

Risk Factors For Respiratory Syncytial Virus (RSV) Bronchiolitis in Children. A hospital Based Study.

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ABSTRACT :

BACKGROUND:

Respiratory syncytial virus (RSV), historically being the major causative agent. RSV causes respiratory disease in young children worldwide and by the age of two years most children have been infected.

OBJECTIVE:

The aim of this study was to investigate the effect of passive smoking alone and in conjunction with breastfeeding and Crowding index and Family history of atopy in determining the risk of bronchitis in Children under of 5 years of age .

METHODS:

We studied 100 consecutive Children aged from (1)day to (60)months (56boys and 44 girls),median age 30 months, who required hospital admission for acute bronchiolitis at the Pediatric Department ,Children Welfare teaching hospital ,medical city complex - Baghdad.

The cases were compared with 100 patients at the same age groups with no history of Bronchiolitis .The following parameters was studied in both groups: Exposure to passive smoking, type of feeding (Breast, Bottle, and Mixed), Family history of atopy, and crowding index.

RESULTS:

High level of exposure to passive smoking on the other hand significantly increase the risk of having bronchiolitis by (2.3) times compared to those with negative exposure. Breast feeding significantly decrease the risk of having bronchiolitis by 5 times compared to those on mixed and bottle feeding.

A positive family history of atopy significantly increase the risk of bronchiolitis by (9.5)times . Subjects with moderately high crowding index (interquartile range)has 6.3 times of having increase the risk of bronchiolitis compared to those of living in uncrowded residence (first quartile crowding index).Highly crowding index (forth quartile)significantly increase the risk by 101 times compared to the those in un crowded (first quartile)residence.

CONCLUSION:

Although Smoking , Lack of Breast feeding and family history of atopy are important risk factors for RSV bronchiolitis But Crowding seems to be the most important risks factors for RSV bronchiolitis in this study.

KEYWORDS: risk factors, respiratory syncytial virus, bronchiolitis.

INTRODUCTION:

Internationally, respiratory syncytial virus (RSV) is the leading cause of lower respiratory tract disease during infancy and is responsible for 50–80% of hospitalizations for bronchiolitis. ⁽¹⁾

Respiratory syncytial virus (RSV) historically being the major causative agent. RSV causes respiratory disease in young children worldwide and by the age of two years most children have been infected ⁽²⁾.

In temperate climates the infection occurs as yearly

winter epidemics and the impact of RSV on human health is demonstrated annually when infants are admitted to hospitals in large numbers ⁽³⁾.

Symptoms vary from a mild upper respiratory tract infection to severe bronchiolitis with hyperinflated lungs and hypoxemia. ^(2, 3)

The first infection is usually the most severe but milder re-infections are common throughout life. The risk of severe illness is highest in infants born prematurely and in those with chronic lung disease, certain congenital heart defects and immunodeficiency disorders ⁽⁴⁾.

Major risk factors for RSV bronchiolitis hospitalization include: pre-term delivery, severe underlying cardiac, respiratory or neuromuscular disease, and immunodeficiency

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The aim of this study was to investigate the effect of some risk factors include: passive smoking alone and in conjunction with breastfeeding and crowding index and family history of atopy in determining the risk of Bronchitis in under of 5 years of age children.

PATIENT AND METHODS:

This a case control study studied 100 consecutive Children (56 boys and 44 girls),with median age 30 months(1day to 5 years), who required hospital admission for acute bronchiolitis at the Pediatric Department ,Children Welfare teaching hospital ,medical city complex ,Baghdad.

The cases were Compared with 100 children at the same age groups with no history of Bronchilolitis . After taking the detail history, clinical examination, CXR(Chest X-ray) and CRP(C-reactive protein) ,The following parameters was studied in both groups:

Detail of exposure to passive smoking, type of feeding (Breast, Bottle, Mixed), Family history of atopy (sneezing, eczema, food allergy, dermatitis, asthma.), and crowding index(NO. Of family members/NO. Of rooms).

