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The Incidence, Common Presentation, Management and Outcome of Children with Bronchiolitis admitted in Dubai Hospital between 2016 - 2017

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List of Abbreviations

LOS: length of stay

ICD: international Classification Disease

SD: standard deviation

WHO: World health Organization

NEB: nebulizers

HX: History

DX: Diagnosis

NAD: no apparent distress

IV: intravenous

RSV: Respiratory syncytial virus

UAE: United Arab Emirates

BD: Bronchodilators

HS: Hypertonic Saline

Introduction

Bronchiolitis is a common lower respiratory illness-affecting young children between the ages of two and twenty - four months worldwide. The number of children admitted with RSV diseases from developing countries in 2005 was more than double that estimated in 1986, and the incidence of RSV-acute lower respiratory tract infection was twice that of industrialized countries **(**Nair et al., 2010**)**. In the USA, emergency department visits and hospitalizations due to bronchiolitis have increased steadily over the last 30 years **(**16, 17**)**, incurring in over 150,000 emergency visits and hospitalizations annually, and exceeding $1.7 billion in combined charges [18, 19, 20, 21]. Little is known about the epidemiology of bronchiolitis infections in the Middle East, including UAE.

Male infants develop more severe lower respiratory illness and wheezing. The reason for the gender difference is unknown, but may relate to differences in lung function between the sexes **(**1**)**. It is characterized by epithelial cell destruction, cellular edema, and airway obstruction by inflammatory

debris and mucus. Most children who become severely ill are under 6 months of age and in this group morbidity and mortality are high **(**2**)**. Although many viruses can cause the clinical picture including influenza, parainfluenza, rhinovirus and Adenovirus; Respiratory syncytial virus **(**RSV**)** infection is one of the most important viral cause of severe acute lower respiratory tract infection, however only a small proportion of children infected with this virus develop severe disease. Clinical manifestations associated with disease severity are influenced by sex, age, previous bronchiolitis, co-morbidities, environmental exposure, and the host's immune response to the infection **(**15**)**. The clinical manifestations include cough, tachypnea, labored breathing, wheezing and fever **(**3**)**. Cough is an early symptom that typically increases in severity over several days. The quality of the cough can be variable, from dry to wet to croupy. Because the airways are obstructed by mucus and necrotic debris, wheezing and crackles are common symptoms **(**4**)** Most cases are associated with fever during the first few days of the illness. Fever is usually low grade and may no longer be present at the time of hospitalization. Clinical judgment remains the gold standard for hospital admission of infants with bronchiolitis.

In summer, it is hot and can be very humid, whereas in winter, temperature can drop significantly in this region. These weather variations can exacerbate respiratory infections and chronic lung diseases in susceptible individuals. A review of RSV infections in the Middle East region shows that the occurrence of RSV infections is in the winter season peaking around January as in other parts of the world, with the same age groups affected.

Previous studies have shown that the mainstays of therapy include airway support, supplemental oxygen, and support of fluids and nutrition. Frequently tried pharmacological interventions, such as ribavirin, nebulized bronchodilators, and systemic corticosteroids, have not been proven to benefit patients with bronchiolitis. Bronchodilators can cause hypoxia and increase bronchial compressibility by reducing smooth muscle tone **(**14**)**. Antibiotics do not improve the clinical course of patients with bronchiolitis, and should be used only in those patients with proven concurrent bacterial infection. Steroids seem to bring no clinical improvement, except in infants with protracted wheezing after bronchiolitis and patients with preexisting BPD **(**14**)**

This aim of this study is to help shed light on the epidemiology children admitted with the diagnosis of bronchiolitis or RSV bronchiolitis in one of the largest government hospitals in UAE over a period of a year, along with observing the seasonal and gender variation of these admissions, their common presenting signs and symptoms, most common organism isolated in relation to seasons, frequently prescribed treatment plan they received and whether it had relation to their length of stay.

Materials and methods

This research was a retrospective descriptive, record based study done in Dubai Hospital, which was established in 1983, and is a government organization under Dubai Health Authority. It has a specialized Pediatric ward that offers its services to all children up till age of thirteen in United Arab Emirates, including locals and expatriates.

The hospital offers both general and specialized pediatric care spread across numerous wards. All children admitted in Dubai hospital have their ICD **(**International Classification of Diseases**)** coding recorded in the electronic filing system; SAM and SALAMA. These systems along with discharge summaries and with the help of medical record department, we identified all children admitted with Bronchiolitis to General pediatric ward on level 4 between September 2016 and September 2017.

For the purpose of this study, all Children under 2 years of age, boys & girls, Nationals and non-nationals with a clinical diagnosis of bronchiolitis with or without an identifiable pathogen were included in the study. All children who did not meet this criterion were excluded. Children with preexisting conditions such as Bacterial pneumonia, Gastro esophageal reflux disease, recurrent viral triggered wheeze, congenital heart disease with heart failure, vascular rings, and chronic pulmonary disease with prolonged and recurrent wheeze, Asthma, cystic fibrosis, foreign body aspiration were excluded. Children not included were also the ones that were discharged against medical advice or preterm infants with prior intensive care unit or neonatal intensive care unit stay.

