RSV-Related Healthcare Burden: A Prospective Observational Study in a resource-constrained setting

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Abstract

Background: Respiratory syncytial virus (RSV) is a leading cause of pediatric hospitalizations globally, impacting overstretched health systems. Comprehensive data is vital for informing RSV vaccination policies.

Methods: From January to December 2019, a prospective study was conducted at Bangladesh's largest pediatric hospital to evaluate RSV's burden on the health system. We analyzed hospitalization rates, lengths of stay, and outcomes for children under five using WHO criteria and qPCR testing. We also examined survival probability for children denied admission due to bed shortages, compared with those admitted using the Kaplan-Meier method, and estimated the effects of a maternal vaccine using Monte-Carlo simulations.

Findings: Out of 40,664 children admitted, 31,692 were under five. Of these, 19,940 were eligible for study inclusion with 7,191 meeting inclusion criteria; 6,149 (86%) had samples taken, with 1,261 (21%) testing positive for RSV. The hospital incidence rate was 465 per 10,000 admissions. The median age of RSV patients was 3 months, with a median stay of 5 days. RSV accounted for 8,274 bed days of the total 151,110 observed bed days. In-hospital mortality was 1.9%, increasing to 9.9% during a 90-day follow-up over telephone. Additionally, 9,169 children were denied admission during the study period; of these, 5,969 under-five children were approached, and outcomes of 2,850 admitted versus 3,928 refused were followed. The hazard ratio for death was 1.37 for refused versus admitted children, highest within neonates at 1.7. A 70% efficacious vaccine would equate to adding 50 hospital beds and averting 195 deaths.

Interpretation: RSV significantly contributes to pediatric hospitalizations in Bangladesh, exacerbating healthcare burdens and increasing mortality risks. Maternal vaccination could significantly reduce both direct and indirect RSV burdens, enhancing healthcare capacity and benefiting overall child health in resource-limited settings.

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Introduction

Respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory infection in young children. Annually, RSV infections are estimated to result in 33 million episodes, 3.6 million hospitalizations, and 26,300 deaths [1]. Low- and middle-income countries (LMICs) bear a disproportionate burden of the disease, where over 95% of RSV infections and more than 97% of RSV-attributable deaths occur [1].

Emerging interventions, such as maternal vaccines and long-acting monoclonal antibodies, promise to reduce RSV-related morbidity and mortality [2–4]. There is also growing evidence suggesting that these interventions might have broader benefits, like reducing respiratory illnesses caused by other pathogens, decreasing recurrent hospitalizations, and improving lung health [5–7]. Policymakers across countries are grappling with decisions about introduction, and which groups should be prioritized for these interventions. Making informed decisions necessitates up-to-date and locally relevant epidemiological data. However, there exist large data gaps from LMICs.

In Bangladesh, a densely populated lower-middle income country, with a birth cohort of almost 3 million[8] the healthcare system faces unique challenges due to the high burden of communicable and non-communicable diseases[9]. Data from the country's largest pediatric hospital indicate that approximately 20% of children needing hospitalization—whether for communicable or non-communicable diseases—have to be turned away due to bed shortages [10]. Timely and appropriate care is vital for child survival and well-being. In settings where healthcare resources are stretched thin, a high RSV burden can exacerbate capacity issues, potentially leading to adverse health outcomes for children who cannot be admitted for various reasons. Thus, it is imperative to consider both the direct and indirect effects of RSV infections on child health and the broader health system when making informed policy decisions.

Two prominent multi-country studies, Aetiology of Neonatal Infections in South Asia (ANISA) [11], and Pneumonia Etiology Research for Child Health (PERCH) [12], have highlighted RSV as a primary etiological agent in sepsis and respiratory tract infections in Bangladesh and other countries in Asia and Africa. While these studies underscore RSV's role in community-based child morbidity, gaps remain in understanding the extent of RSV-associated hospitalizations and the broader impact on the healthcare capacity in resource-constrained settings.

To address the current gaps in data and estimate the potential impact of RSV vaccines, we conducted a prospective, observational study at Bangladesh's largest pediatric hospital. We aimed to quantify RSV-associated hospitalizations, bed usage, and outcomes. We also assessed the wider health implications for children denied admission due to bed shortages, providing crucial data to inform policy and intervention strategies.

Methods

Ethical considerations

This study was approved by the ethical review board of the Bangladesh Shishu Hospital and Institute (BSHI). We obtained written informed consent from guardians of children admitted in the hospital from whom nasopharyngeal samples were collected. We obtained informed verbal consent from caregivers when they were registered in the study after hospital admission refusal for telephone follow up. We also obtained informed verbal consent from caregivers of admitted patients selected for follow-up over telephone.

Study Design and Setting

From January to December 2019, we conducted a prospective observational surveillance at the BSHI, previously known as Dhaka Shishu Hospital (DSH), located in Dhaka, Bangladesh. BSHI, with its 653-bed capacity (2019), is Bangladesh's largest pediatric hospital. It offers primary to tertiary care for patients up to 18 years old. Admission decisions for the in-patient department (IPD) are made by physicians in the Emergency Room (ER).

