ORIGINAL ARTICLES

Management of Bronchiolitis with or without Antibiotics –A Randomized Control Trial

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Summary:

Background: There has been epidemics of bronchiolitis in the recent years in Bangladesh. Bronchiolitis is mostly (95%) a viral disease in infants and young children but being treated with antibiotics in 99% of cases in our situation. Antibiotic has little role in the management of bronchiolitis. Very few randomized control trials without antibiotics in the management of bronchiolitis have so far been done.

Objectives: To evaluate the outcome of bronchiolitis with or without antibiotics in a hospital setting.

Methods: A randomized control trial was done during one winter season of 2005 with all cases of bronchiolitis attending a teaching hospital of Dhaka, Bangladesh. Sample size was selected conveniently. One hundred twenty six consecutive cases (one month up to 2years) with clinical bronchiolitis (runny nose followed by wheeze, cough, breathing difficulty perceived by caregiver, chest indrawing and rhonchi on auscultation) who attended the hospital were enrolled in the study. Detailed history and clinical examination were done and the children were randomized into 3 groups: (1) parenteral antibiotic group, paren AB (30) treated with supportive management and IV ampicillin, (2) oral antibiotic group, oral AB (33) treated with supportive management and oral erythromycin and (3) no antibiotic group, no AB (63) treated with supportive management only. The children were managed both in indoor and outdoor but very sick patients particularly those having oxygen saturation <90% were admitted into the hospital or excluded from the study (if not agreed for hospitalization). Oxygen therapy was given to cases having oxygen saturation < 90% and IV fluid (10% dextrose in 0.225% NaCl) was given to severely distressed children. Tube feeding was given to children who were unable to take milk by mouth but not very sick deserving IV fluid. Antibiotic was given according to the protocol. All children were followed up for 23 parameters, hospitalized cases were observed 8 hourly and outdoor (OPD) cases twice in the morning and at noon. Outcome measures were breathing difficulty, feeding difficulty, social smile, fast breathing (R/R > 50/m), hypoxia (oxygen saturation <95%), wheeze, rhonchi and crepitation. Verbal consent of the parents was taken before the study. Whenever patients condition became worse with the given treatment, the children was taken out of the study and more intensive management was given. Parents were also at liberty to discontinue the treatment process whenever they wanted irrespective of the reasons.

Results: Out of enrolled 126 children with bronchiolitis 104 (82.5%) improved and were discharged safely. The improved children in different groups were as follows: paren AB 29(27.8%) , oral AB 32(30.7%) and no AB 43(41.3%). Total 22 cases were excluded from the study, o1 from paren AB, 01 from oral AB and 20 from no AB group. Among them 18 were OPD cases , did not turn out on regular follow up, 2 cases left hospital on DORB and 2 cases were excluded from no antibiotic group for persistence of breathing difficulty and crepitation in the lung and treated with antibiotics. There was no death. Mean TWBC count was around 8500/cmm in all the groups. The mean value of neutrophil and lyphocytes were 33% and 61% respectively. Radiologically about 70% cases had hyperinflation, 52% cases had hypertranslucency and 56% cases had streaky densities. Hundred percent children had breathing difficulty at the time of inclusion into the study in all the groups. The decrement of breathing difficulty was gradual in all the groups and on day 5 only 27% in paren AB , 25% in oral AB and 34% in no AB group had breathing difficulty (p o.66). About 50% children had feeding difficulty at the

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beginning of study in all the groups. The decrement of feeding difficulty was found rapid and similar in all the groups and there was no feeding difficulty on day-5 in all the groups. Only 34% children in paren and oral AB group and 30% in no AB group had social smile on day-1. On day-3 about 90% of children of all the groups started smiling in spite of having fast breathing and chest in drawing. About 91% children had tachypnea (RR >50/m}at the time of inclusion into the study. The decrement of fast breathing was gradual and similar in all the groups and on day five only about 10% children had fast breathing and it was equal in all the groups (p.05). About 54% children had hypoxia during inclusion in all the groups (p0 .49). The improvement of hypoxia was rapid and similar in all the groups and on day-5 only 6.7% had hypoxia. Hundred percent children of all groups had wheeze at the beginning of the study. The decrement of wheeze was gradual and similar in all groups. On day five total 15% children had wheeze and it was almost equal in all the groups (p.82). The decrement of crepitations in all the groups was also gradual. During inclusion into the study about 60% children had crepitations and it was almost equal in all the groups and on day five about 14% children had crepitations in all the groups (p o.97).