Total number of neonate's, infants and children admitted with diagnosis of bronchiolitis were 154. 35 **(**22.7%**)** from this list were excluded based on our exclusion criteria and 119 **(**77.3%**)** were included in the study.

For all those included in the study analyses was done on incidence amongst total pediatric admission and incidence amongst all those admitted under age of 2 years, their common presenting feature sets, common treatment modalities, length of stay, gender, seasonal variation & nationality. All data was analyzed using SPSS.

The study was undertaken after receiving approval from the Dubai Scientific Research & Ethics Committee. Data collection was done by the principal investigator. Data was retrieved from the electronic patient record system where patients' demographic information, medical investigations, and discharge summaries are saved **(**SAM & SALAMA**)** and from the case records section in Medical records department in Dubai hospital. All data were saved to password encrypted flash drives.

Definition of presenting variables

In clinical features used in diagnosing bronchiolitis, upper respiratory prodrome was defined as having dryness, nasal itching and/or obstruction, sneezing; watery nasal discharge; cough and constitutional symptoms such as presence of fever and generalized malaise, followed by increased respiratory effort which encompassed tachypnea, nasal flaring, chest retractions, wheezing, and/or rales**)**. Poor feeding was defined as oral intake that was less than two thirds to half of their normal daily intake. Fever was defined as recorded temperature greater than 38^{o}C either at home or at the hospital.

Bronchodilators included the use of Ventolin and Atrovent nebulization. Steroids used included either Prednisolone, Hydrocortisone or Dexamethasone use. Antibiotics used included Augmentin or Cephalosporin. Other Medications used included use of epinephrine nebulization, Pulmicort nebulization, Singulair, Mucosalvan, Cetirizine, Oxygen supplementation and IV fluids.

Nationals were UAE citizens and Non-nationals were children with other nationalities residing in UAE. In Children screened for viruses associated with bronchiolitis, other virus's category included all other viruses apart from respiratory syncytial virus, including rhinovirus, adenovirus, norovirus etc.

Results

Total number of children admitted in Dubai Hospital under 2 years of age between September 2016 – September 2017: 168. Total number of children admitted with Bronchiolitis under the 2 years of age between September 2016 – September 2017: 154. Incidence of children admitted with Bronchiolitis between September 2016 – September 2017 was: 91%

Number of children included in the study using inclusion criteria: 112. Number of children excluded from study using exclusion criteria: 42. Incidence of children admitted with simple Bronchiolitis without any other associated illnesses, not requiring intensive care and excluding those who were discharged against medical advice, was: 66.6%.

There was a higher percentage of boys admitted at 58% as compared to girls 42 %.

Most common presentation was cough with respiratory distress and fever in 34% of children. Poor oral intake in addition to identical symptoms as above was present in 30% of children and least common was only isolated cough with respiratory distress in 16.9% of children. 59% of children were admitted in winter months and 41% of children were admitted in summer months. Most common organism

Isolated was RSV 44%. The most common treatment choice was a combination of bronchodilators with other medications in 62% of case, with most common combination being BD with hypertonic saline 55% and BD with Antibiotics 25 %, followed with Bronchodilators use alone 21.4 % and use of Other medications without any bronchodilator at 16.07%. Using Wilcoxon signed rank test there was significant association between the organism isolated **(**RSV, other organisms, or none**)** and treatment modalities implemented **(**bronchodilator use only, bronchodilators with other medications or no bronchodilator use at all**)**. Implementing Wilcoxon signed rank test also showed there was a clear association between the median of different treatment modalities in different seasons, Winter or Summer.

Length of hospital stay in relation to gender and nationality

Mean length of hospital stay for boys was 61 hours **(**2.5 days**) (**95% CI: 51 – 72 hours**)** and a median of 48 hours **(**2 days**)**, with standard deviation of 42.69 hours. In Females the mean length of hospital stay was 56 hours **(**2.3 days**) (**95 % CI: 45 - 68 hours**)**. Median of 48 hours **(**2 days**)**, with standard deviation of 39.17 hours, as demonstrated in figure 1 A . The length of hospital stays amongst nationals showed a mean of 61 hours **(**2.5 days**)**, a median of 48 hours with a 95% confidence interval of **(**51.2 – 72.3 hours**)**, and amongst Non-nationals, the mean LOS was 57.58 hours **(**2.3 days**)**. With a median of 48 hours and 95% CI of **(**46.0 – 96.1**)**, as represented in figure 1 B.

The Length of stay for less than 2 days in all children was seen in 57.14% of children. The length of hospital stay for less than 5 days in children was seen in 92% of children. There was no statistically significant correlation between length of hospital stay and gender of children admitted, boys **(**p = 0.55**)** and girls **(**p= 0.54**)**.

