Original Research Article

Environmental Epidemiology

OPEN

Exposure-response relationship of residential dampness and mold damage with severe lower respiratory tract infections among under-five children in Nigeria

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Background: Previous epidemiological studies demonstrated an increased risk of respiratory health effects in children and adults exposed to dampness or mold. This study investigated associations of quantitative indicators of indoor dampness and mold exposure with severe lower respiratory tract infections (LRTI) among children aged 1–59 months in Ibadan, Nigeria.

Methods: In-home visits were conducted among 178 children hospitalized with LRTI matched by age (±3 months), sex, and geographical location with 180 community-based children without LRTI. Trained study staff evaluated the indoor environment using a standardized home walkthrough checklist and measured visible dampness and mold damage. Damp-moldy Index (DMI) was also estimated to quantify the level of exposure. Exposure-response relationships of dampness and mold exposure with severe LRTI were assessed using multivariable restricted cubic spline regression models adjusting for relevant child, housing, and environmental characteristics.

Results: Severe LRTI cases were more often male than female (61.8%), and the overall mean (SD) age was 7.3 (1.35) months. Children exposed to dampness <0.3 m^2 (odds ratio [OR] = 2.11; 95% confidence interval [CI] = 1.05, 4.36), and between 0.3 and 1.0 m^2 (OR = 2.34; 95% CI = 1.01, 7.32), had a higher odds of severe LRTI compared with children not exposed to dampness. The restricted cubic spline showed a linear exposure-response association between severe LRTI and residential dampness (P < 0.001) but a nonlinear relationship with DMI (P = 0.01).

Conclusions: Residential dampness and DMI were exposure-dependently associated with higher odds of severe LRTI among under-five children. If observed relationships were causal, public health intervention strategies targeted at reducing residential dampness are critically important to mitigate the burden of severe LRTI among under-five children.

Keywords: Dampness; mold exposure; lower respiratory tract infections; under-five children; Nigeria; epidemiology

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The authors declare that they have no conflict of interest with regard to the content of this report.

This work was supported by the College of Health (CHS) PhD Scholarship of the University of KwaZulu-Natal to facilitate field activities.

The data from the case-control study cannot be made available publicly as the consent form signed by participants did not have such a stipulation: individuals interested in obtaining the data required can contact Dr. Fakunle; fakunz@yahoo.com, Department of Public Health, Osun State University, Osogbo, Nigeria.

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Environmental Epidemiology (2023) 7:e247

Received: 17 November 2022; Accepted 23 February 2023

Published online 29 March 2023

DOI: 10.1097/EE9.0000000000000247

Introduction

Lower respiratory tract infections (LRTIs) remain the leading cause of childhood morbidity and mortality worldwide, particularly among under-five children.[1,2] An estimated 921,000 children died of LRTI in 2015, and more than 95% of these deaths occurred in low-and-middle-income countries (LMICs), predominantly in South Asia and sub-Saharan Africa.[3,4] In 2017, community-acquired LRTIs were the single most significant cause of under-five mortality, accounting for 140,520 (19%) of under-five mortality in Nigeria.[5] Nigeria ranks first in Africa and third worldwide for the highest estimated number of childhood deaths from LRTI.[6] Despite reports from several studies on the risk factors of LRTIs, reducing the burden of LRTIs in sub-Saharan Africa remains a significant public health issue that requires a concerted effort, including improving the indoor environment.

Many studies have reported that residential exposure to indoor dampness and mold could trigger adverse respiratory or allergic

What this study adds

Assessment of dampness and mold exposures in residential environments has relied mainly on qualitative measurements of exposure which in most cases lacks useful information about exposure-response relationships. In this work, we showed that quantitative measurement of residential dampness and moisture damage was exposure-dependently associated with a higher risk of severe LRTI among under-five children, thereby demonstrating the importance of public health intervention for promoting good hygienic conditions and reducing the considerable burden of severe LRTI among under-five children in LMICs.

health effects in infants, children, and adults,[6–10] without quantifying exposure to assess exposure-response relationships that could strengthen evidence of causality. Most buildings in LMICs are subjected to continuously fluctuating moisture and temperature conditions, which can cause damage to building materials and increase indoor humidity.[7] These conditions can enhance mold and bacterial proliferation, leading to increased respiratory illnesses, including LRTIs, especially among under-five children.[11,12]

