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Respiratory Syncytial Virus Infection in Children with Bronchiolitis

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Abstract

Background: Respiratory Syncytial Virus (RSV) is the most common organism causing bronchiolitis. Bronchiolitis is almost always diagnosed clinically. As a result, the availability of bedside sensitive rapid RSV antigen tests is critical for timely RSV acute respiratory infection diagnosis.

Methods and materials: This study was conducted to detect RSV antigen positivity and the sociodemographic profile of children with RSV antigen positive bronchiolitis. From October 2022 to March 2023, this observational study was conducted in the pediatrics department of Chattogram Medical College Hospital. Ninety-two nasopharyngeal swabs from children younger than two years, were tested for RSV antigen. The mean and standard deviation were used to express the demographic data. Chi-square analysis was used to examine differences in group proportions.

Results: RSV antigen positivity was detected in 45.7% of the 92 cases, with a mean age of 4.18±3.08 months. Severe bronchiolitis cases were more common (22.8%) among antigen positive cases and had the longest hospital stay. During the months of November (42.4%) and December (29.3%), RSV infection levels peaked. This study describes that during the seasonal epidemics, RSV was the main concern, as the number of positive cases decreased in the months that followed. The signs and symptoms of RSV positive and negative cases were not significantly different.

Conclusion: A simple, low-cost and bedside RSV test can be considered as a valuable diagnostic tool in a low resource setting.

Key words: Bronchiolitis, RSV Antigen

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Introduction

The most significant respiratory condition affecting infants and young children is bronchiolitis, which is mostly brought on by the highly contagious Respiratory syncytial virus (RSV). The rhinovirus, human metapneumovirus, parainfluenza virus, influenza virus, adenovirus, and mycoplasma pneumoniae are additional pathogens. Respiratory syncytial virus (RSV) is the leading cause of viral pneumonia and bronchiolitis worldwide, with >95% of the disease burden occurring in resources limited settings.[1] An estimated 6.6 million cases of RSV LRTI (lower respiratory tract infection) and 1.4 million hospitalizations for RSV-associated acute lower respiratory infections in babies under 6 months were recorded globally in 2019.[2] It is the most frequent reason for hospitalization for respiratory illness in infants under one year old and is associated with 1 in 13 primary care visits, according to estimates.[3] A significant burden is placed on the global healthcare systems by the high rates of hospital admissions of infant and young children owing to ARTI related with RSV.[4] The majority of nations have a seasonal pattern to RSV infection, with temperate regions experiencing peaks in activity during the autumn and winter.[5] Over the past decade, hospital admissions for bronchiolitis have increased alongside rising morbidity and mortality in our country.[6] A survey of 43 hospitals from six divisions in our country revealed that 67% of children who visited the outpatient and inpatient departments had respiratory problems, of which 21%

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were diagnosed with bronchiolitis.[7] Based on the patient's clinical presentation, age, seasonal occurrence, and physical findings, bronchiolitis is diagnosed.[8]

Bronchiolitis usually affects children younger than 2 years with a peak in infants aged 3-6 months.[9] Commonly, symptoms of bronchiolitis begin with rhinitis or congestion and cough with respiratory distress (tachypnea, wheezing and accessory muscle use). Severity of bronchiolitis can vary from mild symptoms to acute respiratory failure.[10] Case definition of bronchiolitis includes children below 2 years, respiratory distress associated with wheeze and preceded by runny nose.[11]

According to severity, bronchiolitis is classified into mild, moderate and severe form by three features, eg: feeding, respiratory distress and oxygenation (SPO_2). Mild is characterized by normal ability to feed, mild or no respiratory distress (No chest indrawing) and no requirement of oxygen (O2 saturation >95%). Moderate is characterized by moderate respiratory distress with some chest indrawing, nasal flaring mild to moderate hypoxemia corrected by oxygen with moderate feeding difficulty. Severe is characterized by unable to feed, severe respiratory distress with marked chest indrawing, nasal flaring, grunting and severe hypoxemia which may not be corrected by extra oxygen.[11] Study done by Rakshit SC et al showed prevalence of bronchiolitis in Hospitalized children is 22.6.[12]

