

Factors Influencing Acute Exacerbation of Bronchial Asthma Among Children in Malaysia

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Abstract: The aim of this study was to determine the factors influencing acute exacerbation of bronchial asthma among children in Malaysia. A cross-sectional study was done to identify the factors influencing acute exacerbation of asthma in the University Malaya Medical Centre. In this study 103 known asthmatic children between the ages of 2 to 12 years were analysed. Among the children, 60% had a family history of asthma, 39% allergic rhinitis and only 17% eczema. The main complaints were coryza (84%) and shortness of breath (88%). Majority of the patients were treated as out-patient (58%) and only two were admitted in Intensive Care Unit. The factors that were significantly associated with mild exacerbation compared to a moderate to severe exacerbation was well-controlled asthmatic, good compliance to medications and those who had regular follow up.

Keywords: Bronchial asthma, exacerbation, factors associated.

INTRODUCTION

Asthma is a major public health problem with a huge social and economic burden affecting 300 million people worldwide [1]. It is the most common chronic respiratory disease, affecting up to 10% of the adults and 30% of the children in the Western world. Proper diagnosis of asthma is mandatory in clinical practice in order to avoid unnecessary use of potentially toxic asthma medications. In the latest International Study of Asthma and Allergies in Childhood (ISAAC III), it was estimated that the prevalence of asthma in Malaysia had increased from 6.4% to 9.4 % in children aged 6-7 years and from 9% to 13 % in children aged from 13-14 years [2]. A major part of the burden of disease is caused by acute exacerbation in general practice and emergency department in the hospitals. Despite advances in asthma management, acute exacerbation continues to occur and impose considerable morbidity on patients and constitute a major burden on health care resources [3, 4].

Although the majority of these children are not hospitalized, the exacerbation is associated with significant cost and morbidity. As part of the Global Initiative for Asthma (GINA) guidelines in maintaining well-controlled asthma is the prevention of asthmatic exacerbations [5]. Exacerbations can be defined as the presence of either one of the following:

- signs and symptoms of airflow obstruction within the past 48 hours (e.g. cough, wheezing, shortness of breath and chest tightness).

- repeated use of short-acting beta-agonists within the past 48 hours.

MATERIALS AND METHODS

A cross-sectional study was conducted from November 2010 until November 2011 at the University Malaya Medical Centre (UMMC). All children between the ages of 2 years to 12 years with acute exacerbation of bronchial asthma in the Trauma & Emergency (UMMC) and the General Paediatric Wards (including Paediatric Ward 2, 4, 5 and Paediatric Intensive Care Unit) of UMMC were included in the study. Ethical approval was obtained from the University Malaya Ethical Committee. There were a total of 624 children aged 2 to 12 years seen in the University Malaya Medical Centre (UMMC) Paediatric Trauma & Emergency Unit and the wards for asthma exacerbations during this period. Using the convenience sampling method 124 patients were recruited in this study. Out of 124, the data from 21 children were incomplete and so 103 children were included in the study. A face to face interview using a questionnaire was used in the study. The inclusion criteria were all children between 2 to 12 years of age with acute exacerbation of bronchial asthma who had been previously diagnosed with bronchial asthma and the exclusion criteria was children below 2 years or above 12 years of age, children whose parents or guardians who refused consent for the study and also children diagnosed with asthma but without any exacerbation.

Statistical analysis was carried out using SPSS version 20 (PASW) and Microsoft Excel database. A p value of < 0.05 was considered as significant.

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Table 1: Atopy among Immediate Family Members of the Patient (%)

Condition	Father	Mother	Other sibling	>1 family member	None
Eczema	0	8	10	17	84
Allergic rhinitis	16	15	8	29	71
Asthma	20	22	36	59	41

RESULTS

Majority of the children were ethnic Malays 76 (74%), followed by Indians 18 (17%) and the Chinese were 9 (9 %.). There were more males 60 (59%) than females 43 (41 %.). About 48% were between 2 to 5 years of age, 30% were 6 to 9 years of age and 22% were 10 to 12 years of age. Only 42 (41%) of these children were breast fed and 56 (54%) had at least one parent who smoked. Most of the mothers 47 (46%) were housewives, about 24 (23%) were clerical or skilled and about 27 (26%) were professionals. Majority 49 (48%) of the fathers were professionals followed by skilled manual/clerical 30 (29%) and unskilled were 22 (21%). Table 1 shows that 59% of patients had more than one family member with asthma, 29% with allergic rhinitis and 17% with eczema.

Table 2 shows that although asthma was the most common atopic condition in the family, the family history of atopy did not correlate with the severity of asthmatic exacerbation.

