CLINICAL PEDICTORS OF HOSPITALIZATION IN AN ACUTE ATTACK OF BRONCHIAL ASTHMA

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ABSTRACT

The present study was undertaken to identify the clinical predictors of hospitalization in an acute attack of bronchial asthma in subjects aged 2-12 years. Seventy five children with an acute attack of bronchial asthma were evaluated. A detailed clinical history and examination was recorded and baseline investigations sent before starting therapy. All subjects were treated with injection adrenaline (two doses) and those who did not respond were hospitalized. Twenty subjects who were hospitalized were compared with 32 cases who were discharged and did not have a relapse on follow up.

After multivariate analysis, the factors independently predictive of hospitalizatton were, pulsusparadoxus (>10mmHg; QR = 1.02), younger age (below 5 years, OR = 0.98) and severe accessory muscle use (OR = 89.6). Presence of any 2 of these 3 clinical pedictors has a high sensitivity (90%) and specificity (96%). The investigative variables significant after multivariate analysis were low pH (OR=0.00) and polymorphonuclear leucocytosis (>70%) on peripheral smear (OR=1.12). The sensitivity of this model was similar (90%) but specificity was lower (90.6%). The addition of investigative variables to clinical model did not improve the predictability. It is concluded that it is possible to identify at presentation, children with acute bronchial asthma who require hospitalization and clinical variables are sufficient for this purpose.

Keywords: *Bronchial asthma, Outcome, Hospitalization, Bronchodilator*

Bronchial asthma is a leading cause of both acute and chronic morbidity in children. In developed antions, it accounts for almost one-third of all the chronic conditions occurring annually in children and for nearly one-fourth of days lost from school because of chronic illness(l). There is a paucity of similar estimates from the developing countries.

Pediatricians on duty in the emergency ward often have to decide whether a child with an acute asthmatic attack would require hospitalization, and more intensive therapy. The usual practice which varies from place to place, consists mainly of giving a trial of bronchodilator therapy and reassessment. In the context of a developing country with meagre resources, criteria which could predict the need for hospitalization would result in more effective manpower utilization. Additionally, there may be a loss of precious time for inducting vigorous therapy fof a severe attack which could adversely affect the length of hospital stay and mortality.

There is thus an urgent need to develop clinical predictors of immediate hospitalization especially in the context of developing countries. However, there is limited data even from developed countries on this aspect and that too relates to older subjects (>5 years). The present study was, therefore, designed to identify clinical predictors for the need for hospitalization in an acute attack of asthma in children in the age group 2-12 years.

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Subjects and Methods

The present study was conducted in the Department of Pediatrics, Maulana Azad Medical College and Associated Lok Nayak Jai Prakash Narain Hospital on 75 children with an acute attack of bronchial asthma in the age group 2-12 years. Bronchial asthma for the purpose of the study was defined as per Sibbald's criteria(2), "Recurrent episodes of wheezing which occur in response to allergens, exercise or emotions as well as with symptoms suggestive of respiratory infection. On auscultation there should be high pitched wheeze over most parts of the lung". An acute attack was defined as any attack for which emergency consultation was needed. Patients with pulmonary tuberculosis, emphysema, or other known heart, liver, or lung disease or with skeletal disorders involving the spine were excluded.

After informed consent, the following baseline parameters were recorded. A detailed clinical history was elicited with special emphasis on duration of the attack, age of onset of the disease, its duration, frequency of attacks, number of hospitalizations, time since last attack, history of allergy or worm infestation, treatment history, and family history of asthma. Duration of attack was defined as the interval between the point of time when the patients or parents first perceived the respiratory symptoms to be worse than normal to the time they sought emergency medical assistance. Age at onset was taken as the time at which the parents could first remember episodes of acute respiratory distress.

Detailed clinical examination was carried out including anthropometry, pulse and respiratory rate, blood pressure, pulsus paradoxus, presence of cyanosis, and deformity of the chest wall, use of accessory muscles of respiration and chest auscultation. The pulse and respiratory rate were expressed as percentage of the mean(3) for that age and sex. Pulsus paradoxus was measured according to a standard method described in children(4). Accessory muscle use and rhonchi were graded as absent, mild, moderate or severe and numerical values (0, 1, 2, 3, respectively) assigned. The duration of inspiratory breath sounds was graded as normal or decreased.