The associations between objectively measured residential dampness and mold exposure and respiratory health may reflect underlying causal relationships between fungal exposures and respiratory health effects.[12] The assessment of residential dampness and mold exposures in most epidemiological studies has relied mainly on qualitative measurements of exposure, such as the presence or absence of moisture or visible molds or moldy odor in different areas within the home environment,[7,13,14] which in most cases do not assess quantitative exposure-response relationships. Notably, our previous study among under-five children in Nigeria showed that qualitative measures (presence/absence) of dampness and mold in the child's sleeping area are significantly associated with LRTI even after adjusting for other covariates.[15] Also, the few available studies that have quantitatively measured exposure to dampness and molds were associated with childhood wheeze and asthma.[16,17] Thus, more studies using specific exposure data, such as the quantitative measures of dampness and mold exposure, including the assessment of the Damp–Mold Index (DMI), a subscale of the standardized respiratory hazard index (RHI), are needed.

A meta-analysis showed that under-five children who resided in homes with visible mold and moisture damage were significantly more likely to develop LRTI than in homes with no visible mold.[18] However, quantitative information about exposure levels and more evidence of potential causal association are required to inform policy and practice, especially in developing counties such as Nigeria, where the availability of more advanced methods of assessing exposure is lacking. The objective of this study was to evaluate the association of dampness/moisture and mold damage in the residential indoor environment with severe childhood LRTI and determine potential exposure-response relationships.

Materials and methods

Ethics approval and consent to participate

Access to the participating hospitals was granted by the Oyo State Ministry of Health in Nigeria and the authorities of the participating hospitals. The Ethics Committees of the University of KwaZulu-Natal (Ref No: BE545/17), the University of Ibadan/University College Hospital (Ref No.: UI/EC/17/0077), and the Oyo State Government, Ibadan Nigeria (Ref. No.: AD13/479/462) approved by the study.

Study site, design, and data collection

The study design and sites are detailed elsewhere.[15,19] Briefly, 178 cases were matched to 180 controls for sex, age (±3 months), and geographical location. Severe LRTI cases were recruited from three hospitals within Ibadan, namely Otunba-Tunwase Children Emergency Clinic of the University College Hospital, Ade-Oyo Maternity Teaching Hospital, and Oni-memorial Children Hospital. Controls were under-five children without LRTI identified from the same community as the cases and recruited after obtaining consent from the caregiver. The majority of these communities were semi-urban inhabited mostly by the Yoruba-speaking population.

A validated child health questionnaire[20] was administered by trained public health personnel to caregivers of cases and controls to obtain essential information, including socio-demographics (age and sex), and household characteristics. The status of the child was assessed by a trained nurse using a clinical proforma to collect vital child health information such as breastfeeding and immunization status, anthropometric measurements, respiratory symptoms/signs, and X-ray findings.

Definition and selection of cases and controls

As detailed in the published protocol,[19] children under the age of 5 years visiting the selected hospitals were screened, assessed for eligibility (admitted for LRTI and residing in Ibadan), and caregivers were administered the consent form. LRTI diagnosis was carried out by a doctor based on findings from the X-ray report. Controls who were of the same age group and sex as the cases were identified and recruited from the same community as cases during household visitation after thorough screening by the same doctor that assessed the case for the presence/absence of respiratory signs in the past 30 days. Therefore, control subjects who reported signs and symptoms of LRTI in the past 30 days before the study were excluded from the study.