Recent guidelines and evidence-based reviews advise against routinely using diagnostic tests because they have not been found to have a significant impact on the clinical course of bronchiolitis, with the exception of pulse oximetry.[8,13] Typically, tests are used to rule out alternative diagnoses (e g, bacterial pneumonia, sepsis, or congestive heart failure).[14] Thus, accurate and prompt diagnosis of RSV-associated acute respiratory infection (ARI) can have major impact on patient care. Because concurrent serious bacterial infection with RSV is uncommon, especially in children.[15]

For the quick detection of RSV-associated ARI, bedside sensitive fast RSV tests are essential. It might lessen the need for extra diagnostic tests and unnecessary antibiotics, lessen the need for hospitalization. Virus isolation by DNA testing or PCR is expensive and time-consuming, whereas antigen testing is a bedside and user-friendly method to identify the target antigen within 30 minutes. This test may aid in the accurate diagnosis of RSV, allow for supportive treatment decisions. This study also ensures the availability of high-quality hospital data about bronchiolitis for physicians, researchers, decision makers and healthcare planners. A positive result can enable targeted isolation strategies to prevent cross-infection or enable cohort care for a group of sick children. [4,16] So, the purpose of the study is to detect RSV antigen positivity in children with their sociodemographic profile of bronchiolitis cases admitted in the hospital.

Objecrtive:

To determine respiratory syncytial virus antigen and sociodemographic profile of bronchiolitis cases in hospitalized children.

Materials and Methods:

It was a descriptive cross-sectional study done in the department of Pediatrics, Chittagong Medical College Hospital, Chattogram, Bangladesh from October 2022 to March 2023. The Study population were Children below two years, admitted in the pediatric ward who were clinically diagnosed as bronchiolitis and were taken by Convenient sampling.

The calculated sample size was 263 but due to time and money constraint, one hundred cases of children with bronchiolitis were taken as sample to test RSV antigen who fulfilled the inclusion criteria. Children with bronchiolitis were diagnosed clinically. Children below 2 years, suffering from respiratory distress associated with wheeze and preceded by runny nose were taken as bronchiolitis cases. According to severity, bronchiolitis was classified into mild, moderate and severe form by three features, eg: feeding, respiratory distress and oxygenation (SPO2). With detail history and clinical examination, bronchiolitis cases were diagnosed. A predesigned structured case record form containing all the variables of interest was used for data collection. After diagnosis, routine investigation like Chest X-ray & CBC were done. Then antigen testing done by 'STANDARD Q RSV' Antigen Test kit by SD BIOSENSOR. It is a rapid chromatographic immunoassay for qualitative detection of RSV antigen present in nasopharyngeal swab or aspirate and the results is available in 15 to 30 minutes.

With all aseptic precaution nasopharyngeal swab was collected by nasopharyngeal swab stick. This swab

sample of the patient was inserted into the extraction buffer tube; after extracting the liquid, the swab was disposed as waste disposal biohazard protocol. Then nozzle cap was tightly press onto the tube and 4 drop of mixed sample was applied to the test device. The test device was read after 15-30 minutes. Two colored band (C-control line, T-test line) were appeared within the result window, indicate RSV antigen positive. The results were then recorded in case record form. Four cases were discarded due to incomplete history and another four cases were discarded due to confusing kit results. Ninety-two cases were enrolled in this study

Data were presented by suitable tables, and diagrams. All data were calculated using SPSS version 23 software. Demographic data were expressed as mean ± standard deviation (SD) or frequency (percentage). Differences between proportions of groups were analyzed for statistical significance using the chi-square test. The level of statistical significance was set at $p < 0.05$. A written informed consent form was signed by the parent or caregiver of the participating children before enrolling them into the study. Ethical clearance was taken from the ethical review committee of Chittagong Medical College (Memo no: PG.009.2022/271).