Investigations carried out included hemogram with total eosinophil count, arterial blood gases, peak expiratory flow rate (PEFR) and X-ray chest. For arterial blood gases, blood was collected anerobically in a heparinized syringe from the radial or brachial artery, taking all recommended precautions, while the patient was at rest and breathing room air. It was then analyzed immediately for PaO_2, $PaCO_2$, and % pH using standard electrodes by a Eischweiler 2000 blood gas analyzer. Peak flow measurements were made using the Mini-Wright Peak Flow Meter (Clement Clarke, Columbus, Ohio). Each subject was asked to blow three times and the best of the three readings was recorded. The values were expressed as percentage of the predicted normal for that weight, height and sex using regression equations previously developed in Indian children(5).

Treatment was instituted according to a fixed protocol. Each patient was given a dose of injection epinephrine (0.01 ml/kg of 1:1000 dilution subcutaneously upto a maximum of 0.3 ml). If there was no evidence of clinical response within 20 minutes, the same dose was repeated. The use of epinephrine as a bronchodilator instead of β_2 agonist was based on the following considerations: (i) A vast majority of the

General and District hospitals are using this as a first mode of therapy since the relatively expensive nebulizer therapy is not available. The objective of the study was to document the clinical predictors in such a setting; *(ii)* With the parenteral route, one could be certain of drug absorption; and *(iii* The efficacy of subcutaneous epinephrine and nebulizer bronchodilator therapy is almost similar(6).

The need for admission was determined by conventional assessment, *i.e.,* minimal or absent responsiveness to the trial of bronchodilator. Discharge criteria were minimal or absent wheezing and lack of dyspnea and accessory muscle use. All decisions were made by the senior Registrar on duty in the emergency ward, who was not aware of the PEFR or the blood gas values.

Each child discharged from the emergency room was followed up to determine occurrence of relapse. Relapse was defined as a recurrence or exacerbation of symptoms within 10 days, so that a visit to a hospital's Emergency Department or an unscheduled visit to a physician's office was required. The children were divided into four groups depending upon the outcome: (i) *Group I* comprised of 20 children who did not respond to epinephrine and were hospitalized; (ii) *Group II* comprised of 32 children who were discharged and did not have a relapse on follow up; *(iii) Group III* comprised of 7 children who were discharged but relapsed within 10 days; and *(iv) Group IV* comprised of 16 children who were discharged, but could not be followed up and therefore their relapse status is not known.

All variables were subjected to univariate analysis by the Pearson Chi Square test. The variables which differed significantly between the admitted and treated groups were then subjected to multi-variate logistic regression analysis to adjust for confounders. Sensitivity and specificity curves were then constructed for each factor significant on multivariate analysis to determine a cut off point which best predicted outcome.

Results

Only Group I and Group II subjects were analyzed to determine the clinical predictors of hospitalization because Group III was too small and the relapse status was unknown in the last group. *Table I* depicts the summary statistics of Groups I and II for the various factors studied. *Table II* depicts the univariate risk factors after controlling for age. The significant clinical factors with respect to clinical history and examination were a younger age group, moderate to severe use of accessory muscles, a lower level of hepatic dullness, a significant pulsus paradoxus (PP), moderate to severe rhonchi on auscultation and decreased respiratory breath sounds. Significant investigative risk factors included hypercarbia, hypoxia, acidosis, and a higher polymorph count.

Table III shows the results of multivariate analysis along with the best cut off points, sensitivity and specificity values for each variable except pH. After adjusting for various confounders, the clinical factors independently predictive of hospitalization were a younger age, severe accessory muscle use and significant pulsus paradoxus. The best cut off points derived from sensitivity and specificity curves were age less than 5 years, severe accessory muscle use and a PP of more than 10 mm Hg. After multivariate analysis, the investigative factors independently predictive of outcome were a polymorphonuclear leucocytosis and acidosis.