Dampness and mold damage exposure assessment

Recruited cases and controls were followed-up within 24 hours of enrollment, and their households were subjected to a home survey. Trained inspectors used a validated walkthrough checklist[21] to document real-time observations on housing conditions. Each room in homes of cases and controls was visually inspected for signs of dampness and mold damage, coupled with the location and the size of the damaged surface recorded on the checklist. Mold damage (m^2) was defined as the largest damaged area from mold, or mold and water on a single surface in any room. Dampness (m^2) was defined as the maximum damaged area from either water, mold, or both on a single surface in any room. We examined dampness and mold damage as both continuous and categorical variables. Categorical variables included four categories for dampness/moisture damage and three categories for mold damage. Category 0 for dampness and mold exposure variables was homes with no dampness or no mold damage, respectively, while categories 1, 2, and 3 represent dampness and mold damage area of <0.3 m^2, 0.3–1.0 m^2, and >1.0 m^2, respectively.[22] In addition, we assessed the Damp–Mold Index (DMI)[7]; an 8-item subscale derived from the RHI,[23] in homes of cases and controls to further quantify the level of exposure. The DMI includes items on the presence or absence of "any mold on wall," "any mold on joint," "musty smell," "quite damp," "very damp," "minor leaks," "major leaks," and "ponding of water under house." The presence of any of the components of the DMI was given a score of 1 except for "very damp" and "major leaks" that was scored 2 each totaling 10 points.

Definition of household characteristics and selection of covariates

We previously described the links between indoor residential characteristics and LRTI in a Directed Acyclic Graph, which was used to select covariates.[15] Occupant density was defined as the total floor area divided by the total number of persons present. Child's characteristics such as a prior episode of LRTI, breastfeeding status, and the number of other siblings who are under-five were obtained. Housing tenure was considered as owning or renting a residential apartment. The presence/absence of pets of any type and smokers in the house were also inspected in homes of cases and controls.

Statistical analysis

All data were entered into Excel spreadsheets and subjected to logic checks to ensure validity and consistency. A validated and complete dataset was exported to SPSS version 25.0, and R statistical program (version 4.0.0) for further analyses.

We assessed participants' socio-demographic and housing characteristics between cases and controls using McNemar's test for paired categorical outcomes and t-test for continuous outcomes. We further analyzed associations between dampness and mold exposure and severe LRTI status using conditional logistic regression with adjustment for housing characteristics. In the categorical analyses of the association between dampness and mold exposure and severe LRTI, each exposure category was compared with the reference category of no dampness or mold damage. In addition, models with continuous exposure variables for dampness and mold damage, including DMI were constructed to estimate the odds ratios (ORs) associated with each 1 m^2 or 1 unit increase in DMI. Multivariable logistic regression analysis was used to determine the associations between dampness and mold exposure and severe LRTI, adjusting for child, environmental, and housing characteristics such as age, sex, geographical location, number of siblings under-five years, breastfeeding status, history of LRTI, season, housing tenure, occupant density, pet ownership, and cigarette smoking. A restricted cubic spline with 3 knots was used to simulate the exposure-response association between the predictor variables (dampness, mold damage, and DMI) and severe LRTI among under-five children using R-software version 4.1.

Results

Detailed socio-demographic and household characteristics of the children have been presented in a previous report.[15] As shown in Table 1, residential crowding (<38 m^2/person: 77.0% vs. 51.7%), living in a rental house (74.2% vs. 59.0%), pet ownership (38.8% vs. 20.2%), and the presence of any smoker in the house (11.2% vs. 5.1%) were significantly more often observed among cases than controls.

Results of univariate analysis of the association between dampness/mold damage and severe LRTI are presented in Table 2. In the unadjusted model, increasing damp/moisture damage (<0.3 m^2: OR = 1.77, 95% confidence interval = 1.00–3.11; 0.3–1.0 m^2: OR = 2.59, 95% CI = 1.13–5.94; >1.0 m^2: OR = 3.27, 95% CI = 0.95–12.61) was associated with severe LRTI. In the adjusted model for all age categories (Figure 1A), damp/moisture damage <0.3 m^2 (adjusted odds ratio (aOR) [95% CI] 2.11 [1.05–4.36]), and between 0.3 and 1.0 m^2 (aOR [95% CI] 2.34 [1.01–7.32]), were associated with severe LRTI. When stratified by age categories, a higher odds of LRTI was observed for damp/moisture damage <0.3 m^2 (aOR [95% CI] 3.32 [1.25–10.43]) among children less than 6 months of age (Figure 1B), which was not the case for children who were aged 6 months and above (Figure 1C). Stratification by sex revealed no association between damp/moisture damage categories and severe LRTI. (Figure 1 D,E). Damp/moisture damage as a continuous variable was also associated with a significant increase in the risk of severe LRTI (per 1 m^2 increase: OR = 5.23; CI = 1.65, 16.77), even after stratified analysis by age categories (<6 years old: OR = 4.21; CI = 1.04, 18.62; ≥6 years old: OR = 6.14; CI = 1.16, 18.23) and sex (male: OR = 6.40; CI = 1.21, 18.86; female: OR = 3.40; CI = 1.30, 15.43). In terms of mold exposure, univariate and adjusted models did not show any significant association between categories of mold damage and severe LRTI among under-five children. A similar trend was observed for continuously modeled mold damage across age and sex categories. Univariate associations between DMI and severe LRTI (Table 2) revealed a consistent risk of severe LRTI with increasing levels of DMI. A DMI score ≥6 was significantly associated with severe LRTI (aOR = 2.48; 95% CI = 1.08, 5.44) in the unadjusted analysis which was lost after adjustment for essential covariates.