Most of these patients' asthma was diagnosed early. About 80% of the patients were diagnosed with asthma before the age of five, about 32 % by the 2nd year, 54% by the 3rd year and 68% by the 4th year with only 21% of patients diagnosed after the age of five years. Follow up of the patients was examined among the patients and it was noticed that 69% had some follow up, whether it was with a general physician or private paediatrician. About one third (32%) of the patients had regular follow up in the University Hospital paediatric asthma clinic. Thirty one percent (31%) of patients did not have any follow up and some of these patients sought self-care by buying asthmatic medications from private pharmacists. Control of asthma was measured using the GINA Guidelines 2006 for control of asthma. It was noticed that 29% of the patients were well controlled, 52% were partially controlled and 19% were uncontrolled. Most of the patients in this study were from the partially controlled group with less than one third from well controlled. It was noticed that 22% of patients were seen with acute exacerbation of asthma.

Table 2: Family History of Atopy among the Asthmatic Children

History of atopy		p value	OR (95% CI)
Asthma	Father	0.86	0.92 (0.21-4.16)
	Mother	0.68	1.61 (0.42-6.19)
	Sibling	0.47	0.79 (0.17-3.65)
	>1 member	0.60	1.00 (0.42-2.37)
	None	0.60	0.91 (0.14-6.14)
Allergic rhinitis	Father	0.48	0.21 (0.02-1.76)
	Mother	0.23	0.76 (0.09-5.88)
	Sibling	0.37	0.22 (0.02-2.39)
	>1 member	0.64	1.81 (0.65-5.05)
	None	0.64	0.12 (0.01-1.43)
Eczema	Father	-	-
	Mother	0.89	-
	Sibling	0.04	-
	>1 member	0.13	0.29 (0.07-1.15)
	None	0.14	-

Table 3: Factors Associated with Severity on Acute Exacerbation of Asthma

Variables	Moderate-Severe N (%)	Mild N (%)	p-value	OR (95% CI)
Gender				
Male	37 (60.7)	24 (39.3)	0.91	1.00
Female	25 (59.5)	17 (40.5)		0.95 (0.43, 2.13)
Age (years)				
2 - 5	30 (61.2)	19 (38.8)	0.96	1.00
6 - 9	18 (58.1)	13 (41.9)		0.88 (0.35, 2.19)
10 - 12	14 (60.9)	9 (39.1)		0.99 (0.36, 2.72)
Race				
Malay	46 (60.5)	30 (39.5)	0.39	1.00
Chinese	7 (77.8)	2 (22.2)		2.28 (0.44, 11.74)
Indian	9 (50.0)	9 (50.0)		0.65 (0.23, 1.83)
Body Weight (kg)				
<10	10 (58.8)	7 (41.2)	0.86	1.00
11 – 20	24 (66.7)	12 (33.3)		1.40 (0.43, 4.60)
21 – 30	13 (52.0)	12 (48.0)		0.76 (0.22, 2.63)
31 – 40	9 (60.0)	6 (40.0)		1.05 (0.26, 4.32)
>40	6 (60.0)	4 (40.0)		1.05 (0.21, 5.16)
Monthly Family Income (RM)				
<3000	32 (62.7)	19 (37.3)	0.62	1.00
3000 – 8000	28 (59.6)	19 (40.4)		0.88 (0.39, 1.98)
>8000	2 (40.0)	3 (60.0)		0.40 (0.06, 2.59)
Mother's Age (years)				
31 – 40	48 (61.5)	30 (38.5)	0.52	1.00
>40	13 (54.2)	11 (45.8)		0.74 (0.29, 1.86)
Father's Age (years)				
31 – 40	39 (61.9)	24 (38.1)	0.66	1.00
>40	23 (57.5)	17 (42.5)		0.83 (0.37, 1.87)
Gestational Age at Birth				
Term	60 (60.6)	39 (39.4)	0.67	1.00
Pre-term	2 (50.0)	2 (50.0)		0.65 (0.09, 4.81)
Birth Weight (kg)				
<2.5	7 (58.3)	5 (41.7)	0.89	1.00
2.5 – 4.0	55 (60.4)	36 (39.6)		1.09 (0.32, 3.70)
Father Asthmatic				
Yes	13 (61.9)	8 (38.1)	0.83	1.00
No	49 (59.8)	33 (40.2)		0.90 (0.33, 2.42)
Mother Asthmatic				
Yes	13 (56.5)	10 (43.5)	0.66	1.00
No	49 (61.3)	31 (38.8)		1.24 (0.48, 3.17)
Sibling Asthmatic				
Yes	24 (64.9)	13 (35.1)	0.40	1.00
No	38 (57.6)	28 (42.4)		0.73 (0.32, 1.68)
Other Medical Condition				
Eczema	9 (64.3)	5 (35.7)	0.46	1.00
Allergic Rhinitis	3 (42.9)	4 (57.1)		0.42 (0.65, 2.66)
Others	14 (73.7)	5 (26.3)		1.56 (0.35, 6.94)
No	36 (60.2)	27 (42.9)		0.74 (0.22, 2.46)

(Table 3). Continued.