TABLE I–*Summary [Mean (SD)] Statistics of Different Variables*

Variables	Group I (n = 20)		Group II (n = 32)	
	Mean	(SD)	Mean	(SD)
Age (mo)	60.6	(34.9)	85.9	(38.9)
Duration of attack (h)	23.9	(17.1)	56.3	(127.5)
Age at onset of disease (mo)	22.5	(28.4)	41.8	(39.3)
Duration of disease (mo)	37.5	(23.7)	44.1	(35.2)
No. of attacks per year	11.8	(10.3)	8.8	(6.7)
Previous hospitalization (in last 6 mo)	2.3	(4.0)	2.5	(6.7)
Recent hospitalization	0.3	(0.6)	0.1	(0.4)
Time since last attack (days)	79.3	(92.4)	107.1	(116.1)
Height for age (Z-score)	−1.3	(1.4)	−1.2	(1.1)
Weight for age (Z-score)	−2.4	(1.1)	−2.2	(0.8)
Weight for height (Z-score)	−2.2	(1.3)	−2.2	(0.7)
Duration of breast feeding (mo)	6.9	(6.6)	7.4	(6.6)
Pulse (% of normal)	143.0	(16.0)	137.8	(23.6)
Respiratory rate (% of normal)	251.0	(54.4)	203.0	(49.8)
Pulsus paradoxus (mm Hg)	17.9	(8.2)	4.8	(6.1)
pCO_2	40.3	(8.7)	33.5	(4.7)
pO_2	57.8	(10.6)	72.7	(13.0)
pH	7.3	(0.04)	7.4	(0.07)
Base excess	−5.5	(3.4)	−3.0	(3.5)
Polymorph count (%)	70.7	(11.6)	60.7	(11.0)
Eosinophils (%)	6.1	(4.4)	6.8	(6.8)
Hemoglobin (g/dl)	10.0	(2.2)	10.7	(1.4)

The sensitivity, specificity and cut off values for pH were not calculated because the mean values in Groups I and II were close to 7.3 which is clinically not very significant.

Multivariate analysis was utilized to select the combination of variables that best predicted admission. The clinical model predicted admission in 18 out of 20 cases, *i.e.,* out of 20 admitted cases 18 had pres-

TABLE **II-** *Univariate Risk Factors for Hospitalization*

Factor	Odd's ratio	p value
History		
Age	0.16	0.031
Duration of attack	0.98	0.25
Age at onset of disease	0.99	0.52
Duration of disease	1.01	0.56
Previous hospitalization	1.02	0.56
Recent hospitalization	2.39	0.164
Time since last attack	0.99	0.68
Family history of asthma	2.34	0.20
Height for age	0.69	0.190
Weight for age	0.71	0.314
Weight for height	0.97	0.920
History of worm infestation	0.75	0.621
History of allergy	0.36	0.260
Family history of smoking	0.71	0.582
Duration of breastfeeding	0.99	0.953
Clinical Examination		
Use of accessory muscles	241.05	0.003
Level of hepatic dullness	3.48	0.008
Breath sounds	48.38	0.003
Rhonchi	4.48	0.004
Pulse rate	0.97	0.110
Pulsus paradoxus	0.79	0.0004
Investigations		
$PaCO_2$	1.17	0.006
PaO_2	0.90	0.006
pH	0.00	0.003
Base excess	0.98	0.081
Polymorph count	1.09	0.007
Total eosinophil count	0.99	0.981
Hemoglobin	1.14	0.498

TABLE III–*Results of Multivariate Logistic Regression Analysis*

Variable	Odd's ratio (95% CI)	p value	Sensitivity (%)	Specificity (%)
Clinical				
Age	0.98 (0.92-0.96)	0.017	70	69
Acc. Musc. Use	89.66 (15.6-515.9)	0.013	85	90
Pulsus paradoxus	1.02 (0.93-1.11)	0.055	60	88
Investigative				
pH	0.00	0.002	*	*
Polymorph count	1.12 (1.07-1.16)	0.006	65	81

* Explained in the text.

ence of any two of the three significant clinical predictors. Only one out of 32 cases who were discharged had two or three clinical risk factors at presentation. Thus, the clinical model had a very high sensitivity (90%) and specificity (96%). The model with combination of investigative variables had identical sensitivity (90%) but lower specificity (90.6%). The addition of investigative variables to the clinical model did not significantly improve, the predictability of the model.

