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Authors: Dr Logan Manikam[1], Spencer Rutherford[2], David Emes[3], Meghan Cupp[4], Radhika Sharma[5], Dr Kaushik Sarkar[6], Dr Dewi Aisyah[7], Dr Samantha Field[8], Prof Andrew Hayward[9], Dr Hector Altamirano[10], Dr Neha Batura[11], Prof Rajib Dasgupta[12], Prof Muki Haklay[13], Dr Emily Nix[14], Paula Christen[15], Prof Monica Lakhanpaul[16]

Affiliations: Department of Epidemiology and Public Health, UCL[1], Population, Policy and Practice Department, UCL[2], Freetown City Council, Freetown, Sierra Leone[3], Jeevan Ashram Sanstha[4], Indonesia One Health University Network[5], Health and Wellbeing Department, Southwark Council[6], Bartlett School of Environmental Design and Engineering, UCL[7], Institute for Global Health, UCL[8], Jawaharlal Nehru University[9], Department of Geography, UCL[10]

Orcid ids: 0000-0001-8923-9373[2]

Contact e-mail: s.rutherford@ucl.ac.uk

To whom it may concern,

The paper under review, *Assessing the infection burden and associated risk factors in children under 5 across Jaipur's urban slums: A feasibility study using a One Health approach,* presents findings from a formative feasibility study which will inform future research activities for a much larger research project which will be undertaken by the Childhood Infections and Pollution (CHIP) Consortium.

This project (called the CHIP project) will aim to identify risk factors and infection pathways for children under 5 in slums in India, Indonesia, and Chile. The CHIP project will employ a One Health approach to identify infection pathways through biological sampling, observational research, cross-sectional surveys, analysis of routinely collected data, and interviews with community members and stakeholders.

The aim of this formative research, therefore, was twofold;
1) To assess the feasibility of undertaking the above activities in a slum setting in India.
2) To identify preliminary risk factors and variables of interest for infections in children under 5 in slum environments.

Prior to COVID-19, data collection activities had begun to take place in Jaipur. Feasibility studies have also been undertaken in Indonesia and Chile.

Best Regards,
The CHIP Consortium

Assessing the infection burden and associated risk factors in children under 5 across Jaipur's urban slums: A feasibility study using a One Health approach

To whom it may concern,

Best Regards,
The CHIP Consortium Co-Investigators

Abstract

Purpose: Infectious diseases are one of the leading causes of death among children under five (U5s) across both India & globally. This is worse in slum environments with poor access to water, sanitation & hygiene (WASH), good nutrition & a safe built environment.

Globally, a One Health (e.g. human, animal & environment) approach is increasingly advocated by WHO, FAO & OIE to reduce infections & antimicrobial resistance. As U5s living in peri-urban slums are exposed to household and community owned companion & livestock animals and pests, the CHIP Consortium hypothesized that utilizing a One Health approach to co-produce behavior change & slum upgrading interventions may reduce this burden where other WASH & nutrition interventions have failed.

This study aimed to assess the feasibility of utilising a One Health approach to assess U5 infection & risk factor prevalence in Jaipur's urban slums prior to undertaking prospective cohort studies involving culture and culture independent sampling of U5s and animals across our study sites in Jaipur, Jakarta & Antofagasta.

Methods: We administered a Rapid Household Survey to 25 purposely selected households across six slums. The questionnaire evaluated infection prevalence, health seeking behaviors, the built environment, presence of animals & pests, and individual to household-level demographics. Associations were calculated using correlations among continuous variables to show strength of significance between continuous variables.

Results: We found a high incidence of infections in children under five at 40%. This was most significantly correlated with accessibility of sanitary toilets (r = .62) and household expenditure. Vaccination coverage and child characteristics (such as size) were minimally correlated, while the presence of animals (pets or pests) was not correlated; the latter was likely due to the design of the survey.

Conclusion: This study found a higher infection prevalence than previous studies. We also found higher correlations with infection incidence among household-level characteristics, indicating that effective interventions need to address both the built and socio-economic

environments. A pilot prospective cohort study, which includes researcher observations for the presence of animals to account for inconsistencies in the survey, is now underway.

Key Words: One Health, Infectious Diseases, Children Under Five, Slum, India

Introduction

Infectious diseases, particularly respiratory and diarrhoeal diseases, have been the leading cause of child mortality over the past two decades [1]. Home to 20% of the world's children, India is the largest contributor to global mortality in children under the age of five (U5s) and is among the top ten countries contributing to the global childhood infection burden [2]. In terms of disability adjusted life years (DALYs), diarrhoeal and respiratory infections are also two of the five leading causes of ill health in children [3]. Additionally, child and maternal nutrition and air pollution levels were also identified as leading risk factors for DALYs in 2016 [3].