Variables	Moderate-Severe N (%)	Mild N (%)	p-value	OR (95% CI)
Exposure to Smoking				
Yes	36 (64.3)	20 (35.7)	0.36	1.00
No	26 (55.3)	21 (44.7)		0.69 (0.31, 1.52)
Ever Breastfed				
Yes	56 (60.2)	37 (39.8)	0.78	1.00
No	6 (60.0)	4 (40.0)		0.82 (0.20, 3.28)
Breastfed \geq 4 months				
Yes	23 (54.8)	19 (45.2)	0.33	1.00
No	39 (63.9)	22 (36.1)		1.51 (0.66, 3.49)
Compliance to Medication (n = 69)				
Yes	16 (43.2)	21 (56.8)	0.01	1.00
No	24 (75.0)	8 (25.0)		3.94 (1.40, 11.04)
Follow-up				
General Practitioner	11 (64.7)	6 (35.3)	0.68	1.00
Private Pediatrician	13 (61.9)	8 (38.1)		0.89 (0.23, 3.35)
UMMC Asthma Clinic	14 (42.4)	19 (57.6)		0.40 (0.12, 1.35)
None	24 (75.0)	8 (25.0)		1.64 (0.46, 5.87)
Control				
Well	10 (33.3)	20 (66.7)	<0.001	1.00
Partial	34 (64.2)	19 (35.8)		3.58 (1.39, 9.20)
Uncontrolled	18 (90.0)	2 (10.0)		18.00 (3.47, 93.38)
Trigger				
Exercise	3 (60.0)	2 (40.0)	0.42	1.00
Dust	6 (66.7)	3 (33.3)		1.33 (0.14, 12.81)
URTI	48 (63.2)	28 (36.8)		1.14 (0.18, 7.26)
Cold	5 (38.5)	8 (61.5)		0.42 (0.05, 3.43)
Outcome (previous)				
Admitted	34 (79.1)	9 (20.9)	0.001	1.00
Discharged	28 (46.7)	32 (53.3)		0.23 (0.09, 0.57)
Fever				
Yes	28 (57.1)	21 (42.9)	0.70	1.00
No	34 (63.0)	20 (37.0)		1.18 (0.52, 2.66)
Coryza				
Yes	53 (61.6)	33 (38.4)	0.68	1.00
No	9 (52.9)	8 (47.1)		0.80 (0.27, 2.37)
Shortness of Breath				
Yes	55 (60.4)	36 (39.6)	0.91	1.00
No	7 (58.3)	5 (41.7)		0.93 (0.27, 3.24)
Wheeze				
Yes	38 (65.5)	20 (34.5)	0.25	1.00
No	24 (53.3)	21 (46.7)		0.62 (0.28, 1.40)
Apnoea				
Yes	0 (0.0)	0 (0.0)	n/a	n/a
No	62 (60.2)	41 (39.8)		
Diarrhoea				
Yes	1 (25.0)	3 (75.0)	0.18	1.00
No	61 (61.6)	38 (38.4)		4.75 (0.48, 47.52)

(Table 3). Continued.

Variables	Moderate-Severe N (%)	Mild N (%)	p-value	OR (95% CI)
Vomiting				
Yes	7 (63.6)	4 (36.4)	0.88	1.00
No	55 (59.8)	37 (40.2)		0.91 (0.25, 3.33)
Pulse Rate (pulse per minute)				
≤120	17 (45.9)	20 (54.1)	0.03	1.00
>120	45 (68.2)	21 (31.8)		2.52 (1.10, 5.78)
Respiratory Rate (per minute)				
<20	1 (50.0)	1 (50.0)	0.16	1.00
20 – 40	41 (53.2)	36 (46.8)		1.14 (0.07, 18.87)
>40	20 (83.3)	4 (14.7)		5.00 (0.26, 97.68)
Hb level (n = 37)				
9 – 13	27 (87.1)	4 (12.9)	0.20	1.00
>13	3 (50.0)	3 (50.0)		0.23 (0.02, 2.20)
Virology				
Virus isolated	13 (59.1)	9 (40.9)	0.91	1.00
Virus not isolated	49 (60.5)	32 (39.5)		1.06 (0.41, 2.77)
Antibiotic Use (n = 40)				
Yes	17 (81.0)	4 (19.0)	0.80	1.00
No	16 (84.2)	3 (15.8)		1.31 (0.16, 10.57)
Admission to PICU (n = 40)				
Yes	2 (100)	0 (0.0)	0.87	n/a
No	31 (81.6)	7 (18.4)		

The presenting complaints during these exacerbations showed that eighty four percent (84%) of patients complained of cough and cold (coryza symptoms), 91% shortness of breath and 56% complained of wheezing as the main complaint. None of the patients presented with apnoea and less than 15% presented with diarrhoea and vomiting. Most of the patients (70.8%) perception were that the cause of their current asthma exacerbation was an upper respiratory infection and the second common trigger (13%) reported was due to cold weather or cold drinks. Only 5% of patients had exercise induced exacerbations.