RESULTS:

In this study, the gender had no statistically significant association with bronchiolitis. The slight increase in risk of having the condition attributed to male gender was not significant statistically. (Table1).

The low level of exposure to passive smoking increase the risk of bronchiolitis by only 20% (1.2 time increase) compared to those with negative exposure. The risk was however too small to be statistically significant .High level of exposure to passive smoking on the other hand significantly increase the risk of having bronchiolitis by (2.3) times compared to those with negative exposure.(table 1).

Breast feeding significantly decrease the risk of having bronchiolitis by 5 times compared to those on mixed and bottle feeding.

A positive family history of atopy significantly increase the risk of bronchiolitis by (9.5) times. (Table 1).

Subjects with moderately high crowding index (interquartile range)has 6.3 times of having increase the risk of bronchiolitis compared to those of living in uncrowded residence (first quartile crowding index).Highly crowding index (forth quartile)significantly increase the risk by 101 times compared to the those in un crowded (first quartile)residence.(table 1).

As shown in (table2),age group (1-6 months)was the most frequent (60%) age group involved in bronchiolitis.

To asses the net and independent effect of selected risk factors after adjusting for age and gender on the risk of having bronchiolitis as the outcome variable. A multiple logistic regression model was used (table 3).

The age and gender had no important or statistically significant association with the out come after adjusting for other independent variables included in the models.

A high level of exposure to passive smoking increase the risk of getting disease by(2.4) times compared to those with negative history of exposure ,but this effect was not statistically significant after adjusting for other independent variables included in the model.

A positive history of atopy in the family significantly increase the risk of bronchiolitis by ⁽⁹⁾times which is statistically significant.

Breast feeding has protective effect and significantly decrease the risk of getting the disease by 3 times compared to those on mixed and bottle feeding.

A moderately crowded (interquartile range)residence ,significantly increase the risk of having bronchiolitis by (7.7)times .While highly crowded (fourth quartile)residence is associate with significant increase the risk of (145.7) times compared to un crowded (1st quartile)residence ,after adjusting for remaining independent variables included in the model.

The overall model was statistically significant and was associated with an overall protective accuracy of 81. % (table 3).

Table 1: Case-control difference in relative frequency of selected risk factors.

	Controls		Cases (Bronchiolitis)		OR	95% confidence interval OR	P (Chi-square)
	N	%	N	%			
Gender							
Female	44	44	36	36	Reference		
Male	56	56	64	64	1.4	(0.8 - 2.5)	0.25[NS]
Total	100	100	100	100			
Exposure to passive smoking							
No smoking member	44	44	31	31	Reference		
Low exposure (other members of family)	30	30	26	26	1.2	(0.6 - 2.5)	0.56[NS]
High exposure (mother)	26	26	43	43	2.3	(1.2 - 4.6)	0.012
Total	100	100	100	100			
Breast feeding							
Bottle/mixed	53	53	86	86	Reference		
Breast	47	47	14	14	0.2	(0.1 - 0.4)	<0.001
Total	100	100	100	100			
Family history of atopy							
Negative	89	89	46	46	Reference		
Positive	11	11	54	54	9.5	(4.5 - 19.9)	<0.001
Total	100	100	100	100			
Crowding index							
First (lowest) quartile (<= 3.0)	57	57	11	11	Reference		
Inter-quartile range (3.1 - 5.0)	41	41	50	50	6.3	(2.9 - 13.6)	<0.001
Fourth (highest) quartile	2	2	39	39	101	(21.2 - 481.2)	<0.001
Total	100	100	100	100			

NS: Not significant

Table 2: Case-control difference in age distribution.

	Study group				P (Chi-square)
	Controls		Cases (Bronchiolitis)		
Age group (months)	N	%	N	%	
Neonate (<1)	10	10	13	13	0.001
(1-6)	33	33	60	60	
(> 6-12)	20	20	12	12	
(> 12-24)	30	30	11	11	
(> 24-60)	7	7	4	4	
Total	100	100	100	100	

Table 3: Multiple logistic regression model with the risk of having bronchiolitis as the dependent (explanatory) variable and selected explanatory (independent) variables.