India is one of the largest consumers of antibiotics globally, propagating the spread of emerging antimicrobial resistance (AMR) [9]. The threat of AMR is attributed to a complex set of factors that include poor public health infrastructure, rising income, a high disease burden and undernutrition [10]. The emergence of AMR is further compounded by low-cost, unregulated antibiotic sales [11] and high rates of antibiotic prescription, with antibiotics prescribed to roughly 30% of all patients seeking care [12]–[14]. Diagnostic uncertainty, patients' expectation to receive antibiotics, practice sustainability, influence from pharmaceutical company representatives, and inadequate knowledge are factors influencing physicians' prescribing practices [15]. A Red Line Campaign has been launched to curb over-the-counter antibiotic use in India [11]; however, systemic challenges in public health care delivery, such as low immunisation rates [17], [18], continue to contribute to the burden of drug-resistant infections [11].

Childhood infections are widespread in Indian slums, with a reported annual prevalence of 8% and 8.5% for diarrhoeal and respiratory infections, respectively [4]. Access to safe water, sanitation, and hygiene (WASH), nutrition and the built environment are important infection determinants, especially in slum areas [5]. Whilst country-led programmatic efforts to improve WASH have included toilet construction, better solid waste management, and raising awareness through the Swachh Bharat Mission (the urban component of India's flagship programme), implementation issues are evident [8].

It's known that the risk of transmitting zoonotic infections can be as high as 60% of all known infections and 75% of emerging infectious pathogens [6]. This led to the recommendation of using the One Health approach by the tripartite WHO-FAO-OIE to address infections and AMR [19]. With pests (e.g. rats) and both livestock (e.g. cows) and companion (e.g. dogs) animals potentially more common in slums, the transmission risk of infections may be even higher.

With mixed results from randomized controlled trials of WASH and nutrition interventions, the Childhood Infection and Pollution (CHIP) Consortium hypothesized that utilizing a One Health approach to co-develop behavior change and slum-upgrading interventions may work in reducing the infection and AMR burden in U5s in urban slums.

In advance of prospective cohort studies across Jaipur (India), Jakarta (Indonesia) & Antofagasta (Chile) involving culture and novel culture independent (i.e. metagenomics) sampling of U5s, caregivers, pests, companion and livestock animals, we aimed to assess the feasibility of utilizing a One Health approach to assess infection and risk factor prevalence in U5s in Jaipur's urban slums.

Methods

Household Survey
We developed a household-survey to capture information on participant demographics, health behaviours, illness history, and care-seeking practices. The infection prevalence was estimated through participants self-reported symptoms. Cases of illness in U5 children were recorded by the head of household reporting on children's cases of illness in the last 30 days, symptoms, care sought for illness, and duration of illness (whether condition required multiple bouts of care seeking). Data on micro-level factors such as water availability, economic status and living conditions were also collected.

The questionnaire was divided into six sections: household member details, care-seeking behaviours for children under 5 years, household socioeconomic status, built environment, animals, and health behaviours. Questions included basic demographic data (age, sex, occupation), details regarding care-seeking (What type of illness occurred? Did you seek treatment advice), and One Health factors (Do you cook in your home? Does your household have any pets?). Full details of the household survey and questions delivered in each section can be found in Appendix 1.

The survey was developed by adapting questions from the WHO Household Survey for Medicine Use [21] with other surveys previously utilized by our team, and then adding questions to explore human-animal interactions from a One Health perspective. All questionnaires were translated into Hindi and delivered by a native Hindi speaking facilitator to establish the appropriateness of the questions as well as their cultural and contextual validity. Appendix 1 contains a full copy of the questionnaire in English. The Hindi version can be requested through email to the study authors.

The survey was delivered with the assistance of Hindi speaking facilitators from a local charity, Jeevan Ashram Sanstha (JAS), which has experience working with and engaging slum dwellers in local projects. All JAS facilitators were proficient in both Hindi and English and were able to deliver the survey questions in Hindi, while simultaneously relaying data to be recorded in English by a field researcher (MAC).

Sampling
We selected three localities in Jaipur (Jal Mahal, Shastri Nagar and Vidhyadhar Nagar) within the JAS network (*Figure 1*), and purposely selected households with a known child U5 across six individual slums for interviews in October 2018. Sample households were selected purposively by door to door visits to inquire if a U5 child was resident at the household. The heads of households with a U5 child were invited to participate in an interview. All interviews were conducted within or just outside of the participant's home. At the start of each interview, the aims of the study were explained, and consent was obtained for each participant. Where the participant was unable to sign their consent, a thumb impression was taken instead.