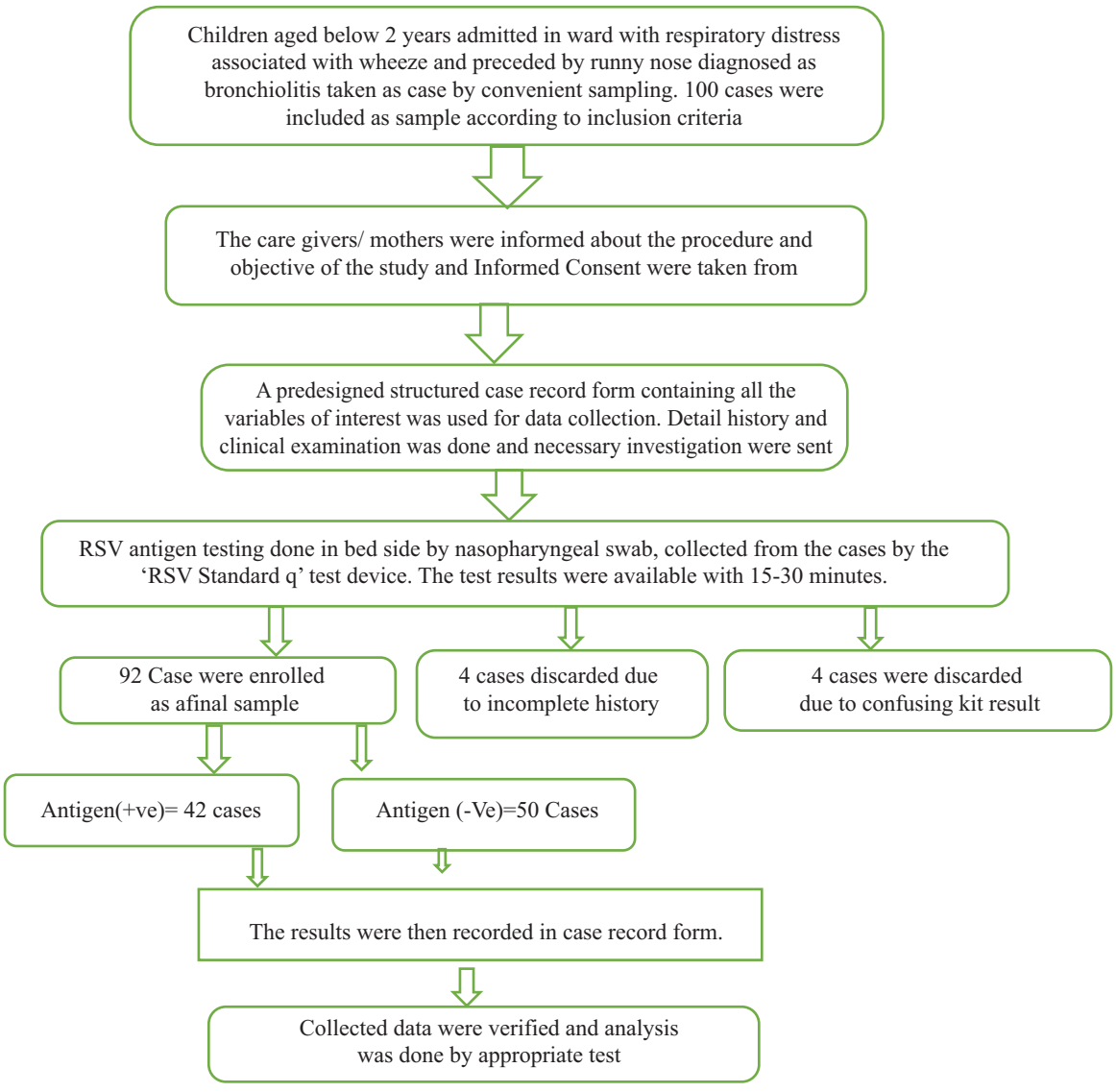

Fig ure 1: *Flow Chart*

Result

In this study among 100 children, 92 were enrolled in the analysis, 4 cases were discarded due to incomplete history and 4 cases were discarded due to confusing results of kit. Among all cases, 42 (45.7%) cases were found RSV antigen positive, 50 (54.3%) cases were found RSV antigen negative(fig-2), and among those, 22 (22.6%) cases were moderate bronchiolitis while 22 (22.63%) cases were severe bronchiolitis. RSV positive severe bronchiolitis were more (21, 22.8%) than RSV negative severe cases (9, 9.8%).