	OR	P
Age in months	0.99	0.71[NS]
Male gender compared to female	0.8	0.64[NS]
Exposure to passive smoking		0.42[NS]
Low exposure (other members of family) compared to negative exposure	1.2	
High exposure (mother) compared to negative exposure	2.4	0.42[NS]
Positive family history of atopy	9.0	<0.001
Breast feeding	0.30	0.021
Crowding index		<0.001
Inter-quartile range (3.1 - 5.0) compared to First (lowest) quartile (<= 3.0)	7.7	
Fourth (highest) quartile compared to First (lowest) quartile (<= 3.0)	145.7	
Constant	0.1	<0.001

P (Model) < 0.001

Overall predictive accuracy = 81.5%

DISCUSSION:

The direction of the association between parental smoking and lower respiratory tracts illness is generally consistent across different study methods of case ascertainment, and diagnostic groupings, Fuat Gürkanetal, found that children admitted to the hospital with RSV bronchiolitis were shown to be acutely exposed to more cigarette smoke after 1 month and much more than the children admitted for non-respiratory diseases. These findings may imply that sudden heavy cigarette smoke exposure may predispose to an acute respiratory infection^(6,7).

Carroll et al-present probably the largest population-based study of term infants with bronchiolitis to determine the association between maternal asthma, maternal smoking, and the incidence and severity of bronchiolitis. In their cohort of >100000 mother-infant dyads, >20% of the infants had 1 health care visit for bronchiolitis. Maternal smoking increased the risk of bronchiolitis by 14%, maternal asthma raised it by 39%, and both together raised it by 47%.⁽⁸⁾.

In this study A high level of exposure to passive smoking increase the risk of getting disease by (2.4) times compared to those with negative history of exposure ,but this effect was not statistically significant after adjusting for other independent variables included in the model. May be due to high percentage of smokers among parents of the

hospitalized children in this study was high. However, a high percentage of parents currently smoking was also recorded in the control group.

The somewhat stronger effect of smoking by the mother than by other household members may be related to a higher degree of postnatal exposure from the mother as principal care giver.

Chatzimichael etal ,studied 240 consecutive infants aged from 6 to 24 months ,who required hospital admission for acute bronchiolitis at the Paediatric Department of Democritus University Hospital, Alexandroupolis, Greece. found that exposure to environmental tobacco smoke worsens the symptoms and the prognosis of bronchiolitis, while breastfeeding seems to have a protective effect even in children exposed to environmental tobacco smoke.⁽⁹⁾.

Similarly a lot of studies ^(10,11,12,13,14) established that increasing the proportion of exclusively breastfed infants seems to be an effective means of reducing infant illness at the community level. The experimental design suggests that the increased incidence of illness among minimally breastfed infants is causally related to lack of breast milk, rather than being attributable to confounding.

In this study Breast feeding has protective effect and significantly decrease the risk of having the disease

by (3) times compared to those on mixed and bottle feeding.

These findings have important implications for pediatric research. First, they strongly suggest that breast milk protection against acute respiratory infections is not universally conferred by passive transfer of humeral immunity⁽¹⁵⁾ or a soluble molecule with anti-infective properties which should be gender indifferent. In fact, breast milk-mediated maturation or activation of a critical protective pathway in the immune system or respiratory tract of girls seems likely⁽¹⁶⁾. A better understanding of the protective components in breast milk is important for strategically improving maternal nutrition and/or supplementing alternative sources of nutrition for infants who receive mixed feedings or no breast milk worldwide.^(17,18)

Overcrowding and bad ventilation appear to be to blamed for the high number of lung infections and one of the most dependable risk factors in our study. A range of mechanisms have been proposed as links between dwelling crowding and disease, including increased exposures to allergens, respiratory irritants and infectious agents in crowded dwellings⁽¹⁹⁾.