Age of admission in relation to Gender and Nationality

Mean Age of Boys admitted was 19 weeks, **(**4.7 months**) (**95% CI 15 – 23 weeks**)** , median of 16 weeks & standard deviation of 16 weeks . Mean Age of Girls admitted was 21 weeks **(**5 months**) (**95% CI 15 – 27 weeks**)**, median of 18 weeks and Standard Deviation of 20 weeks, as represented in Figure 2A. For Nationals mean age of admission was 19 weeks **(**4.7 months**)**, with a median of 16 weeks **(**4 months**)** and 95% CI of **(**14.5-23.6**)**. For Non-national the Mean age of admission 20.9 weeks **(**5.2 months**)**, with median of 12 weeks **(**3months**)** and 95% CI of 26.09 weeks, as represented in Figure 2B. Admission of infants who were less than 6 months of age was 51%. Admissions of infants who were less than 1 year of age was 70.1%

Length of hospital stay in relation to only Bronchodilator use VS Mixed BDL & other medication use.

The mean length of hospital stays for children who received only Bronchodilators was 38.42 hours **(**1.6 days**)**. The mean LOS for children who received Bronchodilators with other medications was 70.31 hours **(**2.9 days**)**, In children who used Other medications and no Bronchodilators at all, mean LOS was 46.44 hours **(**1.93 days**)**. There was statistically significance correlation with use of bronchodilators **(**p:0.01**)** and use of Bronchodilators with other medications: **(**p: 0.00**)** in relation to LOS in hospital, however there was no significant correlation between use of Bronchodilators **(**p: 0.35**)** Vs Use of other medications without bronchodilators **(**0.35**)** and LOS in hospital as shown in Figure 3.

Age in relation to length of hospital stay:

There was a negative correlation between Age and Length of stay of children in the hospital as demonstrated by Figure 4.

Organisms isolated in different Seasons

28% of children were screened for viral organisms. RSV was isolated in 35% children in winter months as opposed to only 9% of children in summer months. 16% of children showed presence of other viruses, and 38% showed presence of no organism as illustrated in figure 5.

Signs & Symptoms Vs Combination Treatment with BD and Other Medications

62.5 % children received a treatment of combination Bronchodilators with Other medications, most common combination being BD with hypertonic saline in 55% of children. Out of them there were equal number of children having only cough, RD with fever in 35%, and Poor feeding association with fever and cough 35%. Second most common combination was BD with Antibiotics, given in 26%. Of children. In these children the most common presenting feature was Cough & RD with fever 44%. 8% of the children received BD with steroids and amongst them, 50% of children had poor feeding, fever, cough & RD. 2.8% of children received a combination of BD, antibiotics & steroids and all these children had cough with distress & poor feeding but no associated fever. Results illustrated in Figure 6. Using Wilcoxon rank test there seems to be no correlation between presenting signs and symptoms and the different treatment modalities used along with bronchodilators.

Presenting Signs & Symptoms and treatment in Different Seasons

In both seasons, winter and summer, solely cough with respiratory distress was present in 16.9% of children. The most common presentation was a combination of fever & cough with respiratory distress **(**Winter: 21%, Summer: 18%**)**, followed by all four symptoms of cough with RD, poor feeding and fever **(**Winter 20%, Summer: 14%**)**. The frequency and severity of symptoms was more frequent in Winter months **(**59%**)** as compared to summer **(**41%**)**, as represented in figure 7. 10% of children admitted in winter and 12% admitted in summer received only bronchodilators. 38% children admitted in winter as opposed to 24% admitted in Summer received Bronchodilators with other medications

12% children admitted in Winter as opposed to 4% in summer received Other medications without bronchodilators. Using Wilcoxon signed rank test, showed there was a clear association between the median of different treatment modalities in the two seasons as shown in Figure 10

Gender role association with presenting Signs & Symptoms

In both boys and girls, the most common presentation was cough with RD & fever **(**Boys: 20.5%, Girls: 14.29%**)** followed by poor feeding and same symptoms as above **(**Boys 16.9 %, Girls: 13.3 %**)** as represented in Figure 8.

Frequency of treatment modalities in different genders

The most common treatment modality in both boys and girls was Bronchodilators in combination with other medications **(**62.5%**)**. Followed Bronchodilators alone **(**21.4 %**)** and use of Other medications without any bronchodilator at **(**16.07%**)** as represented in Figure 9.