Table 1.

Demographic and housing characteristics among cases and controls

Socio-demographic variables	Cases (n = 178); n (%)	Controls (n = 180); n (%)	*P*-value
Sex; male	107 (60.1)	110 (61.8)	0.74
Age (months)			
<6months	112 (62.9%)	113 (63.5%)	0.91
≥6months	66 (37.1%)	65 (36.5%)	
History of LRTI; yes	28 (15.7%)	16 (9.0%)	0.04
Season of enrolment			
Dry	71 (39.9%)	89 (50.0%)	0.05
Wet	107 (60.1%)	89 (50.0%)	
Housing tenure			
Owned	46 (25.8%)	73 (41.0%)	0.002
Rented	132 (74.2%)	105 (59.0%)	
Occupant density (m^2/person)			
14–38	137 (77.0%)	92 (51.7%)	<0.001
39–80	41 (23.0%)	85 (48.3%)	
Mean ± SD	31.7 ± 12.7	42.6 ± 13.9	<0.001
Pet ownership; yes	69 (38.8%)	36 (20.2%)	<0.001
Any smoker; yes	20 (11.2%)	9 (5.1%)	0.03
Breastfeeding status; exclusive	121 (69.1%)	149 (84.2%)	0.001
Number of siblings U5 years; >1	168 (94.4%)	154 (86.5%)	0.01

Two (2) cases were excluded from the analysis because they did not meet the criteria.

Table 2.

Moisture and Mold damages in homes of children under-five

	Cases (n = 178); n (%)	Controls (n = 180); n (%)	Crude OR (95% CI)
Damp/moisture damage (m^2)			
0	115 (64.6%)	141 (79.2%)	Reference value
<0.3	36 (20.2%)	25 (14.0%)	**1.77 (1.00, 3.11)**
0.3–1.0	19 (10.7%)	9 (5.1%)	**2.59 (1.13 – 5.94)**
>1.0	8 (4.5%)	3 (1.7%)	3.27 (0.95, 12.61)
Moisture damage as a continuous variable per 1 m^2 increase			**5.25 (2.20, 14.02)**
Mold damage (m^2)			
0	134 (75.7%)	153 (86.0%)	Reference value
<0.3	32 (18.1%)	20 (11.2%)	1.83 (0.99, 3.35)
0.3–1.0	11 (6.2%)	5 (2.8%)	2.51 (0.85, 7.41)
Mold damage as a continuous variable per 1 m^2 increase			1.18 (0.94, 6.17)
Damp-Mold Index (DMI)			
Dampness			
Feels quite damp (1)	63 (35.4%)	37 (20.8%)	**2.09 (1.30, 3.36)**
Feels very damp (2)	30 (16.9%)	13 (7.3%)	**2.57 (1.30, 5.11)**
Mold			
Any mold on walls/ Ceiling (1)	43 (24.2%)	25 (14.0%)	**1.95 (1.13, 3.36)**
Any mold on joists (1)	16 (9.0%)	9 (5.1%)	1.86 (0.80, 4.32)
Musty smell (1)	30 (16.9%)	19 (10.7%)	1.70 (0.92, 3.14)
Water leaks			
Minor leaks (1)	26 (14.6%)	14 (7.9%)	**2.00 (1.01, 3.98)**
Major leaks (2)	12 (6.7%)	6 (3.4%)	2.07 (0.76, 5.65)
Ponding of water under house (1)	14 (7.9%)	11 (6.2%)	1.29 (0.57, 2.94)
DMI score			
0	108 (60.7%)	138 (77.5%)	Reference value
1	17 (9.6%)	10 (5.6%)	2.17 (0.96, 4.94)
2	8 (4.5%)	2 (1.1%)	**5.11 (1.06, 24.16)**
3	11 (6.2%)	9 (5.1%)	1.56 (0.63, 3.90)
4	8 (4.5%)	3 (1.7%)	3.41 (0.88, 13.15)
5	7 (3.9%)	6 (3.4%)	1.49 (0.49, 4.57)
6+	19 (10.7%)	10 (5.6%)	**2.43 (1.08, 5.44)**