Conclusion: The recovery of bronchiolitis managed with supportive therapy alone was found similar to those treated with combined supportive therapy and antibiotics (either oral or parenteral).

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Introduction:

Bronchiolitis is a common acute contagious respiratory illness of infants and young children involving the lower respiratory tract. It is the most significant respiratory illness of young children[1]. It is a viral disease. The most important causative agent is respiratory syncitial virus (RSV) and it accounts for bronchiolitis in more than 50% cases. Other causative agents are parainfluenzae, influenzae,adenovirus, mycoplas-ma pneumonae, herpes simplex, human metapneumovirus and mumps virus[2,3]. There is no evidence of a bacterial cause for bronchiolitis, although bacterial pneumonia is sometimes confused clinically with bronchiolitis[3].

During an epidemic in Bangladesh RSV was found as the most common responsible agent for bronchiolitis. In a recent study in the different hospitals of Dhaka city in the month of January and February 348 cases were diagnosed as bronchiolitis and were found positive for RSV antibody (1gM or 1gM and Ig G) in 50% cases[4]. In the same study it was found that antibiotics were used in almost all cases (99%). But the fact is that antibiotics have been shown to be of no benefit in the treatment of bronchiolitis[5]. In Canada 57%-81% of infants with diagnosis of bronchiolitis were getting antibiotics, despite the fact that antibiotics have been shown to be of no benefit in the treatment of bronchiolitis. In addition, there is evidence that RSV infection does not predispose to bacterial superinfection regardless of radiologic finding[6]. Kuppermann et al showed in a prospective cohort study that none of the 156 patients with bronchiolitis had bacteremia[7]. Secondary bacterial infections appear uncommon in RSV bronchiolitis. The routine use of antibiotics has not been shown to influence the course of bronchiolitis and there is little rationale for their use. Only when there is evidence of secondary infection should antibiotics be considered[5]. In a standardizing care of bronchiolitis by penny et al they concluded that antibiotics are indicated if bacterial pneumonia is suspected e.g. high fever, toxic appearance, WBC> 15,000 and lobar infiltrate[8]. It has been repeatedly shown that the excessive and often inappropriate use of antibiotics promotes the development of resistant organisms[9]. The incidence of bronchiolitis has been documented in recent years in Bangladesh[10]. We have developed a consensus in the guidelines for the management of bronchiolitis both at home and hospital settings[11]. Bronchiolitis is a viral disease and the most common cause is RSV. It is a self-limiting disease. As bacterial infections are rare in bronchiolitis, antibiotics have little therapeutic value[12]and antibiotics are not recommended unless there is concern for complications such as secondary bacterial pneumonia[13]

Materials and Methods:

This was a randomized control trial conducted during January to July 2005 in a teaching hospital, Institute of Child and Mother Health(ICMH) Matuail, Dhaka. Total 126 consecutive cases (one month upto two years) with clinical bronchiolitis were selected conveniently. Diagnosis of bronchiolitis was made on the basis of following inclusion criteria : age one month up to 2 years, preceding/ existing runny nose, cough, breathing difficulty (as perceived by the