This study had two main components: (i) active surveillance within the IPD to detect RSV infections; and (ii) active surveillance of health outcomes of patients who had to be denied hospitalization due to bed shortages in the IPD, despite needing hospitalization, and a control group of patients who were admitted in the IPD.

RSV Surveillance in the IPD

Children aged 0–59 months admitted to the wards selected for the study with 414 beds were evaluated by study physicians using the WHO RSV hospital-based surveillance case definition [13] (Text S1, appendix page 3). The remaining 239 beds of the total 653 were not selected because they were in wards that do not admit patients with possible infectious diseases (surgery, nephrology, oncology and cardiology wards). Eligible children were enrolled in the study after obtaining written consent from caregivers and obtaining a nasopharyngeal swab sample. Nasopharyngeal swabs were collected by trained nurses and tested using established qPCR methods (Text S2, appendix page 3).

Refusal Surveillance in the ER

Upon arrival at BSHI, families with children potentially needing hospitalization are triaged to the Emergency Room (ER). Here, a physician evaluates the child's condition to determine if immediate hospitalization is necessary. Beds are available on a first come first serve basis. If the physician decides that the child requires hospitalization, but no beds are available, families are referred or advised to seek care elsewhere. During this study, when a child was refused admission due to bed shortages despite requiring hospitalization, trained research assistants documented the ER physician's diagnosis for the patients, and upon obtaining verbal consent from the caregiver, they collected basic details, including the child's age, family address, and contact numbers.

Health Outcome Follow-Up

Among the <5 y children refused admission due to shortage of beds and whose contact information was obtained, families were selected using a computer-based randomization algorithm, and contacted via telephone approximately 2 weeks after hospital-refusal, and the child's health status ("alive" or "deceased"), and date of death (if applicable) was recorded based on caregivers' response. If the child was alive during the 2-week follow-up, a second follow-up call was made three months post refusal. In parallel, from the cohort of children <5 years who were admitted during the same time, children were randomly chosen for follow-up in the same manner. Additional information on in-hospital mortality was obtained from hospital records.

Survival curves were computed using the Kaplan-Meier method. Date of death was collected during follow-up, or from hospital records for admitted cases. Conservative censoring assumptions were made – children refused admission and not followed-up at 14-days were considered censored at day 0, and those not followed up at 90-days were considered censored at 14-days (last successful contact). Admitted children's censoring time was dealt with similarly, except that hospital discharge (either alive or through mortality) was additional information. Multivariate Cox Proportional-Hazards models were used to estimate hazard ratios adjusted for diagnosis cluster (Table S1, appendix page 5), age in months, and sex. We also obtained stratified estimates of hazard ratios.

Estimated impact of RSV maternal vaccine impact analysis (Monte Carlo Simulation)

A Monte Carlo simulation was conducted to estimate the direct and indirect effects of RSV vaccination on hospital admissions and 90-day mortality. The simulation used empirical data on the total number of children requiring admission in 2019 across all age groups and diagnoses, length of stay, and estimated 90-day survival probabilities among refused and admitted cases based on follow-up. We explored the impact on total deaths within 3 months of hospital admission or refusal when a fixed number of beds were occupied under a baseline scenario reflecting the empirical data. Additionally, scenarios with various reductions in the number of

RSV cases were simulated. The median value across 1000 simulations and the 95% prediction intervals are reported. Further methodological details are provided in Text S3, appendix page 4.

Role of funding source

The funder had no role in study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit this manuscript. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Cases hospitalized with RSV:

In 2019, a total of 49,833 children sought care at BSHI and were advised admission, of whom 40,664 could be admitted based on the available beds (Figure 1, Table 1). 31,692 of them were <5, and of them 19,940 were admitted in the screening wards. Of them, 7,191 met the inclusion criteria of the study, and a sample was successfully collected from 6,149 (86%) of these children. Samples could not be collected from the remaining 1,042 eligible cases due to various reasons including the guardian's refusal to participate in the study, use of oxygen mask, and discharge before enrollment or sample collection (Table S2, appendix page 5)). 92% (5658/6149) of all samples were collected within 72 hours of hospitalization (Table S3, appendix page 6).

All 6,149 samples were tested for the presence of RSV using qPCR, and of them 1,261 (21%) samples tested positive. Assuming 1,042 untested eligible cases among 7191 had the same positivity as those tested, the overall proportion of all hospital admissions that were RSV positive was 4.65% or 465 RSV cases per 10,000 <5 hospitalizations (95% CI: 443 to 489).

The highest number of patients were enrolled in the study between June and September (Figure 2A), and these four months accounted for over 70% of the total RSV-positive cases (882/1261) (Figure 2B). During July, August and September, more than 20% of the 414 beds were due to RSV positive cases (Figure 2C).