Demographic Profile of Studied Population:

Among 92 cases, RSV positive infection was more common in children aged 1 to 2 years (30, 32.6%). The mean age of RSV positive children was found 4.18±3.08 months(p=0.95) and the mean weight was 5.72±1.76 kg (ranges 2.5-11kg). The result also shows that there were 2 (2.2 %) RSV positive case in neonatal age group. Two third (67.4%) of the cases were male (p= 0.22). Among all the cases, 64 (69.4%) cases were from urban area. Despite there were more cases of bronchiolitis in rural areas during the study of residency, there were more RSV positive cases in urban areas (P = 0.018). P value is also significant. In terms of total cases, November (42.4%) and December (29.3%) have the highest levels of infection. (66, 71.7%) (p=0.04). (Table-1)

Although there are other viruses that can cause bronchiolitis, this study also explains that, RSV is the main concern during the seasonal epidemics (November-December RSV positive case 36/ Negative 30, January to May RSV positive 5/ negative 20), where P value (0.045) was determined to be significant here. (Table-1, fig-3)

Table-I

Baseline Characteristics of studied population.

		RSV positive		RSV negative		Chi-square	p-value
		frequency	%	frequency	%		
Age	0 to1 month	2	2.2	3	3.2	0.004	0.952
	1m to <1 year	9	9.8	11	11.7		
	1 year to 2years	30	32.6	36	39.1		
Sex							
	Male	31	33.7	31	33.7	1.449	0.229
	Female	11	12	19	20.7		
Residence							
	Rural	24	26.1	40	43.5	5.633	0.018
	Urban	18	19.6	10	10.9		
Month of enrollment							
	November 2022	20	21.7	19	20.7	12.853	0.045
	December 2022	16	17.4	11	12		
	January 2023	2	2.2	1	1.1		
	February 2023	1	1.1	5	5.4		
	March 2023	3	3.3	5	5.4		
	April 2023	0	0	4	4.3		
	May 2023	0	0	5	5.4		
	Range			mean±SD			
Age	2 days-18 months			4.18±3.08 months			
Weight	2.5-11 kg			5.72±1.76 kg			

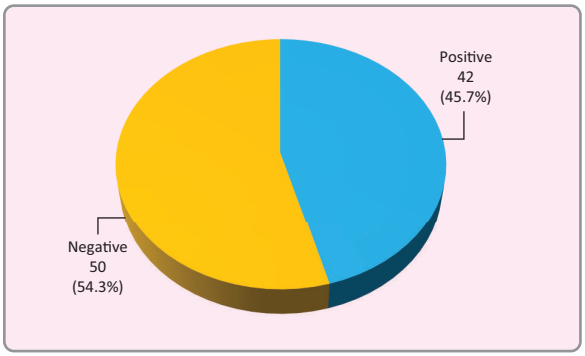

Figure 2: *Distribution of Positivity rate of RSV antigen.*

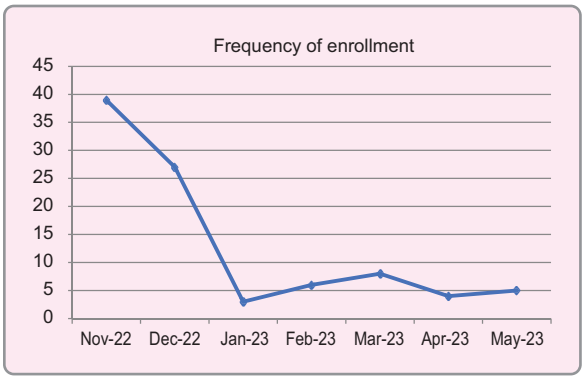

Figure 3: *Distribution of Seasonal variations of bronchiolitis cases*

Table-II

Relevant History of RSV antigen positive cases of bronchiolitis (N=42)

Variables	Frequency	Percentage
Vaccination		
Completed	03	7.1
Ongoing	36	85.7
Not given	03	7.1
History of viral illness in older family member/ siblings		
Present	14	33.3
Absent	28	66.7
History of asthma in first degree relatives		
Present	13	31
Absent	29	69