Numbers in closed bracket indicate the weighting of each factor to give a total score of 10.
DMI indicates Damp-Mold Index.

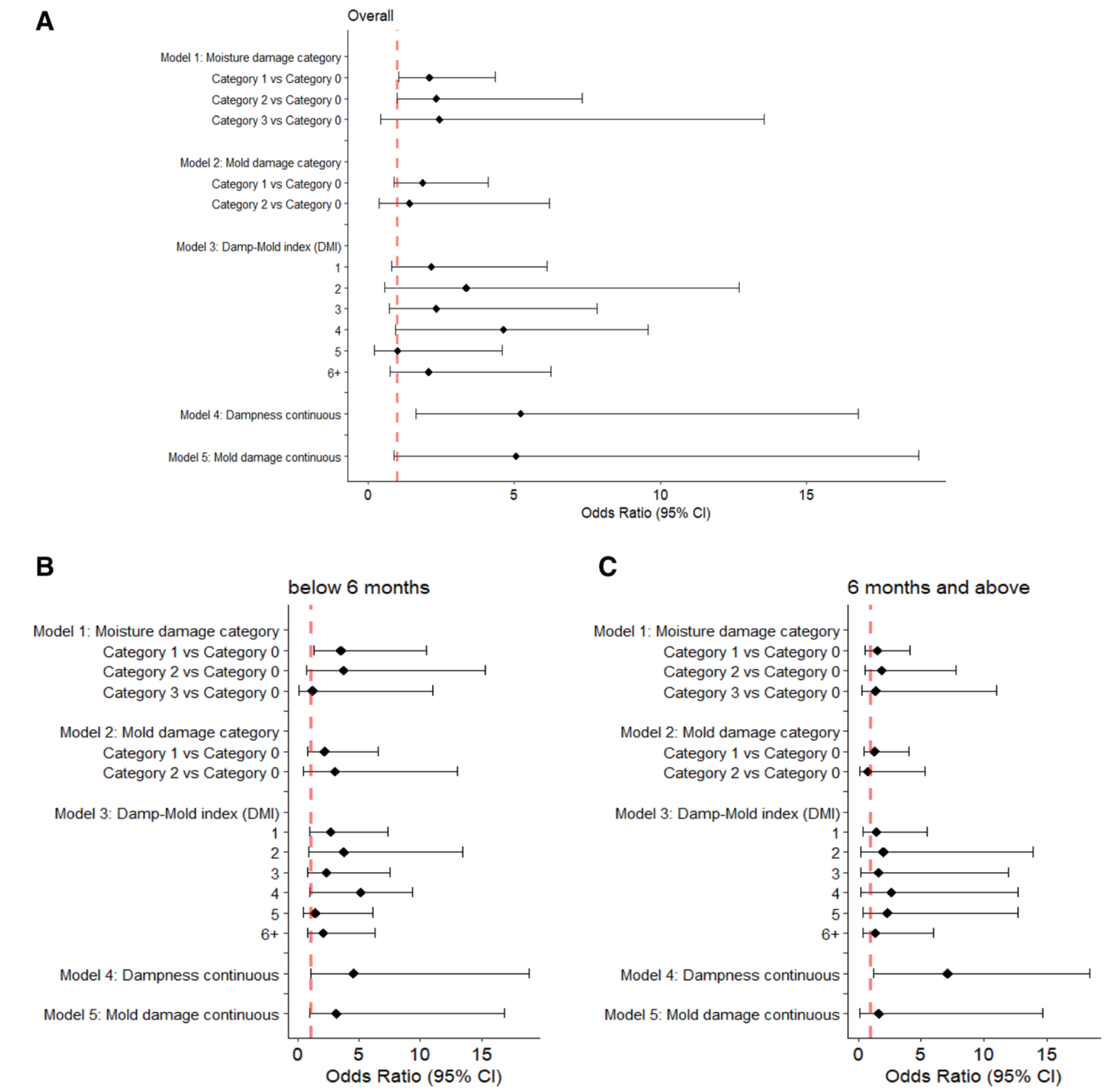

Figure 1. Adjusted odds ratios of having LRTI by exposure variables. **A,** Overall children under the age of 5 years; (**B**). among children under-five <6 months of age; (**C**) among children ≥6 months of age; **D**. Male; **E**. Female. Models were adjusted for age, sex, geographical location, number of siblings under-five, history of LRTI, breastfeeding status, housing tenure, season, occupant density, keeping pets, and environmental tobacco smoking

Figure 2 presents an exposure-response relationship for the association between severe LRTI and the main predictor variables. After adjusting for covariates, a significant linear exposure-response association was observed between residential dampness and severe LRTI among under-five children (Figure 2A). The risk of severe LRTI was significantly correlated with mold damage until after about 0.1 m^2 mold damage area (Figure 2B). Similarly, a significantly increased risk of severe LRTI risk was observed with a DMI of 0–3 but confidence intervals included unity at DMI above 6 (Figure 2C).

Discussion

In this study, we assessed exposure to residential dampness, mold damage, and severe LRTIs among under-five children in Nigeria and found a significant association. Our study shows the significance of childhood residential exposure to quantitatively measured dampness and mold damage in severe LRTI events, demonstrating the importance of public health intervention for promoting good hygienic conditions and reducing the considerable burden of LRTI among under-five children in LMICs. Because children under the age of 5 years spend most of their time in residential environments,[19] if the associations are causal, quantitative assessment of indoor dampness and mold damage can be a useful quick approach in developing interventions to reduce the burden of LRTI among under-five children.

Our findings were consistent with a few available studies, including the Integrating Microbial, Toxicological, and Epidemiological Approaches (HITEA) study; a large European multicountry study.[24] They found that exposure to moisture