A number of epidemiological studies, using different measures of crowding such as total number of residents in the home, number of siblings, number of persons sharing the bed, room occupancy, and population density, have reported an association between crowding and respiratory diseases⁽²⁰⁾.

Another case-control studies conducted in South America Cerqueiro et al. Using three indicators of crowding, reported for inpatients odds ratios of the order of two associated with living in a household with more than 2 persons per room, with more than 4 siblings, and bed sharing. reported an association between household crowding and increased incidence of acute lower respiratory infection in young children⁽²¹⁾.

Kneyber et al found No significant difference between the RSV bronchiolitis and the control group were found regarding a personal history of atopy, a family history of atopy and/or asthma.⁽²²⁾

In this study A moderately crowded (interquartile range) residence, significantly increase the risk of having bronchiolitis by (7.7) times. While highly crowded (fourth quartile) residence is associate with significant increase the risk of (145.7) times compared to un crowded (1st quartile) residence, after adjusting for remaining independent variables included in the model.

Crowding may plausibly increase the risk of respiratory infection by increasing the opportunity for cross infection among the family. The agents of such infections are readily transmitted, usually through air by droplets or aerosols, in crowded and ill-ventilated rooms where people are sneezing, coughing or simply talking.⁽²³⁾

A positive history of atopy in the family significantly increase the risk of bronchiolitis and Seemed to be one of significant risk factor in first order family members for childhood bronchiolitis in this study.

The concept that RSV bronchiolitis accelerates allergic sensitization is further supported by the fact that the relative risk for sensitization was as high in many studies.^(24,25). Many infants with severe RSV bronchiolitis experience recurrent wheezing in later childhood and there is growing evidence that early-life RSV bronchiolitis may predispose some infants to the development of childhood asthma⁽²⁶⁾. The genetic background of the infant, intermittent changes in host cellular immune responses and neural control leading to sustained bronchial hyper-reactivity and recurrent wheezing, timing of RSV infection with respect to allergen exposure, environmental conditions and exposure to endotoxin are all factors suggested to contribute to RSV induced asthma⁽²⁷⁾.

CONCLUSION:

Although Smoking, Lack of Breast feeding and family history of atopy are important risk factors for RSV bronchiolitis But Crowding seems to be the most important risks factors for RSV bronchiolitis, a large study is needed to confirm these findings on the national basis.

REFERENCES:

1. Smyth RL, Openshaw PJ. Bronchiolitis. *Lancet*. 2006;368:312–22.
2. Simoes EA, Carbonell-Estrany X. Impact of severe disease caused by respiratory syncytial virus in children living in developed countries. *Pediatric Infectious Diseases Journal*. 2003;22:S13–20.
3. Janssen R. et al. Genetic susceptibility to respiratory syncytial virus bronchiolitis is predominantly associated with innate immune genes. *Journal of Infectious Diseases*. 2007;196:826–34.
4. Wilson J. et al. Genetic variation at the IL10 gene locus is associated with severity of respiratory syncytial virus bronchiolitis. *Journal of Infectious Diseases*. 2005;191:1705–09.