(Figure 1. Geography of the study localities)

Analysis

Association was calculated using correlation to show strength of significance between continuous variables. Due to the small sample size, an analysis was not conducted for categorical variables. As this was a feasibility study with no power calculations done a-priori, significance was not tested for. Correlations were calculated for key variables using the corr command in R version X.

Results

Participant Demographics
In total, 15 household were sampled with 85 individual household members recorded. Of these 85 individuals, 25 were U5 children. The surveys were delivered across four days (October 12th 2018, October 17th 2018, October 21st 2018, October 25th 2018) over a span of two weeks. In many cases, survey facilitators had worked in the slum areas before and were aware of which households had residents with young children, resulting in these households being preferentially selected. Likely due to this, 100% of households which were approached agreed to participate.

Household Characteristics
The size of households varied significantly; 20% (3/15) were composed of 3 or less individuals,
27% (4/15) 4-5 individuals, 40% (6/15) 6-7 individuals, and 13% (2/15) 8 or more individuals.

47% (7/15) of all participating households had only one U5 child, 40% (6/15) had two U5 children, and 13% (2/15) had three.

A total of 80% (12/15) of households identified as Hindu, while the remaining 20% (3/15) identified as Muslim. 47% (7/15) belonged to other backward classes (OBC), indicating that they belonged to castes which are economically or socially disadvantaged. A full summary of all household characteristics can be seen in *Table 1*.

Table 1. Household Characteristics

Characteristics		n	%
Number of household members	≤3 persons	*3*	20.0%
	4-5 persons	*4*	26.7%
	6-7 persons	*6*	40.0%
	≥8 persons	*2*	13.3%
Number of children under 5	1	*7*	46.7%
	2	*6*	40.0%
	3	*2*	13.3%
Religion	Hindu	*12*	80.0%
	Muslim	*3*	20.0%
Caste	Scheduled Caste	*1*	6.7%
	OBC	*7*	46.7%
	General	*6*	40.0%
	Other	*1*	6.7%
Treatment seeking	District Hospital	*2*	13.3%
	Private Clinic/Hospital/Dispensary	*13*	86.7%
Household monthly spend	≤10,000	*7*	46.7%
	10,001-20,000	*5*	33.3%
	20,001-30,000	*3*	20.0%
Cooking fuel	LPG Natural Gas	*13*	86.7%
	Wood	*2*	13.3%
Water source for drinking	Hand Pump into Dwelling/Yard/Plot	*4*	26.7%
	Public Hand Pump/Tube well/Borehole	*4*	26.7%
	Piped water (Public Tab)	*2*	13.3%

Characteristics		n	%
	Other	*5*	33.3%
Water quality	Very concerned	*3*	20.0%
	Concerned	*4*	26.7%
	Neutral	*6*	40.0%
	Unconcerned	*1*	6.7%
Own sanitary facility	Yes	*8*	53.3%
	No	7	46.7%
Have shared toilet	Yes	*2*	13.3%
	No	*13*	86.7%
Have separated kitchen	Yes	7	46.7%
	No	8	53.3%
Solid waste removal	Back yard of house	*3*	20.0%
	Open plot outside house	*8*	53.3%
	Others	*4*	26.7%
Own animal	None	*13*	86.7%
	Goat	*1*	6.7%
	Chicken/Duck	*1*	6.7%

Individual Characteristics

A total of 42 of the 85 respondents were literate (49%). 55% (24/44) of men, and 7% (3/41) of women in the sample households worked as labourers, while a further 27% (11/41) women were housewives. The average household spend was self-estimated and averaged ₹ 13866 ± 7039 per month. The Aadhar card (a unique ID), was not available for 35% (30/85) of individuals.

Table 2. Individual Characteristics

Characteristics		n	%
Sex	Male	44	51.8%
	Female	41	48.2%
Age	≤5 years	25	29.4%
	6-15 years	10	11.8%
	16-29 years	37	43.5%
	30-44 years	5	5.9%

Characteristics		n	%
	45-59 years	6	7.1%
	60+ years	2	2.4%
Family members	Father	15	17.6%
	Mother	15	17.6%
	Children	38	44.7%
	Grandparents	8	9.4%
	Aunt/uncle	9	10.6%
Have Aadhar Card (ID)	Yes	55	64.7%
	No	30	35.3%
Literacy (children <5 years)	Literate	40	66.7%
	Non-literate	20	33.3%

Children Under Five Years of Age

Cases of infection were categorised as distinct episodes, where the first episode was recorded as the head of household recalling a child's case of illness according to its symptoms or the need for care seeking. Illness in the past 30 days were recorded first as an episode 1 illness. If the illness did not subside after care seeking, or re-emerged after care seeking, a second episode of the illness was logged, and so on.