Table-III

Comorbid conditions among RSV antigen positive cases of bronchiolitis

	Frequency	% of total response	% of cases(n=37)
Prematurity	8	11.5%	21.5%
LBW	9	12.5%	24.3%
Non-breast-feeding	8	11.1%	21.6%
Overcrowding	13	18.1%	35.1%
Passive-smoking	19	26.4%	51.4%
Indoor-air-pollution	18	25.0%	48.6%
Mal-feeding	0	0	0
Total	72	100%	194.6%

Vaccination status, Family history & comorbid conditions of RSV antigen positive cases of bronchiolitis:

In antigen positive bronchiolitis cases, 85.7% children were remaining in ongoing vaccination schedule, 33.3% children's family member had history of viral disease and 31% children had family history of asthma. Overcrowding, Passive smoking and indoor pollution were found the important comorbid conditions for antigen positive cases. (Table-2,3)

Table-IV

Symptoms among RSV antigen positive & RSV antigen negative cases of bronchiolitis

	RSV antigen positive R			SV antigen negative			p-value
	Frequency	% of total response	% of cases (n=42)	Frequ ency	% of total response	% of cases (n=50)	
Fever	30	14.3%	71.4%	31	12.9%	62.0%	0.341
Cough	41	19.5%	97.6%	48	19.9%	96.0%	0.663
Runny nose, viral_ catarrh	32	15.2%	76.2%	42	17.4%	84.0%	0.347
Respiratory distress	39	18.6%	92.9%	43	17.8%	86.0%	0.293
Wheeze	35	16.7%	83.3%	40	16.6%	80.0%	0.682
Feeding difficulty	33	15.7%	78.6%	37	15.4%	74.0%	0.609
Total	210*	100.0%	500.0%	241*	100.0%	482.0%	

*Multiple response

Table-V

Clinical manifestation of RSV antigen positive & RSV antigen negative cases of bronchiolitis

	RSV antigen positive			RSV antigen negative			p-value
	Frequency	% of total response	% of cases (n=42)	Frequency	% of total response	% of cases (n=50)	
Playful	30	9.9%	71.4%	38	12.3%	76.0%	0.619
Irritable	7	2.3%	16.7%	11	3.5%	22.0%	0.521
Lethargy	5	1.6%	11.9%	1	0.3%	2.0%	0.089
Cyanosis	2	0.7%	4.8%	1	0.3%	2.0%	0.590
Flaring of ala nasi	14	4.6%	33.3%	5	1.6%	10.0%	0.006
Normal temp	30	9.9%	71.4%	45	14.5%	90.0%	0.022
Hyperthermia	11	3.6%	26.2%	5	1.6%	10.0%	0.041
Hypothermia	1	0.3%	2.4%	0	0%	0%	0.457
Grunting	11	3.6%	26.2%	4	1.3%	8.0%	0.019
Fast breathing	39	12.8%	92.9%	36	11.6%	72.0%	0.010
Severe chestindrawing	27	8.9%	64.3%	27	8.7%	54.0%	0.318
Tachycardia	16	5.3%	38.1%	11	3.5%	22.0%	0.091
Hyper inflatedchest	14	4.6%	33.3%	11	3.5%	22.0%	0.224
Crepitation onauscultation	26	8.6%	61.9%	29	9.4%	58.0%	0.704
Rhonchi onauscultation	32	10.5%	76.2%	39	12.6%	78.0%	0.837
Head nodding	39	12.8%	92.9%	47	15.2%	94.0%	0.825
Total	304*	100.0%	723.8%	310	100.0%	620.0%	

Common symptoms and signs among antigen positive bronchiolitis cases:

The most common symptom in RSV positive group was cough (97.6%, p-0.66) followed by respiratory distress (92.9%, p- 0.29), runny nose (76.2%, p-0.34), wheeze (83%. p-0.68) and feeding difficulty (78%, p- 0.60).

Regarding physical finding, total 30/42 (71.4%) of RSV antigen positive children were playful (p value 0.61),

64.3% had severe chest indrawing (p value 0.31). Wheezing (32/42) and crepitations (26/42) were present in 76.2% (p value 0.837) and 61.9% (p value 0.70) children respectively. But in some signs eg: normal temp (p value 0.02), flaring of ala nasi (p value 0.006), grunting (p=0.019), fast breathing (p value 0.010), p value were found statistically significant. Children infected with RSV did not differ significantly in terms of other signs and symptoms (except Normal temperature, flaring of ala nasi, grunting, fast breathing) as compared to RSV negative group.