Of the positive cases, 30.6% were females. The median age of PCR-confirmed RSV cases was 3 months (IQR 1.3, 8.3 days) and 70% (881 of 1261) of the cases were within the first six months (Fig 3A, Table 1)). Notably, 17% of infections occurred in the first 4 weeks of life, highlighting the vulnerability of very young babies to RSV. Median hospital stay of RSV cases was 5 days (IQR 4 – 8), and medial stay of all RSV-negative cases and non-tested cases were 4 days (IQR 2 – 7). Throughout the year, RSV cases accounted for 8,274 (5.5%) of the total 151,110 bed days observed.

Of the positive cases, 24 cases (1.9%) died during their stay at the hospital (Table 1). Median age of these cases was 130 days (IQR 77 - 175) and died between 0 - 26 days of hospitalization.

Impact of Bed Shortages on Non-Admitted Patients

During the study period, of the total 49,833 children requiring hospitalization, the hospital was unable to admit 9,169 (18.4%) patients requiring admission due to lack of beds (Figure 1). Of them, we were able to approach and collect contact information of 5,969 families for follow-up; 3,200 patients were not approached because they either came to the hospital at night when the study research assistants were absent (n = 2,324) or were >5 years of age (n = 876). Of the families who provided verbal consent and contact information for telephone follow-up, a random selection of 3,928 (43%) patients were chosen for follow-up. Out of these, 3,435 (87%) could be successfully contacted and followed up at 2 weeks. The primary reasons for missing follow-up included switched-off mobile phones, incorrect phone numbers, or no response to the call (Table S4, appendix page 6). During the first follow up, 2931 (85.3%) children were reported to be alive by their guardian, and 504 (14.7%) were reported to have died. Of the 2,931 patients alive, 2631 (89.8%) could be subsequently contacted during the 3-month follow

up, and 2525 (96%) were reported to be alive, and an additional 106 (4%) had died. The survival probability at the end of follow up was 0.805 [95% CI: 0.791, 0.819] for refused patients (Figure 4a).

During the same time, 2,850 admitted <5-year children were randomly selected for follow-up. Of them, 2,527 (89%) were successfully followed up at 2 weeks. Reasons for unsuccessful follow up included those above, in addition to missing contact information in the hospital records (Supplementary table 6). During the first follow up, 2302 (91.1%) children were reported to be healthy, and 225 (8.9%) were reported to have died. Of the 2,302 patients alive 1,965 (85.3%) could be subsequently contacted during the 3-month follow up, of which 1,883 (95.8%) were alive, and an additional 82 (4.2%) had died (Figure 4). The survival probability at the end of follow up was 0.874 [95% CI: 0.861, 0.887] among those admitted (Figure 4a).

Overall comparison between the two groups revealed a hazard ratio (HR) of 1.69 (CI 1.48 - 1.94) of death in children who were refused admission compared to children who were admitted (Table 3). The HR was 1.37 (CI 1.56 - 1.79) in models adjusted for age, diagnosis and sex. Models stratified by age groups showed that HR of death was significantly greater for refused cases among babies in their first month of life (neonates) (HR 1.93 [CI 1.62 - 2.30]) but not in other age groups. When stratified by diagnosis, HR of death was significantly greater among those with perinatal asphyxia (HR 2.22 [1.68, 2.92]), systemic infections (HR 1.79 [1.13, 2.85]), and preterm low-birth weight 1.85 [1.32, 2.59].

Post-hospitalization RSV-associated mortality

While the study was not designed to specifically follow-up RSV positive cases, of the 2,527 admitted children randomly selected and successfully followed up, there were 205 RSV positive cases. Of these, 18 children died within the 90-day follow-up period. Their median age was 107.5 days (IQR 44.75 - 157) Considering both in-hospital mortality of all RSV admissions and mortality during follow-up of a subset of cases revealed that survival decreased substantially

over time, with a 90-day survival probability of 0.901 [95% CI: 0.865, 0.938] at the end of the follow-up period (Figure 4b).

Potential Impact of Maternal RSV Vaccination

In a Monte Carlo simulation of hospital admissions and refusals for the baseline scenario, based on the empirical data and a 650-bed capacity, on average, 49,968 children required admissions (95% prediction intervals (PI): 49,500, 50,379), and 9,221 (95% PI: 8,869, 9,760) cases were refused admission over the course of the year. This was in concordance with the true burden of total cases requiring admission and refusals – 49,833 and 9,169 respectively. In the vaccine scenario with 70% reduction in RSV cases requiring admission, 48,895 (95% PI: 48,514, 49,315) cases required admission, and 8,103 cases were refused (7,728, 8.695) – a 16.6% refusal rate. Even though total cases requiring admissions in this scenario remained as high as 97.9% (48895/49968) of the baseline scenario, the number of refused cases was 87.8% (8103/9221), due to the freeing up of bed spaces. Figure 5 demonstrates the effects of a 70% reduction in RSV admissions through vaccination, showing its impact on deaths and hospital bed utilization. The plot compares mortality with increase in available beds, demonstrating how reducing RSV cases is akin to increasing bed capacity. Overall, there were 7,002 deaths (6829, 7167) in the baseline scenario, and 6807 deaths (6629, 6930) in the vaccine scenario, a difference of 195 deaths. A reduction in RSV cases was found to decrease both hospital RSV incidence and the overall number of RSV cases seeking admission at the hospital. The estimated reduction in deaths with the 70% efficacious vaccine would be equivalent of adding roughly 50 beds to the hospital although, there is considerable overlap of the variability in the estimates from the different scenarios.

