Of these, 10 contained data from Jigawa and the North-West, 8 from Lagos and the South-West, and 14 with national-level data.

Mortality

The all-cause under-five mortality rate decreased moderately at national level from between 2010 (taken from the 2013 DHS data) and 2017 (from the 2016-2017 MICS data), while rates remained stable in Lagos and Jigawa (Figure 2.A). The national under-five mortality rate was 136 deaths per 1,000 live births in 2010 and 100/1,000 live births in 2017. In Jigawa, there was a slight increase in the under-five mortality rate during the same period, from 187 in 2010 to 191/1,000 live births in 2017, while Lagos, had a slight decrease from 106 in 2010 to 92/1,000 live births in 2017. However, in 2014 and 2016, estimated mortality rates in Lagos were closer to 50 deaths per 1,000 live births. The reason for these outliers isn't clear. The percentage of under-five deaths attributed to ARI was 19.4% in 2015[10], however age-specific state-level cause-specific mortality rates were not found in the literature (Table 1).

Morbidity

We found data points for ARI point prevalence from 2011-2018 (Figure 2.B), taken from the 2011 MICS, 2013 DHS and 2015 and 2018 NNHS datasets. In Nigeria overall, there was a decrease in prevalence from 2011-2015 (from 9.6% to 2.3%) followed by an increase to 4.6% in 2018; the same trend was observed in Jigawa. In Lagos, however, following a decline between 2011-2013 (from 4.2% to 1.1%), the prevalence then increased, with a 2018 estimate of 2.1% for the South West region. However, these values all have wide confidence intervals, especially in Jigawa, and were based on surveys done at a single time point and should therefore be interpreted with caution.

We did not find any published data on pneumonia/ARI case numbers at primary, secondary or tertiary care, inpatient case-fatality rates, or pneumonia/ARI prevalence stratified by severity in Lagos or Jigawa, or national estimates.

Socioeconomic and environmental determinants of ARI

Nine papers described associations between socio-economic factors and ARI, eight using 2013 DHS data, and one using 2011 MICS data. Of these, six papers focused on the national level[11-16], while the other three compared associations between regions[17-19]. The following variables were reported as significantly associated with an increased probability of caregiver reported ARI symptoms: use of unclean cooking fuel, low wealth index, living in the North-West region (versus the South-West or South-South), dry season, lack of handwashing and living in a rural versus urban area.

Our analysis of the MICS 2016-17 dataset for Nigeria, Jigawa and Lagos are presented in Table 2. Caregiver reported fever in the previous two-weeks was the only variable consistently associated with reporting ARI symptoms across Lagos (aOR: 3.93; 95%CI: 0.94-16.42), Jigawa (aOR: 7.18; 95%CI: 3.17-16.27) and at national level (aOR: 3.25; 95%CI: 2.81-

3.76). Rainy season was associated with fewer reported ARI cases, both nationally (aOR: 0.74; 95%CI: 0.60-0.91) and in Jigawa (aOR: 0.21; 95%CI: 0.09-0.51); however, the opposite was observed in Lagos (aOR: 8.64; 95%CI: 1.79-41.72). In the national-level analysis, living in the South-West region (aOR: 0.39; 95%CI: 0.27-0.58) and having a caregiver with no education (aOR: 0.63; 95%CI: 0.49-0.81) were associated with lower odds of ARI. In Lagos, having a Christian caregiver was associated with lower odds of ARI (aOR: 0.34; 95%CI: 0.17-0.68).

Sensitivity analysis using the DHS 2013 data found key discrepancies (Web-appendix 4). At the national-level, living in the North-West region was associated with significantly lower odds of ARI (aOR: 0.36; 95%CI: 0.25-0.50), and caregiver education was no longer significant. In Jigawa, belonging to the poorest wealth quintile was associated with higher odds of ARI (aOR 5.35; 95%CI: 1.13-25.42). In Lagos, no significant association was found with seasonality, while having a Catholic caregiver was associated with higher odds of ARI (aOR: 6.68; 95%CI: 1.22-36.60).

Knowledge and care-seeking

Four papers explored caregivers' level of ARI -related knowledge. All reported that less than 50% of caregivers have knowledge of the disease's symptoms[20-23]. Five papers reported on ARI health-seeking behaviors[21,24-27]. The data suggests a decrease in care-seeking behavior over time (62% in 2011[21] to 24% in 2016-17[24]). The factors found to be associated with adequate care-seeking behavior were: higher levels of caregiver education, high household wealth index, and living in an urban area.