Table-VI

CXR findings of RSV antigen positive cases of bronchiolitis (n=34)

	Frequency	%
Hyper translucency	17	50.0
Hyperinflation	12	35.3
Hyper translucency + hyperinflation	3	8.8
Hyper-inflation + patchy opacity	1	2.9
All three features	1	2.9
Total	34	100

Chest X-ray findings of RSV antigen positive cases of bronchiolitis:

Majority of the patients 80% (34/42) had positive findings on X-ray. Here 50% children had hyper-translucency and 35.3% children had hyperinflation on X-ray finding. (Table-6)

Table-VII

Treatment outcome of RSV antigen positive cases of bronchiolitis (n=42)

	Frequency	%
Improved and discharged	34	81.0
Referred to PICU and improved then discharged	5	11.9
Developed septicemia then improved and discharged	2	4.8
Died	1	2.4
Total	42	100

Treatment outcome of RSV antigen positive cases of bronchiolitis:

On treatment modalities, only five (11.5%) children required ICU, 34(81%) children were improved with treatment and discharged. (Table-7)

Table-VIII

Association of RSV positive bronchiolitis with bronchiolitis Category, Treatment

		RSV positive		RSV negative		Chi-square	p-value
		frequency	%	frequency	%		
Bronchiolitis category	mild	0	0	3	3.3	12.094	0.002
	moderate	21	22.8	38	41.3		
	severe	21	22.8	9	9.8		
Steroid nebulization	yes	24	26.1	25	27.2	0.468	0.094
	no	18	19.6	25	27.2		
IV antibiotic	yes	37	40.2	43	46.7	0.088	0.766
	no	5	5.4	7	7.6		
Outcome							
	DAMA/absconded	0	0	1	1.1	2.998	0.558
	Improved and discharged	34	37	43	46.7		
	Referred to PICU and improved then discharged	5	5.4	2	2.2		
	Developed septicemia then improved and discharged	2	2.2	2	2.2		
	Died	1	1.1	2	2.2		
Total		42	45.7	50	54.3		

Table-IX

Length of hospital stay in relation to RSV antigen test and bronchiolitis severity

		Length of hospital stay (day)		
RSV- antigen	Bronchiolitis-category	Mean	Std. Deviation	Frequency
positive	moderate	2.81	1.569	21
	severe	6.52	1.662	21
negative	mild	2.67	1.155	3
	moderate	3.08	1.194	38
	severe	3.78	2.728	9
	Total	3.18	1.561	50
Mean Hospital stay	3.86±2.15 days			

Association of RSV positive bronchiolitis with bronchiolitis Category, Treatment modality, & treatment outcome

RSV positive bronchiolitis is associated with moderate and severe disease (p-0.002). P value is found significant here. In treatment modality like antibiotic and steroid nebulization, no significant association are found (p value 0.76 & 0.09 respectively). The outcomes are also not significantly different in both category (p value 0.55).

Here, all of our hospitalized (88.1%) children were treated with intravenous antibiotic as coexistent infection cannot be ruled out and chance of secondary infection is more in this tertiary hospital due to excessive patient load (Table-VIII)

Length of hospital stay of antigen positive bronchiolitis cases:

A two-way ANOVA was performed to evaluate the effects of RSV antigen test (positive or negative) and bronchiolitis severity (mild/moderate/ severe) on length of hospital stay showed on Table -9. It Shows RSV positive children did not have any mild instances, and they had more severe cases. (P value 0.002) and all children had an average hospital stay of 3.86±2.15 days. RSV antigen positive cases who suffered from severe bronchiolitis had the longest hospital stay (6.52±1.66 days).