Discussion

Informed decision-making on interventions to prevent RSV infections in young infants requires contemporary and locally relevant epidemiological data. Our study demonstrates the significant

impact of RSV on healthcare resources in Bangladesh, a country characterized by a high burden of infectious diseases and a substantial demand for pediatric care amidst resource limitations.

Our study recorded an overall RSV positivity rate of 21% among the 6,149 patients admitted to the largest pediatric hospital of Bangladesh with respiratory illnesses, corresponding to an RSV hospital incidence of 465 per 10,000 <5 admissions. The median age of confirmed RSV cases was 3 months. These findings are concordant with those of the PERCH study that reported that in Bangladesh 31.2% of children hospitalized with respiratory tract infections tested positive for RSV [12].

The in-hospital mortality rate for RSV-positive cases was 1.6%, which escalated to 9.9% during the 90-day follow-up of discharged patients. The median age of recorded RSV-associated deaths was 4.2 months. These data are comparable to a Zambian study that found RSV in 9% of community deaths and 5% of in-hospital deaths [14]. In Child Health and Mortality Prevention Surveillance (CHAMPS) study, RSV was found in 5.5% of all deaths, with variability across countries: 9.7% in Mali, 10.7% in Ethiopia, and a lower 2% in Bangladesh [15]. Half of the deaths in the CHAMPS study occurred in infants younger than six months.

These findings underscore the critical need for maternal immunization strategies, such as vaccines like ABRYSVO™, which has demonstrated 81.8% efficacy in preventing RSV infections within the first three months of life [16]. Our estimates suggest that maternal immunization could potentially reduce the hospital incidence from 465 to 140 cases per 10,000 <5 admissions.

Beyond the direct impact of RSV infections, our findings also demonstrate the considerable burden infections impose on the healthcare system. For a minimum of three months during the study year, RSV cases occupied more than 20% of the beds under observation, with a median hospital stay for RSV-positive cases at 5 days—longer than the overall median length of stay of 4 days for all admitted patients. In 2019, RSV cases accounted for 8,274 of the total 151,110 bed days observed. As the largest pediatric tertiary hospital in Bangladesh, BSHI, even with its total of 653 beds, is insufficient. Consequently, clinicians often must refuse admission due to

bed unavailability [10]. We followed over 5,000 admitted and refused children up to 90 days to determine the difference in health outcomes and the wider effects of high-burden infections like RSV on the healthcare system. The cumulative mortality proportion for children denied admission was 19.4%, significantly higher than the 14% among those admitted. This discrepancy in mortality risk is quantified by a hazard ratio (HR) of 1.69 across all children under five.

The HR for death was 1.37 among children refused admission compared to those admitted, adjusted for age, diagnosis, and sex. The highest mortality risk was observed in neonates requiring hospitalization within their first month of life, with a HR of 1.93. This disparity highlights the essential role of healthcare access in determining child survival outcomes. Monte Carlo simulation using a 70% efficacious vaccine is estimated to be equivalent to adding approximately 50 beds to the hospital, and averting 195 deaths in only one hospital, each year.

The issue of bed shortages, a prevalent concern across many LMICs, is pressing. In Bangladesh, the rate of 0.8 beds per 1,000 population is markedly lower than in developed nations such as 2.9 in the USA and 2.5 in the UK [17]. With limited infrastructure, preventative strategies become even more vital. Over the past decades, the introduction of multiple vaccines in Bangladesh and improved health systems have led to a decrease in under-5, yet the rate 33 death in 1,000 live birth remain high, underscoring the need for further disease prevention measures [18]. Given the considerable proportion of hospital beds occupied by RSV cases during peak periods, introducing an RSV vaccine could significantly impact bed availability for critically ill infants. Other interventions like administration of monoclonal antibodies in neonates and infants can also be considered. However, the cost and logistical hurdles associated with monoclonal antibody treatments, such as nirsemivab, highlight the need for affordable, scalable, and equitable solutions, particularly in LMICs like Bangladesh where 69% of health expenditures are out-of-pocket [19].

While our 2019 study centered on RSV, a significant dengue outbreak during the same period compounded the strain on hospital resources [20]. In addition, other infectious etiologies of respiratory infections remain to be explored, as evidenced by the high number of cases meeting the inclusion criteria for RSV October to December, despite the absence of RSV detection.

The findings of this study must be viewed considering certain limitations. Primary among them is the necessity to conduct the study in a single hospital due to the high volume of cases and the extensive follow-up required for thousands of patients. While the authors' lived experiences suggest that similar circumstances are likely in other resource-limited settings, a multi-site research would be helpful in developing a more detailed understanding of the RSV burden among children throughout Bangladesh and potentially the wider region. Furthermore, the study's duration was constrained to one year, shortened by the COVID-19 pandemic in the following year. A longitudinal study spanning multiple years could provide more information on the patterns of RSV seasonality, but previous reports from Bangladesh suggest an unpredictable pattern of RSV seasonality [21]. And the overall high burden of RSV in the study hospital aligns with previous studies [11,12]. This study also did not investigate concurrent infections alongside RSV, nor was it set up to confirm deaths directly attributable to RSV. Lastly, potential biases due to human factors may have influenced the clinicians' admissions decisions during times of resource scarcity, even though such decisions should theoretically be unaffected by bed availability constraints.