Of all 25 children within the households surveyed, evidence of infection was found in 40%. The reported symptom for 70% of episode 1 illnesses was cough, while fever accounted for the remaining 30%. 55% (6/11) of childhood illness were reported to subsided after care (episode 1) within the past 30 days, while a further 45% (5/11) of children had either developed an illness which did not subside or developed two illnesses (episode 2) within the past 30 days (*see table 3*).

Table 1. Illness episodes in children U5

Characteristics		n	%	Episode 1		Episode 2	
				n	%	n	%
All		25	100%	10	40.0%	5	20.0%
Sex	Male	11	44.0%	4	36.4%	2	18.2%
	Female	14	56.0%	6	42.9%	3	21.4%
Age	≤2 year	3	12.0%	1	33.3%	1	33.3%
	2-3 years	14	56.0%	7	50.0%	3	21.4%
	4-5 years	8	32.0%	2	25.0%	1	12.5%
	Yes	9	36.0%	3	33.3%	2	22.2%

Table 1. Illness episodes in children U5

Characteristics		n	%	Episode 1		Episode 2	
				n	%	n	%
Currently breastfeeding	No	16	64.0%	7	43.8%	3	18.8%
Previously breastfed	Yes	25	100.0%	10	40.0%	5	20.0%
	No	0	-	0	-	0	-
Had formula milk	Yes	3	12.0%	1	33.3%	1	33.3%
	No	22	88.0%	9	40.9%	4	18.2%
Feeding stuffs cleaning method	Boiled	5	20.0%	2	40.0%	1	20.0%
	Rinsed with soap and water	14	56.0%	5	35.7%	0	0.0%
	Rinsed with water	5	20.0%	3	60.0%	3	60.0%

One Health Factors Correlated with Childhood Infections

A correlation analysis was run to show the strength of significance between continuous variables; the results are depicted in figure 2.

A strong, positive correlation was found between episodes of illness and sharing toilet facilities with others (r = 0.62). Among the 10 children who did not have access to sanitary facilities within the household, 60% (6/10) developed symptoms of illness. In contrast, among the 15 children who had access to sanitary facilities within the household, 27% (4/15) developed a symptom. Episodes of infection also had a weak, positive correlation with distance walked to retrieve water (in kilometers) (r = 0.07).

Monthly household expenditure showed a moderate, negative correlation to illness episodes (r = -0.45), with households who spend less per week (i.e. likely to be earning less) being more likely to develop illness symptoms in children U5 compared to households who spend more per week (i.e. likely to be earning more).

Age was found to have a weak, negative correlation with number of illness episodes (r = -0.22), while parental perceptions of child's size at birth in comparison to other children was also found to have a weak, negative correlation with number of illness episodes (r = - 0.1).

Regarding immunisations, there was a weak, negative correlation between vitamin supplements and illness episodes (r = 0.23); a weak, negative correlation between the number of hepatitis vaccinations completed and illness episodes (r = - 0.15); and a very weak, negative correlation between the number of DPT vaccinations completed and illness episodes (r = - 0.05). There was also a very slight negative correlation between the number of episodes of illness and the number of vaccinations received, according to children's vaccination cards (r = - 0.03).

Notably, there was no significant correlation between the presence of animals in the household and illness episode. This is likely due to survey design limitations and the misinterpretation of