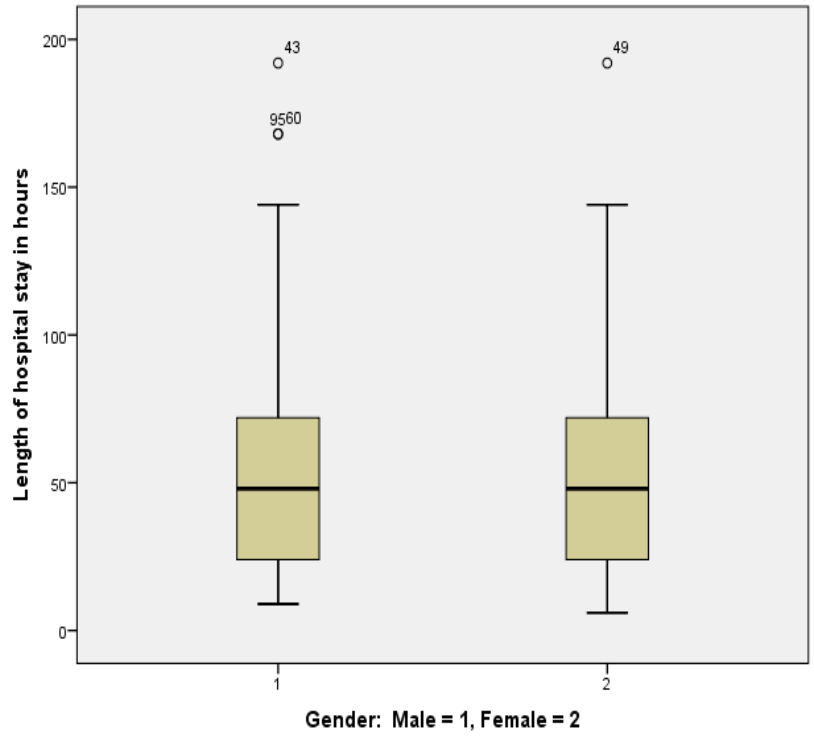

Figure 1. A Box plot: Gender Vs Median Length of hospital stay

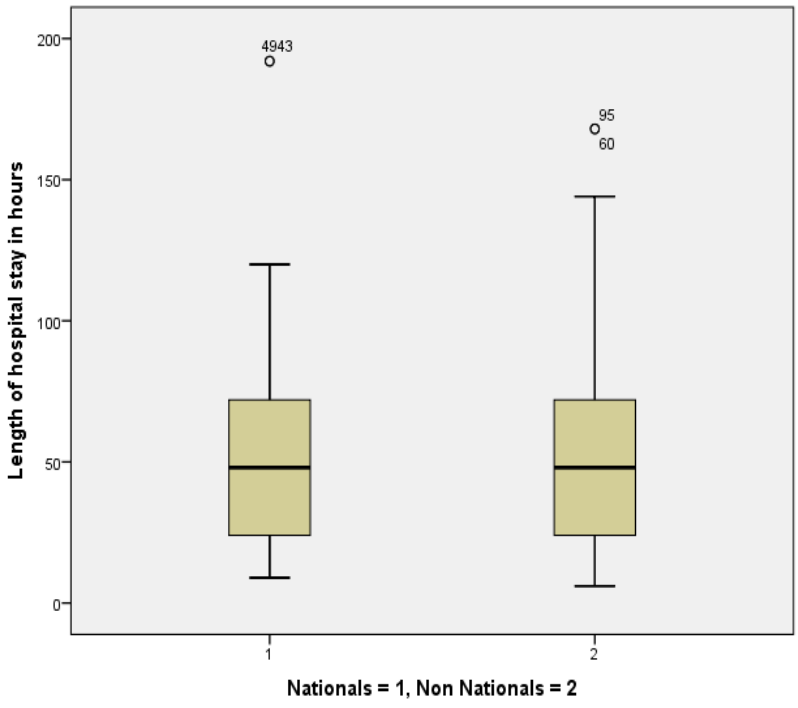

Figure 1. B Box plot: Nationality Vs Median Length of hospital stay

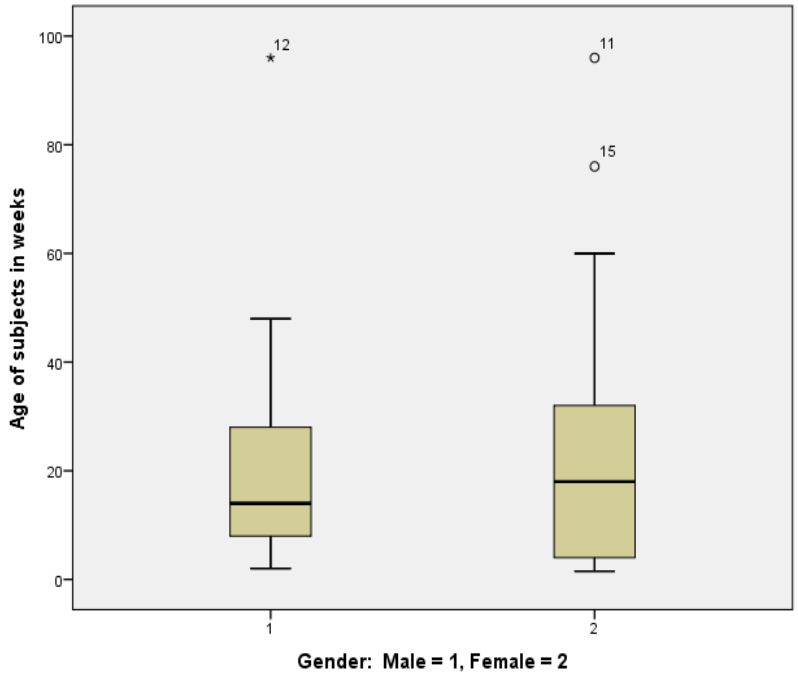

Figure 2. A Box plot: Age of children admitted in Boys and Girls

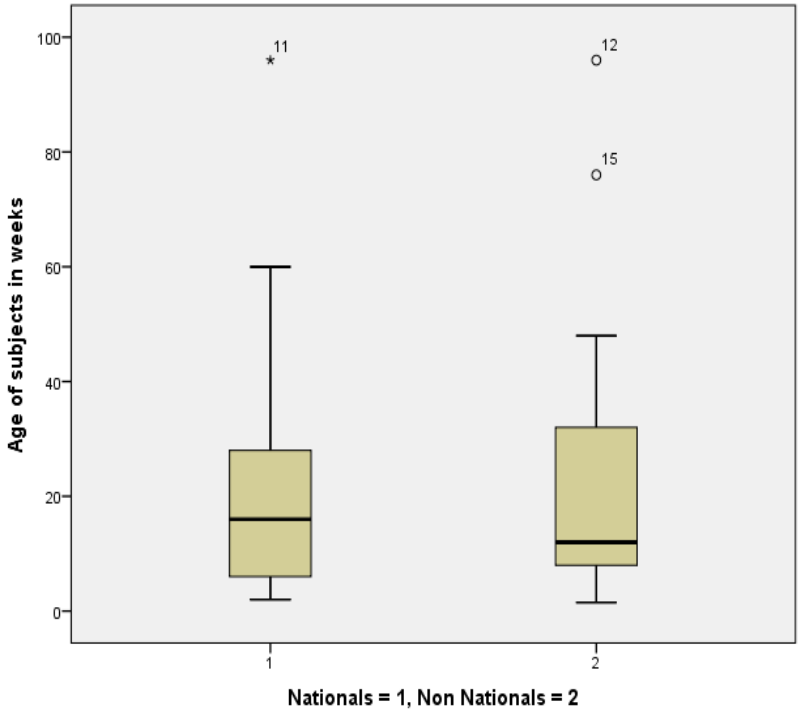

Figure 2. B Box plot: Age of children admitted amongst nationals and non-nationals.

	Mean LOS in hours	LOS (P Value)
Bronchodilators	38.42	0.01
Bronchodilators + other medications	70.31	0.00
Other medications	46.44	0.35

Figure 3. Mean LOS and p values of children who received BD VS BD with other medications, and only other medications