The broader context and global health implications of our study are significant. The challenges highlighted related to shortage of hospital beds in places with high burden of disease are common in many LMICs and the global health community can learn from these findings particularly regarding resource allocation and estimate potential impact of preventive strategies like vaccination. This study also contributes to the growing body of evidence supporting the development and distribution of RSV vaccines or other interventions, which could significantly impact child health globally, specifically in low-resource countries where burden is the highest.

Declaration of Interests

The authors declare no conflict of interest.

Author contributions

S.S. contributed to conceptualization, funding acquisition, study design, implementation, monitoring, data analysis, drafting the initial manuscript, and preparation of figures. S.Sa. was involved in data analysis, preparation of figures, and manuscript editing. N.K. contributed to data analysis and editing. Y.H. participated in data analysis, preparation of figures, and manuscript editing. M.S.I. was responsible for analysis and coordination of the study, and also contributed to editing. S.I. carried out specimen extraction and PCR testing. Z.B.A. coordinated and trained doctors and nurses, assisted in the implementation of the study, in addition to contributing to manuscript editing. M.J.A. was involved in monitoring and management activities, as well as editing. A.M.A. performed data cleaning. P.K.S. contributed to management and patient data analysis. M.R.A. was involved in implementation and management. M.R.A. contributed to editing. S.K.S. contributed to conceptualization, funding acquisition, study design, implementation, monitoring, and manuscript editing. All authors reviewed the manuscript and agreed on the contents.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT to check grammar, spellings, and improve readability of the manuscript. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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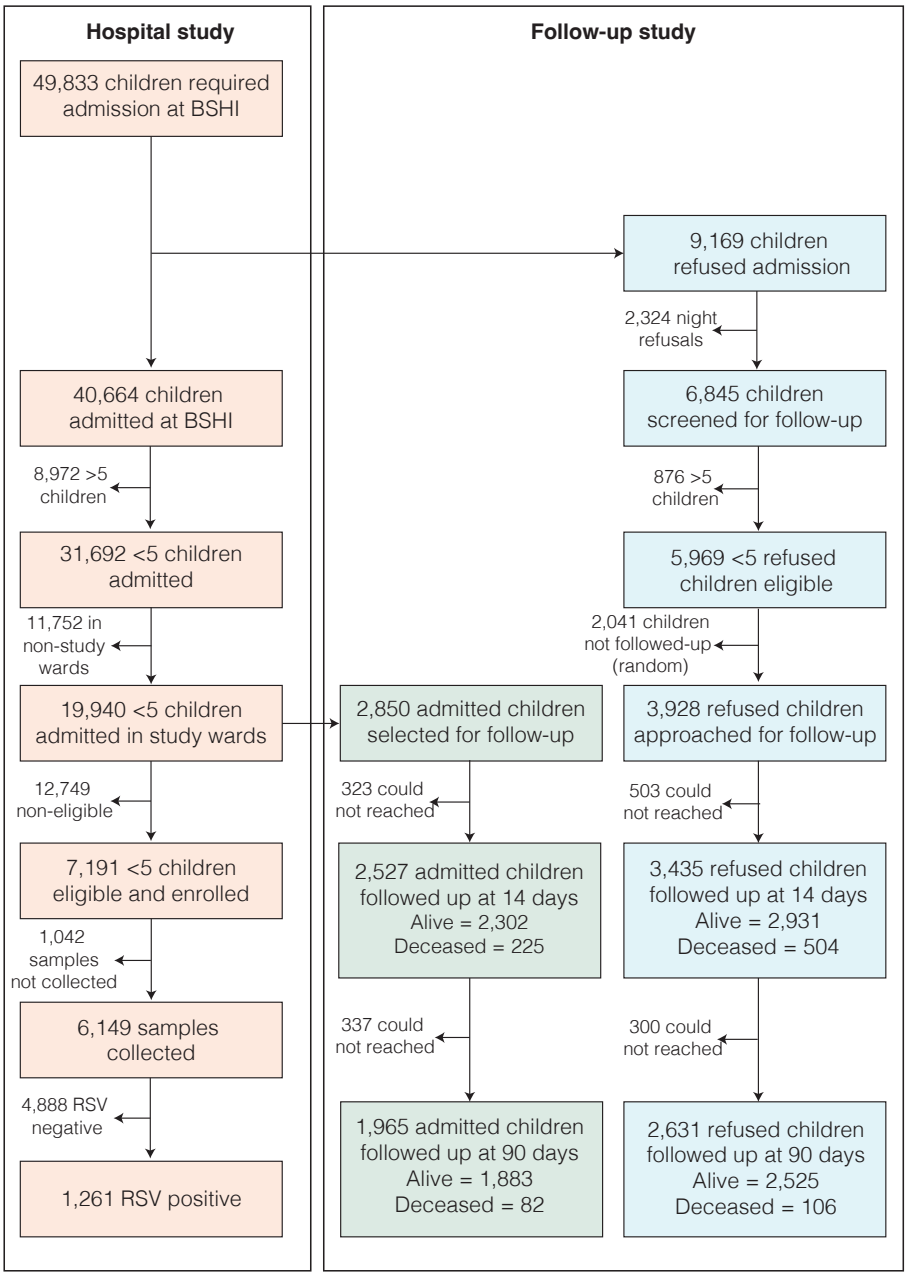