caregiver), lower chest in-drawing, wheeze and rhonchi on auscultation. The exclusion criteria were: child with atopic conditions (asthma, allergic rhinitis, allergic conjunctivitis, atopic eczema), congenital heart disease, high fever >102°F and toxic appearance. Children below 2 years with breathing difficulty attended at outpatient department were identified and included in the study on the basis of inclusion criteria. Parents/attending relations were briefed about the study, its implications, management, follow up, their options to discontinue. The children whose caregiver agreed, were included in the study. A structured questionnaire was filled up through face to face interview with the caregivers at the beginning of the study. Detailed history and clinical examination were done and the children were randomized into 3 groups: (1) paren antibiotics (AB) who were treated with IV ampicillin and supportive management,(2) oral antibiotics (AB) who were treated with oral erythromycin and supportive management and (3) no antibiotics (AB) who were treated with supportive management only. Randomization was done on the basis of odd and even number. All odd number cases were managed with antibiotics (oral and parenteral alternately) along with supportive management and even number cases were managed with supportive management only. A pulse oximeter was used to observe the level of oxygen saturation in blood immediately after inclusion into the study. The very sick patient who had significant hypoxia (O_2< 90%), feeding difficulty and those selected into paren AB group were admitted into the hospital. Among them whose parents did not agree to be hospitalized were excluded from the study. Oral AB group was given syrup erythromycin 30-50 mg/ kg/ day every 6 hours[14], the paren AB group was given IV ampicillin 100-200 mg/ kg/ dose every 6 hours[15] and no antibiotic was given to no AB group. The supportive therapy was given to all cases according to national guidelines for the management of bronchiolitis[16]. All hospitalized children were managed with salbutamol nebulisation 6-8 hourly (0.15 mg/kg/dose), oxygen therapy (when oxygen saturation < 90%), IV fluid 10% dextrose in 0.225% Nacl (incase of severely distressed children), NG tube feeding to children who were unable to take milk by mouth but not very sick deserving IV fluid, paracetamol for fever and oropharyngeal suction when needed. Hospitalized children were followed up 3 times in 24 hours (9: 30am, 2.00pm and 8:00pm) and OPD cases were followed up two times (9:30am and 2:00pm) up to seven days in a structured follow up sheet. All OPD cases were either in oral or no AB group and nebulised in the morning and at noon and advised to take salbutamol syrup at a dose of 0.2- 0.4 mg/kg orally at night. Total 23 parameters were followed up daily which were: cough, runny nose, breathing difficulty, feeding difficulty, socialsmile, restlessness, inconsolable cry, sleeping difficulty, nasal blockade, convulsion, wheeze, chest indrawing, nasal flaring, cyanosis, impairment of consciousness, temperature, respiratory rate, heart rate, liver, spleen, rhonchi, crepitation and arterial oxygen saturation by pulse oximeter. Outcome measures were breathing difficulty, feeding difficulty, social smile, fast breathing (R/R > 50/m), hypoxia (oxygen saturation <95%), wheeze, rhonchi & crepitation. Hematological profile (total and differential count of WBC, Hb%, ESR,CRP) and X-ray chest was done in all cases. Criteria for discharge were satisfactory feeding as per mothers confidence, return of social smile and no significant hypoxia (SaO^2 >90%) in room air. The improvement of individual feature were defined as marked improvement: improvement of the feature in about 90% of children, rapid recovery: marked improvement occurring within 4 days, very rapid recovery: marked improvement occurring within 2 days, gradual recovery: marked improvement occurring beyond day- 4, very gradual recovery: marked improvement occurring at the end of day -7. All data were checked for consistency and correctness and scrutinized by one of the authors. The data were cleaned and entered by data enterers into the Epi-info program and analyzed in the SPSS software program with the help of an epidemiologist. Data recorded in a pretested questionnaire in to computer and analyzed by using SPSS statistical software employing appropriate statistical test like Chi square and determination of p value. Ethical approval was obtained from the Ethical Committee of ICMH and informed consent was taken duly from the parents before enrollment.

Results:

Most of the babies (92.2%) were within first year of life, 67.3% were male and 32.7% were female. Out of

enrolled 126 children 104(82.5%) improved and discharge safely. The improved children (104) who were as follows: paren AB (29) treated with IV ampicillin, oral AB (32) treated with oral erythromycin and no AB(43) given no antibiotics. Total 22 cases were excluded from the study, o1 from paren AB, 01 from oral AB and 20 from no AB group. Among them 18 were OPD cases , did not turn out on regular follow up, 2 cases left hospital on DORB and 2 cases were excluded from no antibiotic group for persistence of breathing difficulty and crepitation in the lung and treated with antibiotics. Hematological profile was like that of bronchiolitis[4, 22] in all the groups. Mean TWBC count was 8500/cmm. The mean value of neutrophil and lymphocytes were 33% and 61% respectively. CRP was found <6 in75% cases, 12 in 11.5% cases and 24 in 12.5% cases. Radiologically, all cases had the similar features suggestive of bronchiolitis[18], hyperinflation in 70%, hypertranslucency in 52% and streaky densities in 56% cases. All the children (100%) had breathing difficulty at the time of inclusion into the study in all the groups. The decrement of breathing difficulty was gradual in all the groups. There was a tendency of early recovery in oral AB and paren AB in comparison to no AB group but the tendencies were not significant p 0.66. On day-5 about 27% paren AB, 25% oral AB and 34% no AB had breathing difficulty (Fig-1). About 50% children had feeding difficulty at the beginning of the study; paren AB 41.3%, oral AB 40.6% and no AB 58% p 0.23. The decrement of feeding difficulty was found rapid and similar in all the groups and on day 5 there was no feeding difficulty in all the groups (Fig-2). About 33% of children had social smile at the time of inclusion in to