Discussion:

This study found almost half (45.2%) cases were positive for RSV antigen. Rakshit SC et al reported prevalence of RSV in Bangladesh was 22.9%[12] Bharaj et al. reported RSV prevalence of 20.3% from Northern India [16] and Yeolekar et al. reported 26% prevalence in Western India.[17] Divarathna M V M et al. reported 47% prevalence of RSV in the community among children of Sri Lanka.[18]

A meta-analysis showed that RSV Rapid antigen detection tests pooled sensitivity and specificity were 80% (95% confidence interval [CI], 76% to 83%) and 97% (95% CI, 96% to 98%), respectively.[19] As there was no facility for doing PCR testing in our hospital, we are unable to do the sensitivity and specificity.

This study found mean age of RSV infected children was 4.18±3.08 months with nonsignificant (p value 0.22) male predominance. Similar male preponderance was reported by different studies. [20,21] The study by Charu Shingh[22] et al. and Radhakrishnan *et al*.[23] found mean age 9 months with a predominance of male. Saleh Ahmed conducted a retrospective study involving 70 children with RSV bronchiolitis and found out a male predominance with children aged <6 months being infected majorly.[24]

A passive smoking was noted in half (51.4%) of our cases, which support the fact it is a recognized risk factor for bronchiolitis, especially maternal smoking.[25] This study found that rural children were affected more but in urban children, more RSV antigen positivity (P value 0.018) were found, this finding is supported by study of Hamid et al.[26]

Present study found higher rate RSV positive cases in winter season (in November and December) and no RSV positive case after March (P value 0.045). This finding matched with the largest prospective study done by Langley JM et al.[27] who found that June to February was the RSV transmission period in Bangladesh. Charu Shingh [22] et al also found RSV positive bronchiolitis

cases presented in winter months that (November to March). Usually, RSV infection is seasonal in most of the countries and RSV seasonality varies considerably between regions.[28]

This study also describes, though there are many viruses causing bronchiolitis, during the seasonal epidemics, RSV is the main concern (November-December RSV positive case 36/ Negative 30, January to May RSV positive 5/ negative 20). P value (0.045) was found significant here.

In our study 21.5% children were born prematurely which is identical to the Charu Shingh et al[22] study in which 20% of cases were born premature. Other study also identified premature birth, as one of the most important factors leading to an increased severity of RSV infection.[29] In our study 25% children had low birth weight, a factor seen to be associated with development of RSV infection. Birth during first half of RSV season (November-January); low birth weight, preschool age, male gender, child care attendance, siblings were found as independent predictors of increased risk of RSV-hospitalization in children in an observational cohort conducted in Canada [30]

Clinical profile showed that respiratory distress (92%), cough (97.6%), fever (71%), wheeze, (83%) and nasal discharge (76%) were most common symptoms. Almost same findings were seen in a study done by Charu Shingh et al [22] and Vahini V, *et al*. [31]

We found 92.9% and 64.3% of children had fast breathing and chest indrawing in this study whereas Ganavi R *et al*.[32] in India observed tachypnea and chest indrawing in 100% of children and Sahleh *et al*. in Saudi Arab found chest wall retractions more than half of his patients.[24]

Sixty nine percent (61.9%) and Seventy six percent (76.2%) of children current study had crepitations and rhonchi on auscultation respectively which finding matched with the studies done by Charu shing in India,[22] Solemani et al in Iran, [33] and Wahab AA et al in Qatar.[34]

In this study, children infected with RSV did not differ significantly in terms of signs and symptoms as compared to RSV negative group. This finding was matched with the finding of study done by Bhandary R, et al. [35]

Limitation of study

1. The lack of use of confirmatory test like RT- PCR for RSV.
2. It was not possible to subtyping of RSV virus.
3. It was a single center study.
4. Sample size was small

Conclusion

Children of RSV positive Bronchiolitis did not differ significantly in terms of sign and symptom (except Normal temperature, flaring of ala nasi, grunting, fast breathing) with the RSV negative group. Many viruses causing bronchiolitis but RSV is the main concern for the seasonal epidemics. More RSV positive case found in urban area (P value-0.018). Severe cases were more among RSV positive cases. (P value significant 0.002) and had the longest hospital stay.

Conflict of interest: We have no conflict of interest to declare.

Recommendation

A simple, low cost and rapid bedside RSV test can be considered as a valuable diagnostic tool in low resource setting. The experience of this study provides useful insight into its utilization. Further larger scale study is needed to accept this with proper rationale and documentation.

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