Figure 1. Flowchart of Sample Collection and Patient Follow-Up.

The figure illustrates the process of sample collection and subsequent patient follow-up for children under five admitted to BSHI or refused admission due to unavailability of bed. Reasons for failures of sample collection and details on those lost to follow-up are provided in Supplementary Appendix Tables S2, S4 - S7.

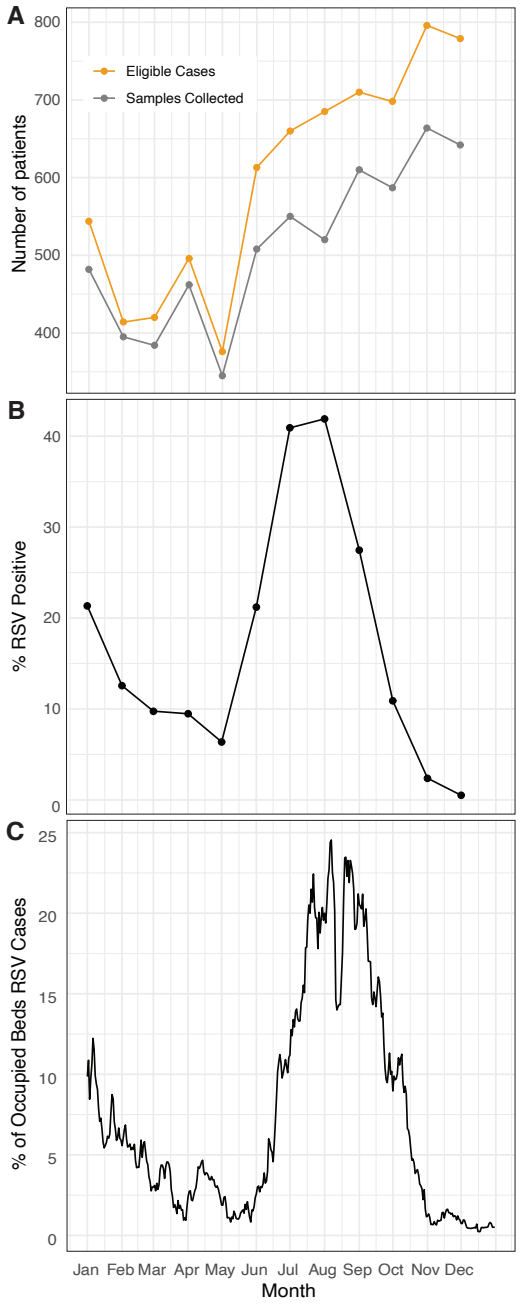

Figure 2. RSV Infections and Bed Occupancy in BSHI in 2019.

A. The total number of patients enrolled into the study each month, and the number of samples collected from these patients. B. Percentage of RSV positive cases detected each month. C. Percentage of occupied beds with RSV positive cases across different months. The dip in bed occupancy seen in mid-August is because of Eid-ul-Adha holidays.