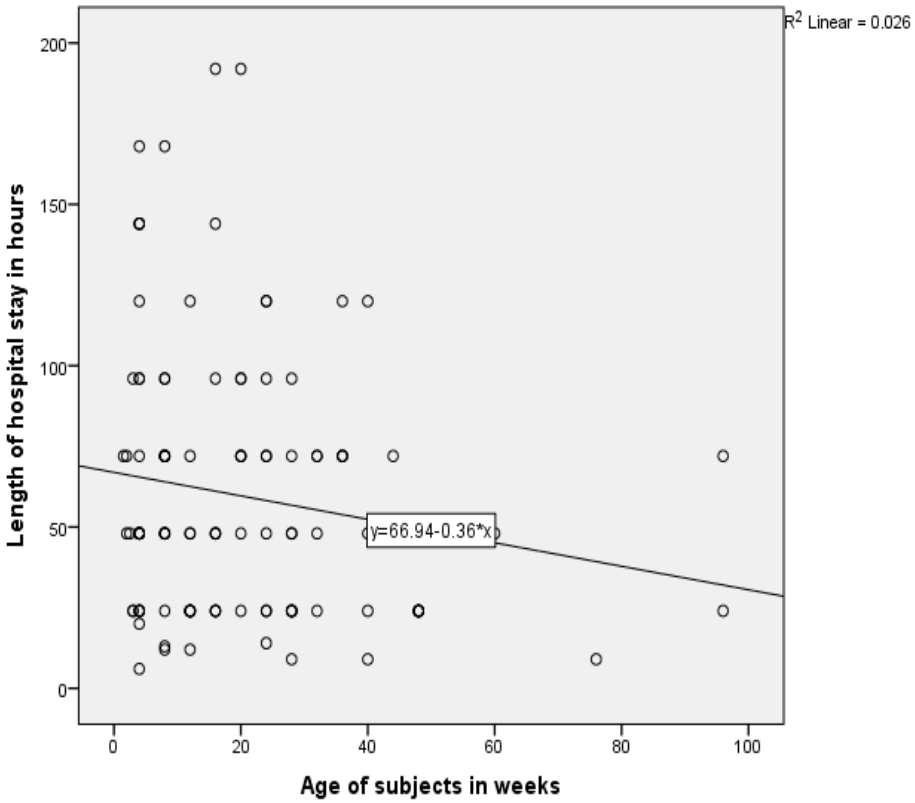

Figure 4. Correlation between Age and Length of hospital stay

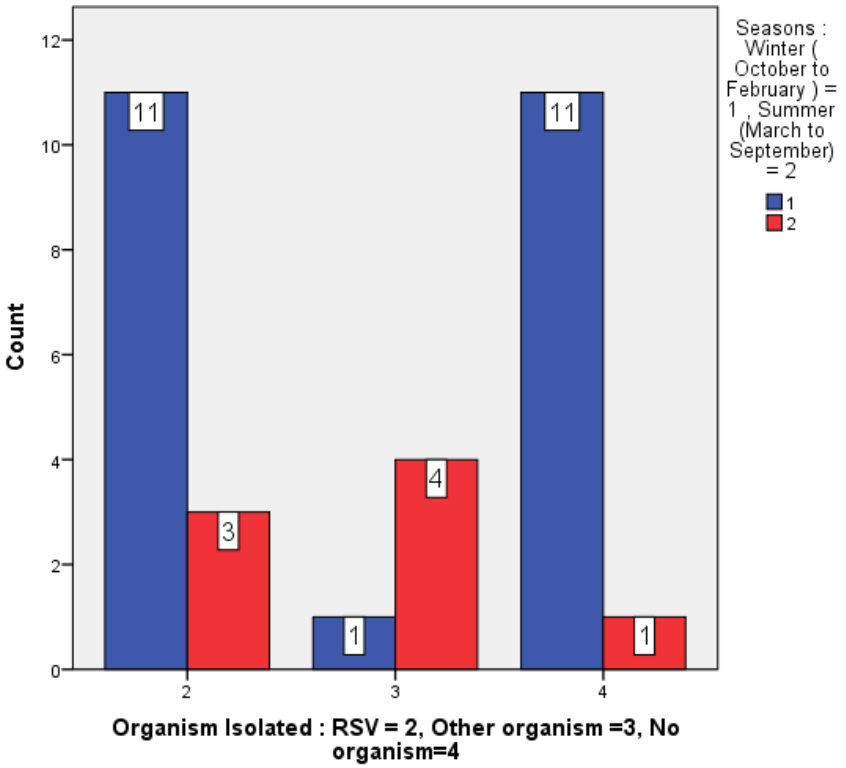

Figure 5. Bar Graph representing Number of Organisms isolated in each Season

Signs and Symptoms	BD with Other Medications = Antibiotics = 1, Steroids = 2, Steroids + Antibiotics = 3, Hypertonic saline = 4, others = 5					Total
	1	2	3	4	5	
Cough + RD	1	2	0	7	0	10
Cough + RD + fever	8	1	0	14	4	27
Cough + RD + poor feeding	3	0	2	4	0	9
Cough + RD + fever +poor feeding	6	3	0	14	1	24
Total	18	6	2	39	5	70

Figure 6. Table illustrating Signs & Symptoms Vs Combination Treatment with BD and Other Medications