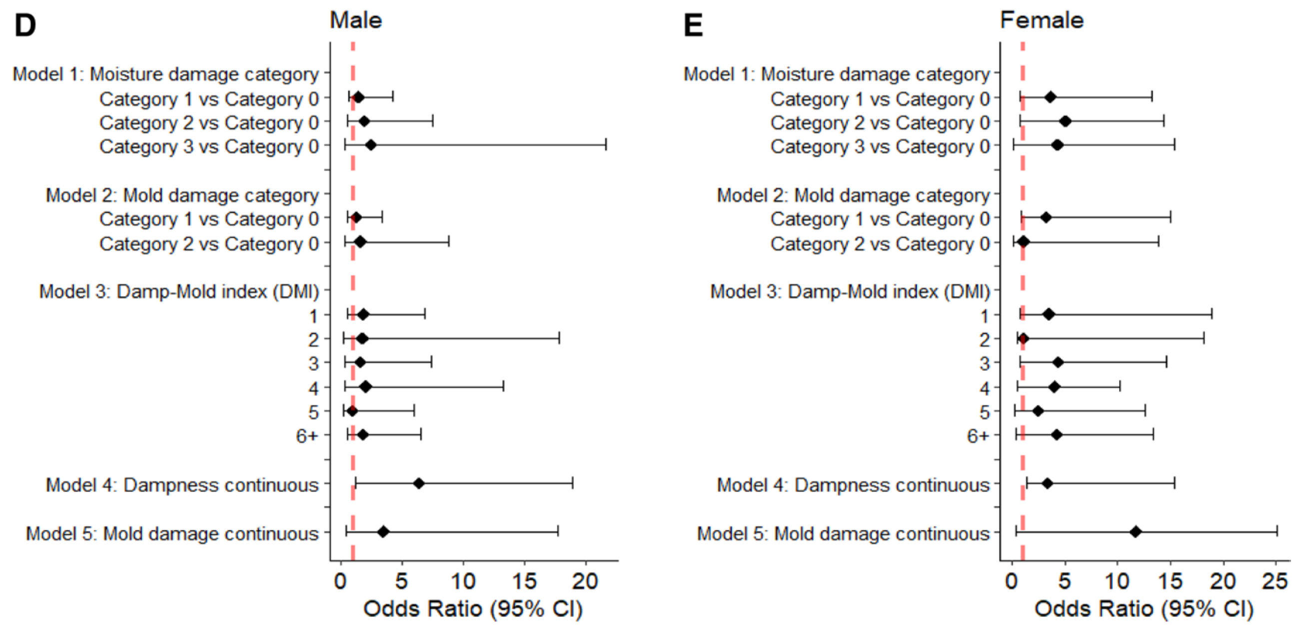

Figure 1. Continued.

damage at home was positively associated with respiratory infections among children with an adjusted country-combined OR of 1.45 (95% CI = 1.26, 1.66) for recurrent respiratory infections in the last year and an adjusted country combined OR of 1.21 (95% CI = 1.06, 1.37) for any respiratory infection in the last 12 months. The strength of the association found in the HITEA study was lower than what was obtained in our study, probably due to the differences in estimating dampness/moisture damage and LRTI ascertainment. Several epidemiological studies have documented an association between a qualitative measure of dampness and respiratory infections among under-five children,[8,12,25] but they were short of reporting an exposure-response relationship. For example, our previous study reported a significant association between LRTI and the presence of visible mold (OR = 3.15; 95% CI = 1.36, 15.02) but a borderline positive association in the current study that used a quantitative measure (OR = 1.88; 95% CI = 0.88, 4.11). This is likely a result of the difference in the measures of exposure. It is therefore important to investigate associations, especially between environmental exposures and health outcomes using more specific approaches such as quantitative measures that provide opportunities to set protective guidelines.[16] A similar study carried out among infants and children below 7 years of age in the United States reported that children residing in homes with ≥0.29 m² of moisture damage were significantly more likely to have wheeze at age 3 years (aOR = 2.2; 95% CI = 1.0, 4.3) and persistent wheeze through age 7 years (aOR = 3.2; 95% CI = 1.3, 7.5).[16,26] The effect of exposure to residential damp/moisture damage in relation to LRTI was observed to differ between children <6 and ≥ 6 months of age. Our findings support a study showing that the odds of acute respiratory infections among children under-five decrease with increase in age.[27] This is likely due to the immature airway of children below 6 months of age[28] as compared to older children. Increased dampness and moisture in the home provide an enabling environment for particles and microbial agents such as bacteria and fungi to survive and remain suspended within the breathing zone which eventually finds their way into the respiratory pathway of occupants thereby causing pathological changes