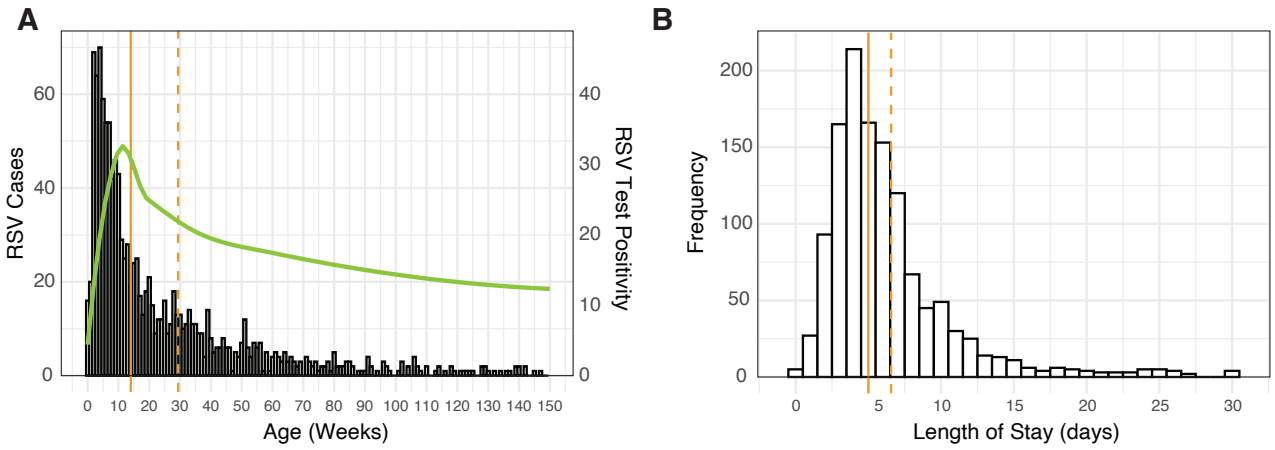

Figure 3. Age distribution of RSV cases and length of hospital stay. A. Age distribution of RSV cases (n = 1,261) in weeks, where the green line represents RSV test positivity in different age groups, the solid orange line indicates the median age, and the dotted orange line shows the mean age. B. Length of hospital stay in days of RSV cases (n = 1,261), with the solid orange line representing the median length of stay and the dotted orange line the mean.

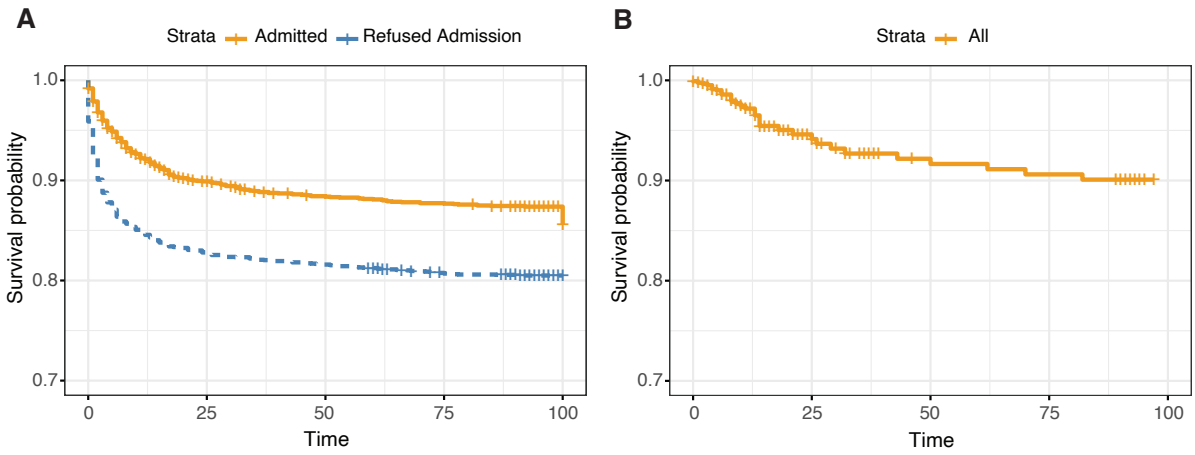

Figure 4. Survival Analysis of Patients followed-up.

A. Survival probabilities of patients who were refused admission with those who were admitted. Cases were censored at discharge if there was no follow-up or at the last successful follow-up. B. Survival curve for only RSV-positive cases: the 24 cases that resulted in in-hospital deaths, alongside the additional 205 cases that were followed up, of whom 18 subsequently died.

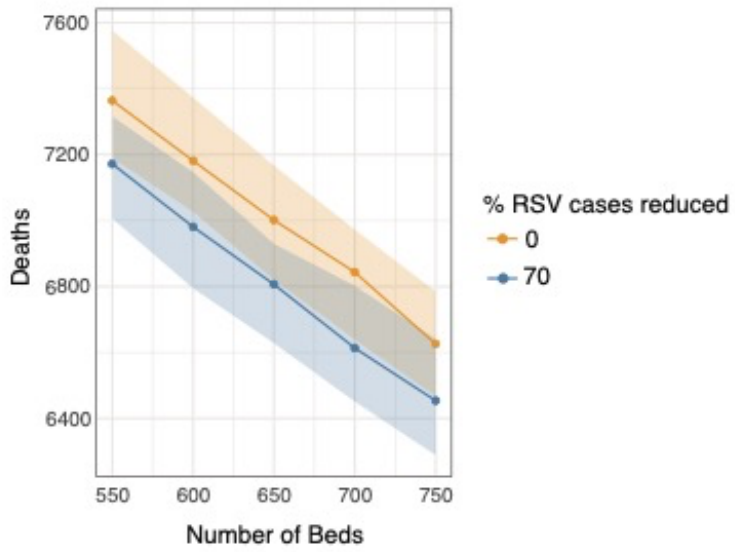

Figure 5. Impact of RSV Vaccination on Hospital Utilization and 90-day Mortality Rates of all children who require admission at BSHI. Effects of a 70% reduction in RSV admissions through vaccination, showing its impact on deaths and hospital bed utilization among children under five. The plot compares mortality against the effective increase in available beds, demonstrating how reducing RSV cases is akin to increasing bed capacity.

Table 1: Clinical attributes study participants enrolled in the study stratified by RSV status.