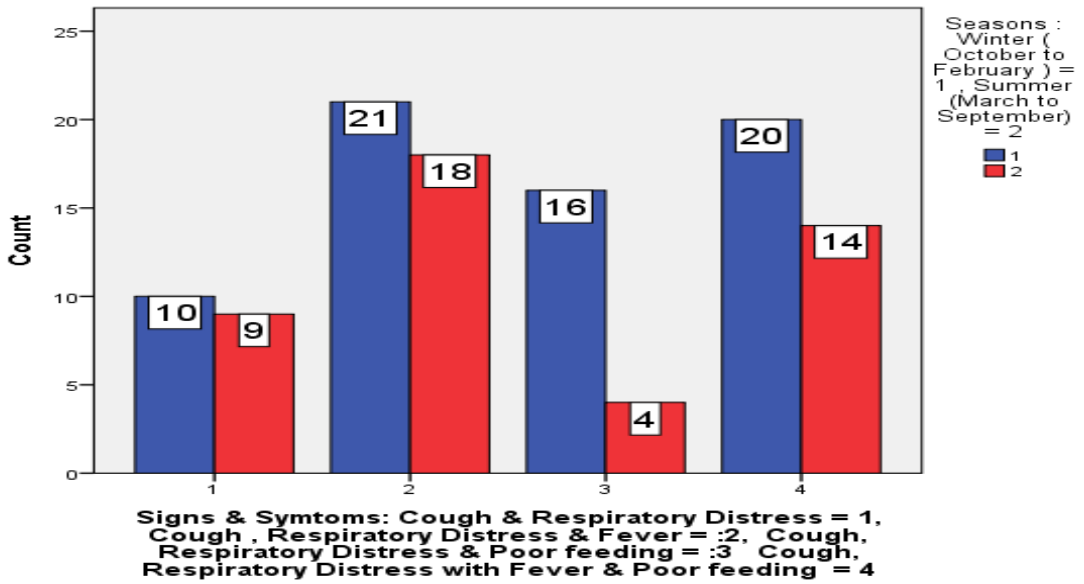

Figure 7. Frequency of Signs & Symptoms in Different Seasons

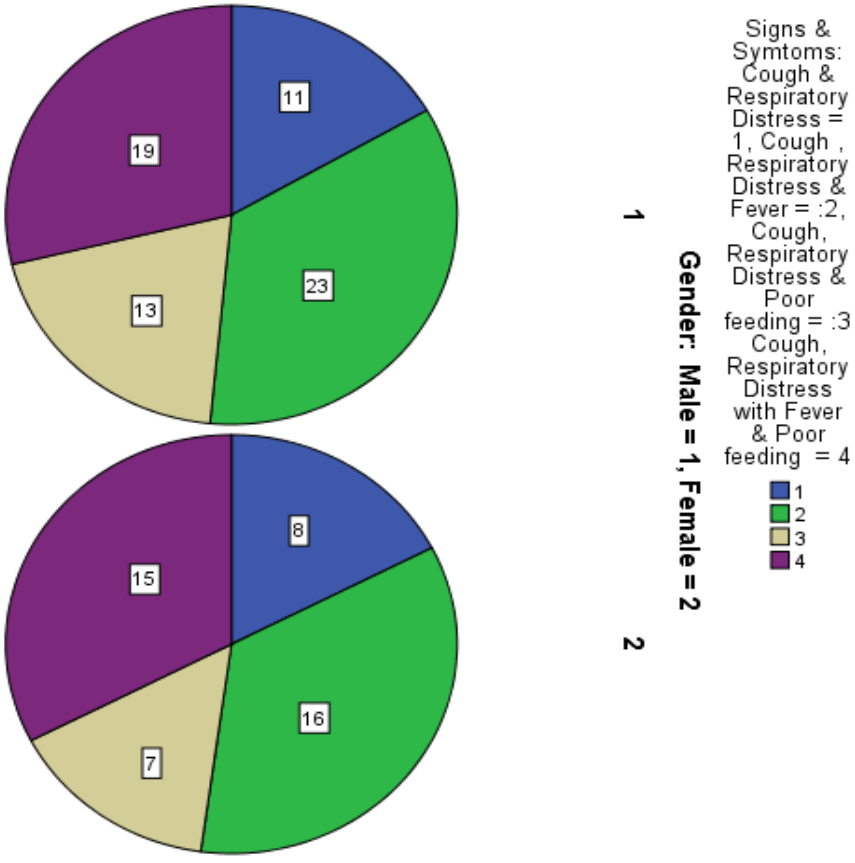

Figure 8. Frequency of Signs & Symptoms in Boys and Girls

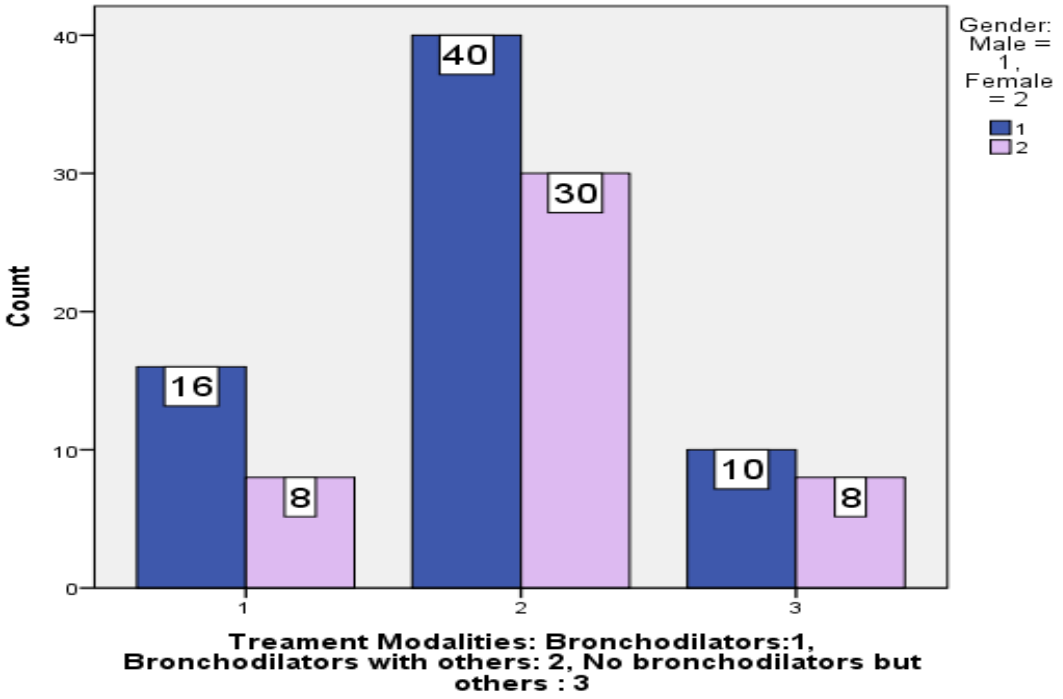

Figure 9. Frequency of various Treatment modalities in Boys and Girl

	Winter	Summer
Bronchodilators	10 %	12%
Bronchodilators + other medications	38%	24%
Other medications	12%	4%

Figure 10. Percentage of various Treatment modalities used in different Seasons

Discussion

Lower respiratory tract infection (LRTI) such as bronchiolitis, constitute the leading cause of global child morbidity and mortality (8). It is a leading cause of hospitalization in infants and young children (6) and it has also been shown that the rates of infant bronchiolitis hospitalization have also increased over the years significantly (9)

From 1997 to 2006 in the United States, the average annual rate of bronchiolitis among children younger than 5 years of age was 27.9 per 1,000 with half a million annual hospitalizations (7). Hospital costs for care related to bronchiolitis in children younger than 5 years of age have been on the rise in the United States and exceeded 1.7 billion US dollars in 2009 (6). It can present with a myriad of symptoms including respiratory distress, cough, feeding difficulty, fever and relative hypoxia.