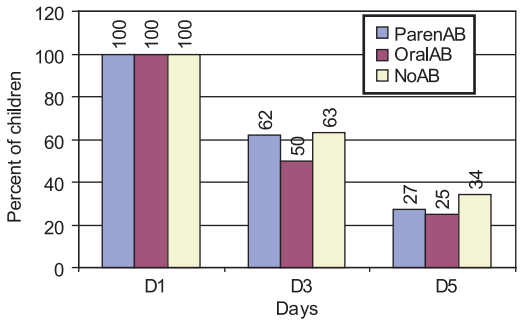

Fig.-1: *Gradual decrement of breathing difficulty in all the groups*

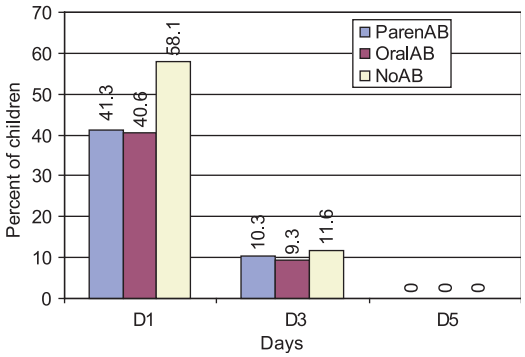

Fig.-2: *Rapid decrement of feeding difficulty in all the groups*

the study in all the groups, paren AB 34.5%, oral AB 34% and no AB 30% p0.90. There was rapid and similar improvement of social smile in all groups and on day 5 100% children in all groups developed social smile (Fig-3). About 90% children had tachypnea (RR>50 per minute) at the time of inclusion into the study, paren AB 86.9%, oral AB 93.7% and no AB 93%. The decrement of fast breathing was gradual and similar in all the groups and on day five total 10% children had fast breathing, paren AB 10.3%, oral AB 9.3% and no AB 11.6% p .05 (Fig -4). Fig 5 showed that about 54% children had hypoxia (SaO2 < 95%) at the time of inclusion in to the study, paren AB 62%, oral AB 46%, no AB 53.4% p 0.49. The improvement of hypoxia was gradual and similar in all groups and on day five total 6.7% had hypoxia paren AB 6.8%, oral AB 9.3%, no