	Overall	RSV Negative/ Not Tested	RSV Positive	p
Number of Patients	**19940**	**18679**	**1261**	
Sex - Female (%)	7582 (38.0)	7196 (38.5)	386 (30.6)	<0.001
Age in months (median [IQR])	5.00 [0.00, 16.00]	5.00 [0.00, 17.00]	3.00 [1.00, 8.00]	<0.001
< 2 wks	5364 (26.9)	5293 (28.3)	71 (5.6)	
2 wks - 3 mnths	4039 (20.3)	3413 (18.3)	626 (49.6)	
4 - 6 mnths	1648 (8.3)	1464 (7.8)	184 (14.6)	
7 mnths - 2 yrs	5693 (28.6)	5381 (28.8)	312 (24.7)	
2 - 5yrs	3196 (16.0)	3128 (16.7)	68 (5.4)	
In-hospital mortality (%)	1266 (6.3)	1242 (6.6)	24 (1.9)	<0.001
Length of Stay (median [IQR])	4.00 [2.00, 7.00]	4.00 [2.00, 7.00]	5.00 [4.00, 8.00]	<0.001
Diagnosis Cluster (%)				<0.001
Respiratory Manifestation	5026 (25.2)	4065 (21.8)	961 (76.2)	
Gastrointestinal Manifestation	2192 (11.0)	2178 (11.7)	14 (1.1)	
Perinatal Asphyxia	2178 (10.9)	2164 (11.6)	14 (1.1)	
Febrile Illness	1464 (7.3)	1445 (7.7)	19 (1.5)	
Systemic Infections	1421 (7.1)	1352 (7.2)	69 (5.5)	
Preterm low-birth weight	899 (4.5)	887 (4.7)	12 (1.0)	
Other	6758 (33.9)	6586 (35.3)	172 (13.6)	

Table 2: Clinical attribute and outcome of participants admitted or refused admissions who were followed-up.

The table represents data of participants for whom data could be collected. Diagnoses was could not be collected for 18% of participants, 14-day mortality was missing for 12% and 90-day mortality was missing for 21%.

	Overall	Admitted	Refused	p-value
Number of Patients	**6772**	**2845**	**3927**	
Sex - Female (%)	2582 (38.1)	1071 (37.6)	1511 (38.5)	0.502
Age in months (median [IQR])	3.00 [0.00, 12.00]	4.00 [0.00, 15.00]	3.00 [0.00, 11.00]	0.006
< 2 wks	2017 (29.8)	804 (28.3)	1213 (30.9)	<0.001
2 wks - 3 mnths	1430 (21.1)	600 (21.1)	830 (21.1)	
4 - 6 mnths	622 (9.2)	226 (7.9)	396 (10.1)	
7 mnths - 2 yrs	1869 (27.6)	764 (26.9)	1105 (28.1)	
2 - 5yrs	834 (12.3)	451 (15.9)	383 (9.8)	
ER Diagnosis Cluster (%)				
Respiratory Manifestation	1463 (26.5)	351 (20.1)	1112 (29.4)	
Gastrointestinal Manifestation	475 (8.6)	182 (10.4)	293 (7.8)	
Perinatal Asphyxia	702 (12.7)	211 (12.1)	491 (13.0)	
Febrile Illness	207 (3.7)	101 (5.8)	106 (2.8)	<0.001
Systemic Infections	496 (9.0)	145 (8.3)	351 (9.3)	
Preterm low-birth weight	382 (6.9)	78 (4.5)	304 (8.0)	
Other	1799 (32.6)	677 (38.8)	1122 (29.7)	
14-day Mortality (%)	729 (12.2)	225 (8.9)	504 (14.7)	<0.001
90-day Mortality (%)	917 (17.2)	307 (14.0)	610 (19.4)	<0.001

Table 3: Hazard ratio (HR) of refused vs admitted participants adjusted by age, sex, and diagnosis.

Adjusted by	Strata	HR [95% CI]
		1.69 [1.48, 1.69]
Age, Sex, Diagnosis		**1.56 [1.36, 1.79]**
Sex, Diagnosis	< 1 mnth	**1.93 [1.62, 2.3]**
Sex, Diagnosis	2-3 mnths	1.19 [0.89, 1.58]
Sex, Diagnosis	4 mnths - 1 yr	1.47 [0.87, 2.48]
Sex, Diagnosis	1-5 yrs	1.05 [0.66, 1.68]
Age, Diagnosis	Male	**1.59 [1.34, 1.9]**
Age, Diagnosis	Female	**1.49 [1.2, 1.84]**
Age, Sex	Respiratory Manifestation	0.96 [0.7, 1.31]
Age, Sex	Perinatal Asphyxia	**2.22 [1.68, 2.92]**
Age, Sex	Systemic Infections	**1.79 [1.13, 2.85]**
Age, Sex	Preterm low-birth weight	**1.85 [1.32, 2.59]**
Age, Sex	Febrile Illness	0.79 [0.14, 4.37]
Age, Sex	Gastrointestinal Manifestation	1.37 [0.51, 3.71]
Age, Sex	Other	**1.32 [1.02, 1.71]**