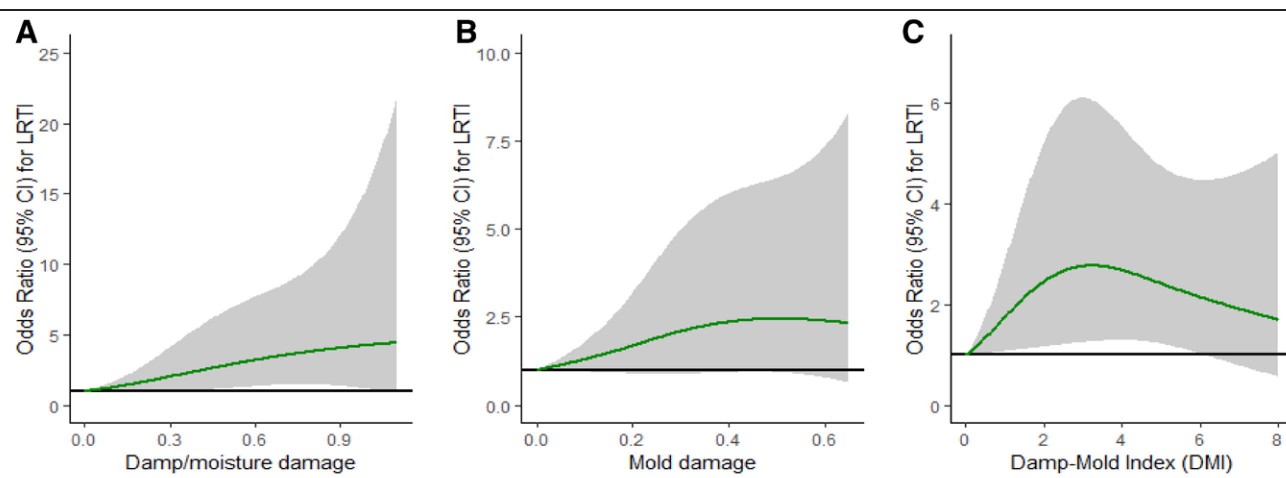

Figure 2. Shape of the exposure-response association between Lower Respiratory Tract Infections (LRTIs) among under-five children and (A) dampness/moisture damage; (B) Mold damage; (C) Damp-Mold Index. The graphs show a restricted cubic spline and 95% CI of the pooled odds ratio (OR) of LRTI by the predictor. The green lines denote the OR, and the grey shades represent the 95% confidence interval. *Notes*: Model adjusted for age, sex, geographical location, history of LRTI, breastfeeding status, number of siblings U5, season, housing tenure, pet ownership, environmental tobacco smoking, and occupant density.

in the host characterized by inflammation of the mucosa lining of the airway.[7,15,29]

Our study showed a linear exposure-response relationship between dampness and LRTI among under-five children after adjusting for confounding factors. With an increase in moisture damage area, the risk of severe LRTI presented a continuous linear trend. Regarding exposure to mold damage, we found a borderline significant positive association between exposure to mold and severe LRTI among under-five children. A similar study carried out in the United States among 779 children reported a significant association between mold damage ≥0.19 m^2 and wheezing at age 3 years (aOR = 2.9; 95% CI = 1.3, 6.4) and early transient wheeze at age 7 years (aOR = 3.5; 95% CI = 1.5, 8.2).[16] The difference in results may be due to the smaller sample size and more severe health outcome used in the current analysis.

As an additional quantification of dampness and mold exposure, we assessed the DMI in homes and found no significantly associated with severe LRTI among under-five children, after adjusting for essential covariates. In contrast, the report from a similar study that assessed the DMI in homes of children <2 years in New Zealand[7] found a significant association with LRTI. The design of the study and sample size might have attenuated the observed association in the current study. A similar study in the United States reported a clear dose-response relationship between increasing RHI and respiratory symptoms such as wheeze among children below 7 years of age.[23] After adjusting for confounders, a nonlinear exposure-response relationship was observed between DMI and severe LRTI among under-five children. With an increasing DMI, the risk of severe LRTI presented a rising trend, then falling. When the DMI was between 0 and 3, the risk of severe LRTI gradually increased, which indicated that the risk of severe LRTI increased with minimal exposure but reduced slightly as the DMI increased to 6. This slight reduction is not entirely apparent but could be due to the insufficient sample size.

The study was limited by the use of respiratory signs and symptoms to define the absence of LRTI among community controls which could have introduced some outcome definition bias. This was minimized by actively engaging the same doctor that reviewed the cases in assessing the controls. Also, the overlap in the definition of mold and moisture damage as similarly applied by Cox et al.,[16] may pose a concern which should be explored in future studies. An essential strength of our study was the quantitative assessment of dampness and mold exposures, which provided detailed information on the exposure-response relationships with severe LRTI outcomes among under-five children. In addition, the case definition used in the current study was a significant strength as this helped minimize the risk of misclassification. Also, we could reduce potential information bias or recall bias because exposure to dampness/moisture damage and mold damage was registered by home visit teams instead of using parental reports, which are subjective and prone to misclassification.

Future studies should include more quantitative exposure data to assess the shape of the relationship and explore potential health-relevant thresholds.

Conclusion

This study revealed that quantitative measurement of residential dampness and moisture damage was exposure-dependently associated with a higher risk of severe LRTI among under-five children. If causal, adopting interventions to manage home moisture and mold damage might help manage the burden of LRTI among children under the age of 5 years.

Acknowledgments

We acknowledge the support received from the College of Health (CHS) PhD Scholarship of the University of KwaZulu-Natal to facilitate field activities. We would like to thank Prof. Regina Oladokun of the Department of Paediatrics, University College Hospital.

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