PEFR was tried in all children who could co-operate. Out of 75 children, 30 were too small or too sick to co-operate. As the number who could perform the test was small, it was difficult to statistically analyze the results. However, certain impressions can be made. All 10 children with a PEFR more than 18% of the predicted normal were successfully discharged. Of the 20 children admitted, 9 were big enough to cooperate. Only one had a PEFR > 10% of predicted normal. Five were too sick to cooperate, and even after the first dose of adrenaline, four out of five could not co-operate while in one, the PEFR was 9% of the predicted normal. Of the 32 children successfully discharged, 23 were big enough to cooperate. Only four (17%) had PEFR <10% of predicted normal. Only one was too sick to cooperate, but after the first dose of adrenaline his PEFR was 48% of predicted normal.

Discussion

Every child presenting to the emergency room with an acute attack undergoes a fixed treatment protocol before getting admitted or discharged. Consequently, many patients can continue to wait for the decision for hospitalizations in a busy and often hectic emergency room. Institution of vigorous therapy may be delayed for such patients thereby increasing their suffering, length of hospital stay and mortality risk.

The present study which included children under 5 years of age also, documented that it is possible to select such children on the basis of clinical profile and/or investigations.

On the basis of clinical profile, the three significant independent predictive factors were: a younger age (<5 years), severe accessory muscle use and pulsus paradoxus (> 10 mm). Earlier available studies in older (>5 years) children(7,8) using appropriate multivariate analysis have not found such results. We could find no study in children less than 5 years. However, it is well known that bronchodilators are less effective in younger children(9). Also, younger children are at increased risk for serious obstruction because of disproportionately narrow small airways, decreased bronchiolar smooth muscle, excessive intraluminal mucous production and decreased static elastic recoil. This could explain their greater risk of admission. Severe accessory muscle use was found to be a significant univariate variable by earlier workers(10,12), however, other studies using multivariate analysis did not find it to be significant(7,8). Significant pulsus paradoxus (>10 mm Hg) alone or along with severe accessory muscle use is indicative of a severe acute attack. Both of these have been found to be independently predictive of lack of responsiveness to treatment. Only disadvantage of pulsus paradoxus is that it may be difficult to assess in very young and irritable children.

The significant investigative variables independently predictive of outcome were acidosis and polymorphs more than 70%. There is paucity of such reports on predictive value of these investigations for hospitalization in children for comparison.

Hypercarbia has been associated with severe asthma in adults in some studies(13,14). Others(15) reported that $PaCO_2$ levels were not related to the severity of the episode. In this study hypercarbia and hypoxia along with arterial pH were significant risk factors on univariate analysis but on multivariate analysis only pH was predictive of admission. It may be pertinent to state that although arterial blood pH helps in predicting children at risk for admission, the facility may not be available in all centres treating patients with an acute attack of asthma. Moreover, in this study the pH values in admitted and discharged groups were not significantly different clinically. Also, patients may not allow an arterial blood gas (ABG) analysis for each attack. For these reasons, although ABG is predictive of admission, it cannot be recommended for routine use.

Polymorphonuclear (PMN) leucocytosis could have been a response to the stress of an acute attack or associated with bacterial infection. Workers have reported PMN leucocytosis to be present in patients with acute asthma(16) but its value in predicting the outcome of an attack has not been analyzed earlier. This is an easy bedside test which can also help in predicting admission.

Using combination of variables of three high risk factors, (age less than 5 years, severe use of accessory muscles, and pulsus paradoxus of more than 10 mm) presence of two or all three of these factors was highly predictive of admission. Severe accessory muscle use was the most sensitive and specific individual risk factor to predict the outcome (sensitivity = 85% and specificity = 90%) but when combination of clinical factors was used the predictability was higher, than all factors individually (sensitivity = 90% and specificity = 96%).

Clinical variables were found to have same sensitivity and higher specificity value than investigative variables. Addition of investigative variables to the clinical model did not improve the sensitivity and specificity thereby proving that bed side clinical assessment was sufficient to predict the need for hospitalization.

Although handicapped by the shortage of sample size, our results suggest that PEFR is a simple noninvasive investigation which appears to have a promising role in this context. Many studies in children and adults have also highlighted the utility of this investigation(7,ll,17,18). However, some workers have not found it to be useful(8,19). Again the cost and availability of the instrument may preclude its widespread use in developing countries.

It is concluded that a younger age (<5 years), pulsus paradoxus >10 mm, and severe use of accessory muscle are significant clinical predictors of hospitalization. Such children may be admitted directly and immediately put on vigorous treatment which could help in more efficient management of time and personnel.

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