Results from our description of the MICS 2016-17 data, describing knowledge of ARI symptoms and care-seeking for treatment, and socio-economic factors are presented in

Web-appendix 5. Knowledge of the two ARI symptoms - fast breathing and difficult breathing - was poor across the settings, with 15% of the caregivers reporting this knowledge nationally, and 12% and 7% in Jigawa and Lagos, respectively. Nationally, relatively little variation in knowledge of ARI symptoms was seen between socio-demographic variables, except for wealth quintile with 10.1% of the poorest group knowing both symptoms, versus 20.9% of the richer group. In Jigawa, higher income households and caregivers with secondary/tertiary education had higher levels of knowledge, while in Lagos, being unmarried was associated with higher knowledge.

At a national level, care-seeking for ARI was higher in high income households (80.0% richest versus 62.7% poorest) and in those with more education (81.6% secondary/tertiary versus 61.3% no education). The numbers at state level were small, limiting comparisons (Web-appendix 5).

Vaccination coverage

Using all data points from 2011-2018, the trend in 3-dose coverage of pentavalent vaccine coverage in 12-23 month-old children showed an overall increase in coverage over time (Figure 2.C). This was seen in all regions, from 37% to 57% at the national level, from 7% to 38% in Jigawa and from 82% to 93% in Lagos. The trend in PCV coverage during the same period could not be plotted, due to the lack of data points at national and state level.

Two papers reported determinants of vaccine uptake, with living in the South-West region[28] and being from a wealthier household[26] associated with higher vaccination coverage. Table 3 presents the percentages of complete vaccination uptake in 12-59 month old children in Nigeria, Jigawa and Lagos from the 2016/17 MICS dataset. Higher percentages of complete vaccination at the national level were found in groups characterized by: being of higher wealth (54%), higher education (50%), single mother (54%), with ARI knowledge (36%), with fewer children in the household (44%), being Christian (50%) and the mother being >19 years old (39%). In Jigawa and Lagos, the patterns were similar, the main exception being religion, as Islamic households had higher rates of completed vaccination in Lagos (62%). Female and male children had similar levels of complete vaccination nationally (40% vs 37%), but in both Lagos and Jigawa, complete vaccination was slightly lower in females than in males (Lagos 54% vs 61%; Jigawa: 5% vs 8%).

Discussion

We conducted a desk-based review of published academic and grey literature, and secondary analysis of household survey data, to synthesize available information on paediatric pneumonia and acute respiratory infections in Nigeria, and specifically Lagos and Jigawa. Despite the high estimated ARI mortality in Nigeria of 19 deaths per 1,000 livebirths, we found crucial evidence gaps and issues in the reliability of the data which is available.

Most notable was the complete lack of data on pneumonia incidence, case-fatality rates, severity and age-stratified morbidity and mortality in our regions of focus. Evidence from other regions in Nigeria suggest a high burden of fast-breathing and severe pneumonias.[18,29] For example, in Kwara state, North-Central region, of cases presenting to the tertiary hospital setting, 41.5% were hypoxaemic and 63.5% had chest-indrawing, and amongst hypoxaemic children, the case fatality rate was 20.5%[30]. These data suggest that reaching appropriate care is delayed, and more evidence is needed to explore if the clinical epidemiology is consistent across regions.

One of the challenges in obtaining reliable information on hypoxaemic pneumonia burden could be the lack of pulse oximeters available in the healthcare system. A study set in the South-West region, but not including Lagos, reported a baseline utilization of pulse-oximeters in children admitted to hospital with suspected pneumonia of 3%[31]. Similarly, for oxygen treatment, a study from South-West Nigeria, again excluding Lagos, in secondary facilities found that the presence of oxygen did not guarantee an adequate supply for the patients[32]. Reasons for this were given as: limited availability of the resource itself, lack of complementary equipment (i.e. nasal prongs); lack of a reliable power source for oxygen concentrators; a perceived high cost for both hospitals and patients; and lack of knowledge/training of the staff on its importance/utilization. Hypoxaemia is a key risk factor for pneumonia mortality, and oxygen is an essential medicine for its treatment. Therefore, context-specific data is needed from other regions, to support intervention adaptation and implementation for different settings.

Synthesizing the published literature and our analysis, five variables had frequently observed associations with under-five ARI in Nigeria: use of unclean cooking fuel, religion, wealth index, region of residence, and caregiver education level. We found that children of caregivers with less education had lower odds of ARI, which contradicts existing evidence[33]. Cross-sectional surveys (like MICS and DHS) rely on self-reported information from caregivers, and those with less education are likely have poorer knowledge of ARI, and therefore would be less likely to report their child having the disease. As caregivers in Jigawa had lower levels of education, the ARI point prevalence for Jigawa may be less reliable than Lagos; therefore, we would advise caution in the interpretation of these associations due to this inherent bias with the self-reported household survey methodology.