Little is known about the epidemiology of bronchiolitis infections in the Middle East, including UAE. In our study, 154 patients were hospitalized at Dubai hospital, one of the largest governmental hospital with Pediatric Unit in United Arab Emirates, during the study period of one year, from September 2016 until September 2017 with a diagnosis of bronchiolitis or RSV bronchiolitis.

The incidence of bronchiolitis was 91% in all children admitted under the age of 2 years. It seemed to be the cause of majority of admissions. Total of 66.6% of patients were included in the study as we wanted to see the incidence of admission in previously healthy children who had a un interrupted hospital stay and study the various presenting signs and symptoms and their respective management, so all children with preexisting conditions such as bacterial pneumonia, Gastro esophageal reflux disease, recurrent viral triggered wheeze, congenital heart disease with heart failure, vascular rings, and chronic pulmonary disease with prolonged and recurrent wheeze, infantile asthma, cystic fibrosis, foreign body aspiration were excluded. Children who were discharged against medical advice were also not included, so there was no interruption in the treatment plan or preterm infants with prior intensive care unit or neonatal intensive care unit stay.

There was a higher percentage of boys admitted at 58% as compared to girls 42 %. Median Age of Boys admitted was 4 months. Median Age of Girls admitted was 4.5 months. In both boys and girls, the most common presentation was cough with Respiratory distress & fever (Boys: 20.5%, Girls: 14.29%) and was did not show variation in both winter and summer months (winter: 21%, summer: 18%) followed by a second most common combination of poor feeding and matching symptoms as above (Boys 16.9 %, Girls: 13.3 %) it was found to be evidently more common in winter months (winter 20%, summer: 14%). The most common treatment modality in both boys and girls was Bronchodilators in combination with other medications (62.5%), and amongst those other medications

most commonly used was hypertonic saline nebulization. This combination was frequently administered in winter months as opposed to isolated use of bronchodilators used in 21.4 % of admitted patients, and use of other medications without any bronchodilator at 16.07%. Mean length of hospital stay for boys 2.5 days and a median of 2 days. In girls, the mean length of hospital stay was 2.3 days, Median of 2 days.

These results demonstrate that both male and Female patients had a similar median age of admission at around 4 - 4.5 months and they had matching common presenting symptoms which included cough, RD and fever. The frequency and severity of symptoms was more frequent in winter months **(**59%**)** as compared to summer months **(**41%**)**, with most common treatment plan including combination of bronchodilators including Atrovent and Ventolin nebulization, along with other medications such as hypertonic saline, antibiotics and steroids. The most common combination used with bronchodilators was with hypertonic saline. There was not a statistically significant difference in length of stay in hospital amongst both boys and girls, or amongst nationals or non-nationals, however there was a negative trend in relation to age and length of stay, with relatively older children having a shorter hospital stay. Half of children were discharged within 2-3 days of hospital stay and majority had been discharged within five days of hospital stay.

There was also a statistically significance correlation with use of bronchodilators alone **(**p:0.01**)** and use of Bronchodilators with other medications: **(**p: 0.00**)** in relation to Length of hospital stay as compared to children who did not receive any bronchodilators at all. However, it showed that there was a longer mean length of hospital stay amongst children who used bronchodilators with other medications as opposed to other medications alone. This suggests that even though bronchodilator use may have a correlation with length of hospital stay it does not necessarily reduce the duration of hospital stay.

Many studies have documented that RSV is responsible for the majority of winter bronchiolitis hospitalizations **(**10**)** and annual RSV detections in the National Respiratory and Enteric Virus Surveillance System correlate closely with annual peaks of bronchiolitis hospitalizations in NHDS data **(**CDC unpublished data, 1990-1996**)**. **(**11,12**)**. Our study supports this. Even though majority of children were not screened for viral organisms, with more children not being screened in winter as opposed to summer months, only 28% of children were screened and amongst them RSV was isolated in 45 % of children, more so in winter months 79%, as opposed to only 21% of children in summer months.

Conclusion

In Conclusion, the incidence of Bronchiolitis in Dubai Hospital between a period of one year in children below 2 years of age from September 2016 till September 2017 was 91%. Majority of children presented at nearly 4 – 5 months of age. Most common presentation in both boys & girls, nationals and non – nationals was cough with respiratory distress and fever. Mostly admissions were during winter months and presented with a more severe combination of signs and symptoms. Even though majority of children were not screened for viral organisms, amongst those who were screened the most common organism isolated was RSV. A combination of Bronchodilators with other medications such as hypertonic saline and antibiotics was frequently used. Use of Bronchodilators, either alone or in combination with other medications had a statistically significant association with mean length of hospital stay but did not necessarily reduce the duration of hospital stay. Half of children were discharged within 2 to 3 days of hospital stay and majority within 5 days of hospital stay.

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