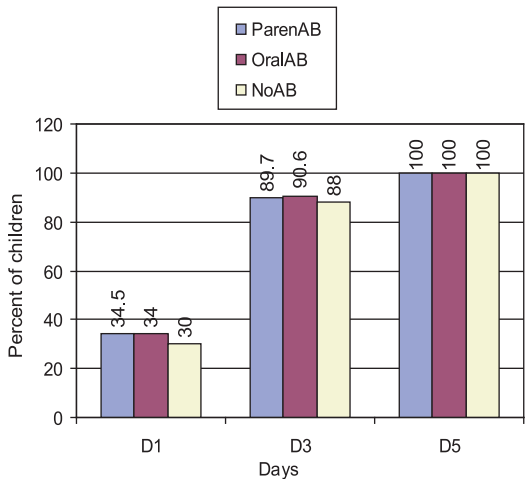

Fig.-3: *Rapid return of social smile in all the groups*

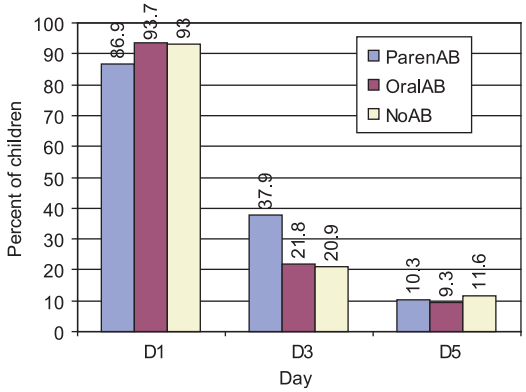

Fig.-4: *Gradual decrement of fast breathing (RR>50/min) in all the groups*

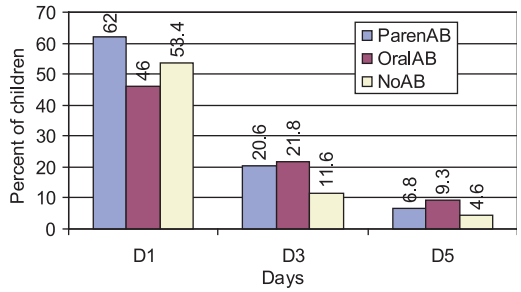

Fig.-5: *Gradual decrement of hypoxia in all the groups*

AB 4.6% . Hundred percent (100%) children had wheeze during inclusion into the study in all groups. On day 5 total 15% children had wheeze, among them paren AB 13.7%, oral AB 20.6%, and no AB 13.9% p.82 (Fig-6). On the day of admission 100%

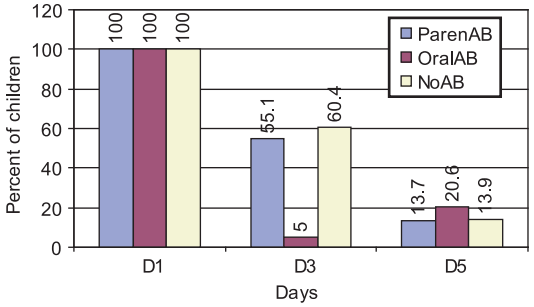

Fig.-6: *Gradual decrement of wheezing in all the groups*

children had rhonchi in all groups. On day 5 about one fifth of total children had rhonchi, paren AB 20.6%, oral AB 25% and no AB 20.9% p.89. About 60% children had crepitation during inclusion into the study. On day 5 total 14.42% children had crepitation, paren AB 13.7%, oral AB15.6% and no AB 14%. Liver and spleen were palpable in 53% and 22% cases respectively.

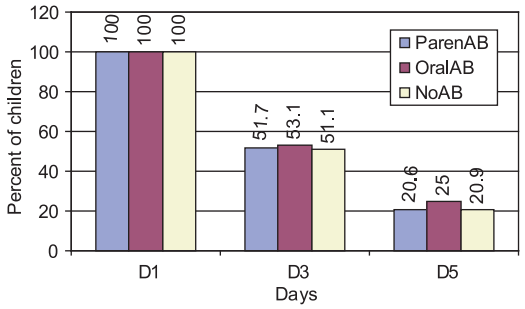

Fig.-7: *Gradual decrement of ronchi in all the groups*

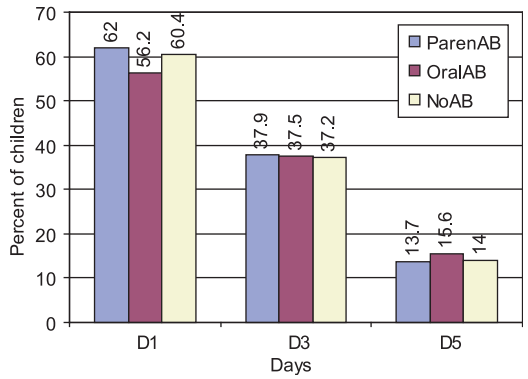

Fig.-8: *Gradual decrement of crepitation in all the groups*

Discussion:

This randomized control trial provides the opportunity to see the outcome of bronchiolitis with or without antibiotic in a hospital setting. We strictly followed the case definition of clinical bronchiolitis [13,17,18]. All children were one month up to 2 years with preceding/ existing runny nose, cough, breathing difficulty , lower chest indrawing, wheeze and rhonchi on auscultation. Hematological profile was similar to other studies[4,19] in all the groups, mean TWBC count was 8500/cmm. The mean value of neutrophil and lymphocytes were 33% and 61% respectively. Radiologically, all cases had the similar

features suggestive of bronchiolitis[13,19,20]. Hyperinflation in 70% and hyper translucency in 52% cases and streaky densities in 56% cases. Liver and spleen were palpable in 53% and 22% cases respectively because of downward displacement of these organs by the hyperinflation of the lungs. In this study the children were randomized into three groups according to odd and even number successively following enrollment into the study. The patients in three groups were as follows: paren AB (29). oral AB (32) and no AB (43).