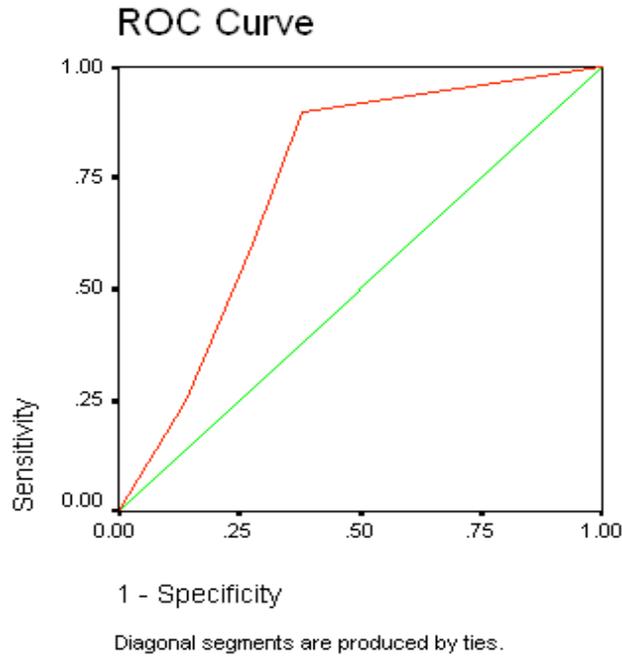
A multiple regression was done for factors that were associated with mild and moderate to severe exacerbation of asthma (Table 3). Most of the variables studied were not associated with acute exacerbation of asthma. The variables associated with acute exacerbation of asthma was compliance to medication, follow up of the patient in one of the clinics and whether the asthma was well controlled or not as well as the outcome of the exacerbation ($p < 0.05$).

Table 3 shows the bivariate regression findings where most of the variables were not significant for

acute exacerbation. The factors that were significant were compliance to medication, whether the patient had previous admissions or whether asthma was well controlled or not. If there was poor compliance to medication there is was 3.94 times more likely that the patient would get acute exacerbation. In the multivariate analysis, factors significantly associated with moderate to severe exacerbation of asthma ($p < 0.05$) were compliance to medication, control of asthma and outcome of previous admissions. Patient discharged from ward was 0.23 less likely to suffer from moderate to severe exacerbation of asthma compared with patient admitted to the ward. A Receiver Operating Characteristic curve (ROC) was performed on the multivariate model. The model was computed by multiple logistic regression controlling for variables including compliance to medication, control, outcome and pulse rate. The model has an area under the curve of 0.743 (95% confidence interval: 0.615 - 0.871).

DISCUSSION

In our study it was found that the only factors that were significantly associated with acute exacerbation were compliance to medication, whether the patient had previous admission or whether asthma was well



controlled. If there was poor compliance to medication there was a 3.94 times likely that the patient would get acute exacerbation whether viruses were present or not. In the multivariate analysis, factors significantly associated with moderate to severe exacerbation of asthma ($p < 0.05$) were compliance to medication, control of asthma and outcome of the previous admission.

Patients complained that the upper respiratory tract infection was the most common trigger followed by cold weather or cold drinks. Our study showed that a well-

controlled asthmatic who is compliant to medications and has some form of regular follow up would have a mild exacerbation compared to a moderate to severe exacerbation.

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REFERENCES

- [1] Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004; 59(5): 469-78. <http://dx.doi.org/10.1111/j.1398-9995.2004.00526.x>
- [2] Pearce N, Ait-Khaled N, Beasley R, *et al.* ISAAC III study of worldwide trends of asthma. *Thorax* 2007; 62: 757-65. <http://dx.doi.org/10.1136/thx.2006.070169>
- [3] Jackson DJ, Sykes A, Mallia P, Johnston SL. Asthma Exacerbation: origin, effect and prevention. *J Allergy Clin Immunol* 2011; 128(6): 1165-74. <http://dx.doi.org/10.1016/j.jaci.2011.10.024>
- [4] Malai P, Johnston SL. How viral infections cause exacerbation of airway diseases. *Chest* 2006; 130(4): 1203-10. <http://dx.doi.org/10.1378/chest.130.4.1203>
- [5] Tregoning JS, Schwarz J. Respiratory viral infections in infants: causes, clinical symptoms, virology, and immunology. *Clin Microbiol Rev* 2010; 23: 74-98. <http://dx.doi.org/10.1128/CMR.00032-09>