Being from a poorer household was consistently associated with an increased ARI risk, and relates to the use of unclean cooking fuel and region of residence. In Jigawa, the use of unclean cooking fuel was almost universal, with exposure to unclean cooking fuel having several biological mechanisms that increase the probability of developing an acute lung infection[34]. We did not explore other forms of environmental smoke exposure, such as tobacco use in the household, as the estimated prevalence is low (e.g. <1% of women reported being current smokers in the recent 2018 DHS)[35]. However, a recent review suggests smoking rates may be much higher, and therefor this relationship warrants further exploration[36].

Northern Nigeria is characterized by low education levels, poor access to adequate health facilities, and a vast majority of the population living in rural areas with high poverty rates. It is no surprise, then, that the secondary data analysis showed an increased odds of ARI with living in the North – opposed to the richer, increasingly urban, with higher vaccination coverage southern region. These differences between the two regions highlight how standardized national level solutions may not be functional in the context of Nigeria, and emphasize the need for local data to create tailored interventions for each setting.

This interconnection between poverty, the North-South divide and ARI prevalence can be inferred as well from the findings on caregivers' education, knowledge and care-seeking behavior. Both the literature review and secondary data analysis corroborated that wealthy and highly educated caregivers are prone to seek treatment or advice when identifying ARI symptoms in their children. The same was observed when conducting the analysis of secondary data on vaccination uptake, finding higher vaccination uptake when caregivers were educated and wealthy. This is likely to reflect increased agency around care-seeking, such as better accessibility of health-care services, increased ability to afford transportation cost, medical fees and medicines, and a better understanding of the importance of health-seeking behavior[37].

We found mixed results around the role of the rainy and dry season in the reporting of ARI. The dry season is characterized by the dusty Harmattan wind, with air flowing from the North-Eastern Sahara Desert. Harmattan dust is a damaging air pollutant, with its mineral dust particles carrying harmful metals and other contaminants. This can penetrate the respiratory system, putting human health at risk[38]. The effect of the Harmattan is stronger in Northern Nigeria – due to proximity to the Saharan desert – possibly explaining the different results seen between Jigawa and Lagos[39]. However, as the data were collected through cross-sectional surveys, the timing of data collection could affect the associations seen between reporting of ARI symptoms and season. Continuous measurement of pneumonia and ARI morbidity and mortality, across all seasons, and between regions is needed to have a full picture of the role of the rainy and dry seasons in Nigeria.

In this paper, most of the data came from MICS, DHS and NNHS datasets or mathematical models based on these datasets. There are several inherent limitations that can affect the reliability of data collected from national household surveys, namely: reporting, recall and misclassification biases, and the inability to infer causal relationships with cross-sectional data. The MICS, NNHS and DHS sample sizes at the national level allowed us to measure statistically significant associations. However, under-reporting of paediatric ARI is likely, as it relies on caregiver report[40], and we found low-levels of ARI knowledge. This limited our ability to do a multivariable analysis of predictors of ARI knowledge and care-seeking, with small numbers of reported cases and potential bias in those who do report symptoms.

Household surveys only report data on ARI symptoms, not specifically on pneumonia. Even if WHO and UNICEF recommended that ARI should be described as "presumed pneumonia" (Web-appendix 2), 'ARI' is an umbrella term that is likely to include a whole spectrum of diseases, such as acute bronchiolitis and common colds. Therefore, the conclusions we can draw from household surveys on pneumonia-specific prevalence and associations are limited.

Considering Nigeria contributes an estimated one in seven global paediatric pneumonia deaths each year, there is an urgent need to address the considerable data gaps we identified in this study. Specifically, prospective empirically observed studies with clinically diagnosed pneumonia and its risk factors, diagnosis, treatment and outcomes, are needed to address the biases seen with household survey data. Promoting high-quality routine data at all levels of the healthcare system, to provide estimates of the real pneumonia burden and severity classification, could go some way to addressing this gap. Further exploration of the importance of caregiver's education in relation to the wellbeing of their children, and the relevance of the child's gender in health-related matters is also required. However, poverty, and factors related to poverty, was consistently associated with acute respiratory infections. Therefore, interventions to try and reduce the pneumonia/ARI burden need to be pro-poor, and ensure the promotion of equity.

Author contributions

The study was conceived by CK, TC, AGF, AAB, HG, EDM and RB, with input from all authors. The literature searches and synthesis was conducted by AIu, and secondary data analysis was conducted by ZA, with support from TC and CK. The paper was drafted by AIu and ZA. All authors commented, read and approved the final manuscript.

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