Paren AB group was given intravenous (IV) ampicillin as was the recommendation of WHO for the treatment of severe pneumonia of hospitalized children in the Integrated management of Childhood Illness (IMCI) guideline[15]. The only non-viral cause of bronchiolitis is Mycoplasma pneumonae in 5% of cases. The median age of bronchiolitis in our situation was 3 months[4] and Chlamydia trachomatis is also a cause of afebrile pneumonia in infant of under 6 months of age [21,22] . Considering these two factors, oral erythromycin was chosen for another choice of antibiotic apart from IV ampicillin. All the children were managed with salbutamol nebulisation in addition to other supportive management whenever needed like IV infusion of 10% dextrose in 0.225% saline, oxygen therapy, NG tube feeding, oropharyngeal suction and paracetamol suspension for fever. All the children were treated free of cost to encourage the parents to stay in the hospital or to come on regular follow up in outdoor . In spite of all efforts twenty (15.8%) parents discontinued the treatment and excluded them from the study. All admitted cases were followed up 8 hourly and outdoor cases were followed up in the morning and at noon using a structured follow up sheet. The follow up features were 23 variables, 10 symptoms and 13 signs including estimation of oxygen saturation of blood by pulse oximeter. We were very liberal to address the ethical issue and the children whose condition deteriorated, were taken out of the study and further evaluation was done and treated accordingly. We were always vigilant on the child's condition in the hospital so that we could take out the child from the study group whenever needed, we also instructed the parents/caregivers who continued treatment at home to comeback immediately in the hospital when they felt that the condition of the child became precarious. Two cases were excluded from the study and given more intensive management as they were not improving by supportive management only. The parents were also at liberty to discontinue the treatment whenever they felt like. Twenty (15.8%) parents discontinued the management although initially agreed to be included in the study ,among them 18 parents (OPD case) did not come back for follow up and 2 parents left the hospital on risk bond during study and they were also excluded from the study. The limitation of the study was that we could not follow up all the cases for 24 hours as some cases (about one third) were outdoor cases and they were only followed up in the morning and at noon and number of dropout cases were very high (22%).Though all the cases were targeted for follow up for 7 days, some cases left the hospital after 5 days as parents felt improvement of their child and they were discharged on request and some OPD cases were also allowed to discontinue follow up on request as they registered significant improvement.. For this reason data was analyzed up to day 5. In this study it was found that the recovery was essentially similar in all the groups whether treated with IV antibiotic or oral antibiotic or no antibiotics. Recovery like social smile, feeding difficulty, breathing difficulty, chest indrawing and oxygen saturation in all the groups were almost similar. The improvement was rapid in the parameters of feeding difficulty and social smile in all the groups and it was on day 3 of hospitalization. The improvement was gradual in all the groups in the features like breathing difficulty, fast breathing, hypoxia, wheeze, rhonchi and crepitation. .It took 5 to 7 days for marked improvement.

One randomized control study so far conducted long ago on the use of antibiotic in bronchiolitis and it found no evidence to support the use of antibiotics for bronchiolitis[23] which corroborates present study results. Another randomized, double blind, placebo-control trial conducted and showed that clarithromycin had statistically significant effects on the clinical and laboratory findings in respiratory syncitial virus bronchiolitis. But the study was conducted with small sample size (21 infants)[24].

Conclusion:

The recovery of bronchiolitis managed with supportive therapy only, was found similar to those treated with antibiotics (either oral or parenteral) and supportive therapy. The recovery was rapid and similar in the features like feeding difficulty and social smile. The recovery was gradual and similar in other feature like breathing difficulty, tachypnea, hypoxia, wheezing, rhonchi and crepitation.

Recommendation: Further multi centre study with large sample size is needed to recommend or refute the role of antibiotic in bronchiolitis.