5. Amanatidou V. et al. T280M variation of the CX3C receptor gene is associated with increased risk for severe respiratory syncytial virus bronchiolitis. *Pediatric Infectious Diseases Journal*. 2006;25:410–14.
6. Strachan DP: Hay fever, hygiene and household size. *BMJ* 1989 ;299:1259-60.
7. Fuat Gürkan , Asuman Kızıl , Elif Dal and Fazilet Karakoç The effect of passive smoking on the development of respiratory syncytial virus bronchiolitis, *Epidemiology*.2000;16:56-60.
8. Carroll KN, Gebretsadik T, Griffin MR, et al. Maternal asthma and maternal smoking are associated with increased risk of bronchiolitis during infancy. *Pediatrics*. 2007;119:1104 –12.
9. Chatzimichael A Tsalkidis A, Cassimos D etal, The role of breastfeeding and passive smoking on the development of severe bronchiolitis in infants. *Minerva Pediatr*. 2007;59:199-206.
10. Major Michelle ,S. Flores MD: The Relationship of Breastfeeding to Antimicrobial Exposure in the First Year of Life. *Sage journal health science* ,october 2010.
11. Sinha A, Madden J, Ross-Degnan D, Soumerai S, Platt R. Reduced risk of neonatal respiratory infections among breastfed girls but not boys. *Pediatrics*. 2003;112.
12. Wright AL, Bauer M, Naylor A, Sutcliffe E, Clark L. Increasing breastfeeding rates to reduce infant illness at the community level. *Pediatrics*. 1998; 101:837 –44.
13. H Roine I, Fernandez JA, Vasquez A, Caneo M. Breastfeeding reduces immune activation in primary respiratory syncytial virus infection. *Eur Cytokine Netw*. 2005;16 :206 –10.
14. Anson LA, Korotkova M. The role of breastfeeding in prevention of neonatal infection. *Semin Neonatol*. 2002;7:275 –81.
15. Van de Perre P. Transfer of antibody via mother's milk. *Vaccine*. 2003;21:3374 –76.
16. Ryan-Poirier KA, Kawaoka Y. 2-Macroglobulin is the major neutralizing inhibitor of influenza A virus in pig serum. *Virology*. 1993;193:974 –76.
17. Buescher ES, McWilliams-Koeppen P. Soluble tumor necrosis factor-alpha (TNF-alpha) receptors in human colostrums and milk bind TNF-alpha and neutralize TNF-alpha bioactivity. *Pediatr Res*. 1998;44 :37 –42 .
18. Dani-Louise Dixon, Kim M. Griggs, Kevin D. Forsyth, Andrew D. Bersten :Lower interleukin-8 levels in airway aspirates from breastfed infants with acute bronchiolitis, *Pediatric Allergy and Immunology*,2010;21:691-96.
19. Simoes EA. Environmental and demographic risk factors for respiratory syncytial virus lower respiratory tract disease. *J Pediatr*. 2003;143:S118 –26.
20. Tina E Faber, Jan LL Kimpen & Louis J Bont :Respiratory syncytial virus bronchiolitis: prevention and treatment, expert opinion on pharmacology , 2008; 9: 2451-58.
21. Cerqueiro MC, Murtagh P, Halac A, Avila M, Weissenbacher M: Epidemiologic risk factors for children with acute lower respiratory tract infection in Buenos Aires, Argentina: a matched case-control study. *Rev Infec Dis* 1990;12:S1021-28.
22. Kneyber etal : Long-term effects of respiratory syncytial virus (RSV) bronchiolitis in infants and young children: a quantitative review, *Acta Paediatrica* 2000;89: 654–60.
23. Ballard TJ, Neumann CG: The effects of malnutrition, parental literacy and household crowding on acute lower respiratory infections in young Kenyan children. *J Trop Pediatr* 1995;41:8-13.
24. Murray M, Webb MS, O'Callaghan C, Swarbrick AS, Milner AD. Respiratory status and allergy after bronchiolitis. *Arch Dis Child* 1992;67:482–87 .
25. U. Schauer, S. Hoffjan, J. Bittscheidt, A. Köchling, S. Hemmis, S. Bongartz and V. Stephan. RSV bronchiolitis and risk of wheeze and allergic sensitisation in the first year of life. *Eur Respir J* 2002; 20:1277-83.
26. Kotaniemi-Syrjanen A, Reijonen TM, Korhonen K, Korppi M: Wheezing requiring hospitalization in early childhood: predictive factors for asthma in a six-year follow-up. *Pediatr Allergy Immunol* 2002;13:418-25.
27. Openshaw PJ, Dean GS, Culley FJ: Links between respiratory syncytial virus bronchiolitis and childhood asthma: clinical and research approaches. *Pediatr Infect Dis J* 2003;22:S58-S64.