the word 'pets', as only 7% of households (1/15) reported their presence. Future studies will utilise researcher observation of the home environment that includes identification of livestock & companion animals including where they stay alongside the presence of pests such as rodents.
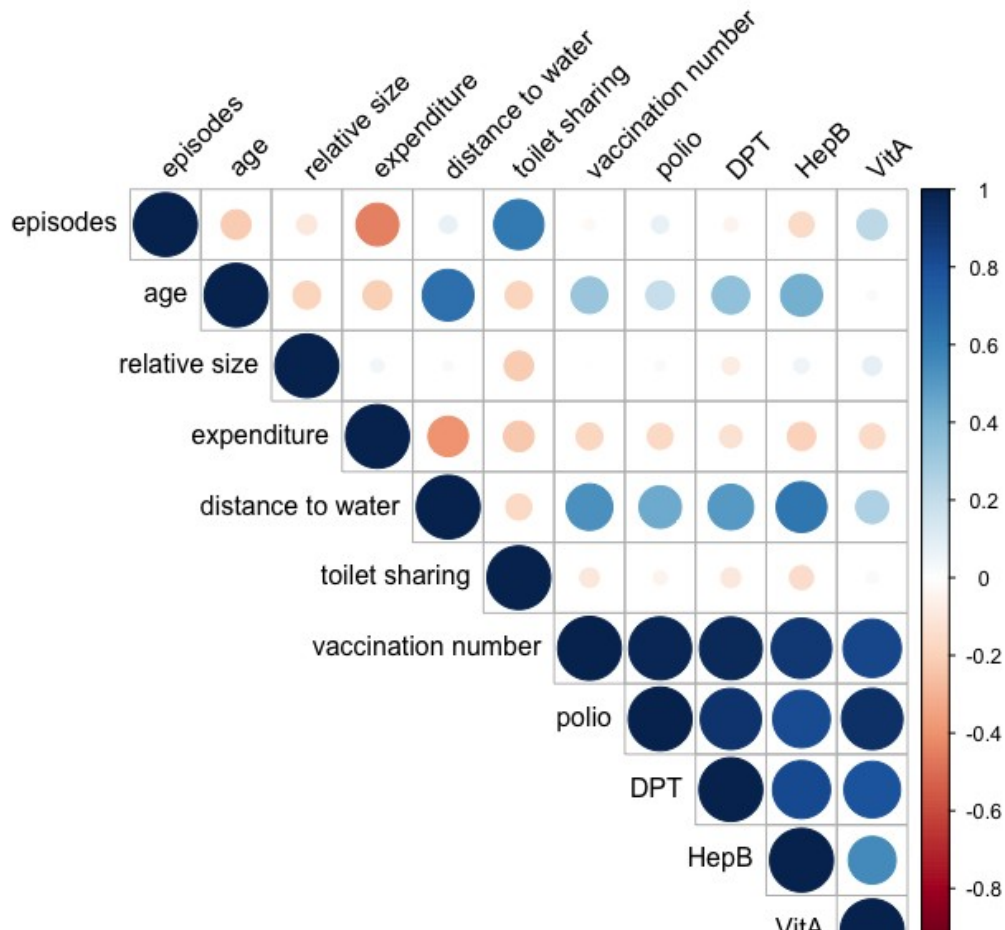
(Figure 2. Correlations between variables of interest)

Discussion

In summary**,** this feasibility study identified a high infection prevalence in U5 children residing in Jaipur's urban slums. Infection symptoms was mostly associated with monthly household expenditure and access to WASH facilities. Treatment seeking behaviour was primarily from private facilities with low vaccination compliance. This reflects the marked dependence of slum dwellers on the private health system and the intrinsic weakness of the public health care system in promoting immunization awareness.

Our findings indicating strong and moderate correlations between illness episodes with sanitation access and socioeconomic status is well-supported in the literature [8][22]. It is interesting to note that our study found a much higher prevalence of infections among children U5 (40%) compared to previous research [4]. A potential explanation is that our infection criteria was based on parental perceptions. Future consortium studies involving culture and culture independent sampling to identify pathogens in the presence of infection symptoms will address this limitation.

Significantly, our investigation of One Health (e.g. animal, environmental) factors highlight the need for an integrated approach to improve the built environment, sanitation and solid waste management practices, preventive practices for zoonotic infections, and health seeking behaviour to reduce childhood infections and the risk of antimicrobial resistance. This sets the scene for subsequent longitudinal CHIP Consortium studies utilising a One Health approach involving both household surveys and sampling of U5s, caregivers and household/community animals/pests (e.g. rats, dogs, cats, goats, cows) to identify respiratory and diarrhoeal disease transmission pathways between humans, animals and the wider environment [23].

There were a number of study limitations that will be addressed in subsequent cohort studies; (1) participants were purposively selected, (2) infections were self-reported, (3) more questions scoping out detailed antibiotic histories are needed, (4) lack of sampling to assess the ecology of resistant bacteria in the human-animal-environment interface and (5) need for researcher observation of the home environment to identify pests, companion and livestock animals.

One addressed, future formative research studies will allow identification of One Health infection pathways to be interrupted with co-developed of integrated interventions to improve the slum-built environment & WASH alongside better animal husbandry and preventive practices to reduce the U5 infection & antimicrobial resistance burden in targeted slums.

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