Reference:

1. Cherry JD: Newer respiratory viruses: their role in respiratory illness of children. Adv paediatr.1973;20, 225-290.
2. Weliver R Cherry JD. Bronchiolits and infectious asthma. In Feigin RD, Cherry JD(eds): Textbook of Paediatric infectious diseases, Philadelphia: WB Saunders, 1987 p 278-287.
3. Behrman RE, Kliegman RM, Jenson HB, Stanton BF Nelson Textbook of Pediatrics 18th edition 2007; 1773-1777.
4. Kabir ARM, HaqN, Amin R, Hossain A, Khatoon S, Shahin A et al. Evaluation of hospitalized infants and young children with bronchiolitis – a multi center study. Mymensingh Med J 2003 Jul; 12(2): 128-133.
5. Friis B, Andersen P, Brenoe E, Hornsleth A, Jensen A, Knudsen FU et al.Antibiotic treatment of pneumonia and Bronchilitis. Arch Dis Child 1984;59: 1038-1045.
6. Henderson M, Rubin E. Misuse of antimicrobials in children with asthma and Bronchilitis, A review. The Pediatrics Infect Dis J 2001;20: 214-215.
7. Kuppermann N, Bank DE, Walton EA, Senac MO Jr, McCaslin I. Risk for Bacteremia and Urinary Tract Infections in Young Febrile Children with Bronchiolitis. Arch Pediatr Adolesc Med Vol. 151. 1997; 1207-1214.
8. Adcock PM, Sanders CL, Marshall GS. Standardizing the care of Bronchiolitis Arch Pediatr Adolesc Med 1998;152: 739-44.
9. Spach DH, Black D. Antibiotic resistance in community acquired respiratory tract infections; Current issues Ann Allergy Asthma Immunol 1998;81: 293-302.
10. Kabir ARML. Bronchiolitis: was there an epdemic? Bangladesh J Child Health 2002;26(1/2): 1-2
11. Kabir ARML. Amin MR, Mollah AH, Khanam S et al. Proposed Guidelines for the management of bronchiolitis. Bangladesh J Child Health 2004; 28(3): 95-99.
12. Hall CB, Powel KR, Schnabel KC, Gala CL, Pincus PH, Risk of secondary bacterial infection in infants hospitalized with respiratory syncitial virus infection. J padiatr, 1998;113:266-271.
13. Fitzgerald DA, Kilham HA. Bronchiolitis: assessment and evidence-based management. Medical Journal of Australia 2004; 180: 399-404.
14. McIntosh N, Helms JP, Smyth LR Forfar and Arneil,s: Textbook of Pediatrics 6th edition 2003; 1315-1508.
15. Integrated Management of Childhood Illness (IMCI): treat the child manual. Government of the People,s Republic of Bangladesh, World Health Organisation and UNICEF, 2001.
16. Hassan MR, Hossain MA, Mahmud AM, Kabir AR, Amin MR, Rahman MM, Bennoor KS. National Guidelines: Asthma, Bronchiolitis, COPD, Asthma Association, Bangladesh, 2005.
17. Wohl MEB, Chemic V, State of the art: bronchiolitis. Am Rev Respir Dis 1978;118:59-81.
18. Duiverman EJ, Neijen HJ, van Strik R, Affoutit MJ, Kerrebijin KF, Lung function and bronchial respornsiveness in children who had infantile bronchiolitis. Pediatr Pulmonol 1987;3:38-46.
19. Ackerman BD: Acute bronchiolitis clin Pediatr 1962;1: 75-81
20. Ahmed F, Kabir ARML. Radiological evaluation of 162 cases of bronchiolitis. Bangladesh J Child Health 2003; 27: 6-9.
21. Tripple MA, Beem Mo, Sexon EM: Clinical characteristics of the afebrile pneumonia associated with Chlamydia trachomatis infection in infants less than 6 months of age. Pediatrics 1979;63:192-197.
22. Harison HR, English MG, Lee CK, et al. Chlamydia trachomatis infant pneumonitis : Comparison with matched controls and other infants pneumonitis. N Eng J Med 1978; 298: 702-708.
23. Spurling GK,Fonseka K, Doust J , Del Mar C. Antbiotics for bronchiolitis in children. Chochrane Database Syst Rev 2007; 24(1):CD 1. 005189.
24. Tahan F, Ozean A,Koc N.Clarithromycin in the treatment of RSV bronchiolitis; a double-blind, randomized, placebo controlled trial.Eur Respir J 2007; 29(1): 91-7.