International Journal of Contemporary Pediatrics
Manikumar K et al. Int J Contemp Pediatr. 2019 Nov;6(6):2610-2617
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20194741

Original Research Article

Simple predictors to differentiate acute respiratory infections from acute asthma in children 6 months to 5 years

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Revised: 27 August 2019
Received: 29 May 2019
Accepted: 31 August 2019

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ABSTRACT

Background: Acute respiratory infections constitute one of the principal causes of morbidity and mortality in children less than five years of age in developing countries. For logistic reasons, WHO recommended case management is structured towards treatment as pneumonia in preference to acute asthma. It is warned that wheezing can occur during pneumonia and therefore, care must be taken when treating wheezing not to miss treating pneumonia with an antibiotic. Current WHO ARI CASE MANAGEMENT guidelines, in a child presenting with cough and rapid breathing, there is a predilection for over -treatment of pneumonia and under treatment of asthma.
Methods: Totally 245 children were included in the study. They were classified into asthmatic and LRI prone with the help of simple predictors.
Results: The combination of fever, chest indrawing and persistent tachypnoea after bronchodilator has an excellent specificity of 96.12% in predicting the presence of pulmonary infiltrate**.** The presence of more than two episodes of similar respiratory distress, previous H/O of nebulization and family H/O asthma, either alone or in combination may point more towards asthma as a cause of cough and respiratory distress.
Conclusions: In a child presenting with cough and fast breathing with a previous similar episode, trial nebulization can be given before investigating further for pneumonia.

Keywords: Antibiotics, Asthma, Bronchodilator, Pneumonia, Simple Predictors, WHO Criteria

INTRODUCTION

Acute respiratory infections constitute one of the principal causes of morbidity and mortality in children less than five years of age in developing countries.

It is estimated that 3.9 million children die annually from ARI, most of them been from developing countries.[1,2]

Pneumonia refers to an infection of the lungs, which can be caused by a variety of microorganisms, including viruses, bacteria, fungi, and parasites.

Signs and symptoms

Symptoms of pneumonia vary, depending on the age of the child and the cause of pneumonia. Some common symptoms include:

- Fever
- Chills
- Cough
- Unusually rapid breathing
- Breathing with grunting or wheezing sounds
- Labored breathing that makes a child's rib muscles retract

- Vomiting
- Chest pain
- Abdominal pain
- Decreased activity
- Loss of appetite (in older children) or poor feeding (in infants)
- In extreme cases, cyanosis

When pneumonia is caused by bacteria, the child usually becomes sick relatively quickly and experiences the sudden onset of high fever and unusually rapid breathing. When pneumonia is caused by viruses, symptoms tend to appear more gradually and are often less severe than in bacterial pneumonia. Wheezing may be more common in viral pneumonia. In developing countries, like India, with high infant mortality rates, pneumonia is contributed mainly by bacteria. Agents causing pneumonia are far wide when compared to adult population.

The current WHO strategy for control of mortality due to ARI relies heavily on STANDARDISED CASE MANAGEMENT.[3] This includes utilization of simple signs and symptoms with high sensitivity and specificity to be adopted at first level health facilities by paramedics. Thus, among children with ARI three main groups have been identified.

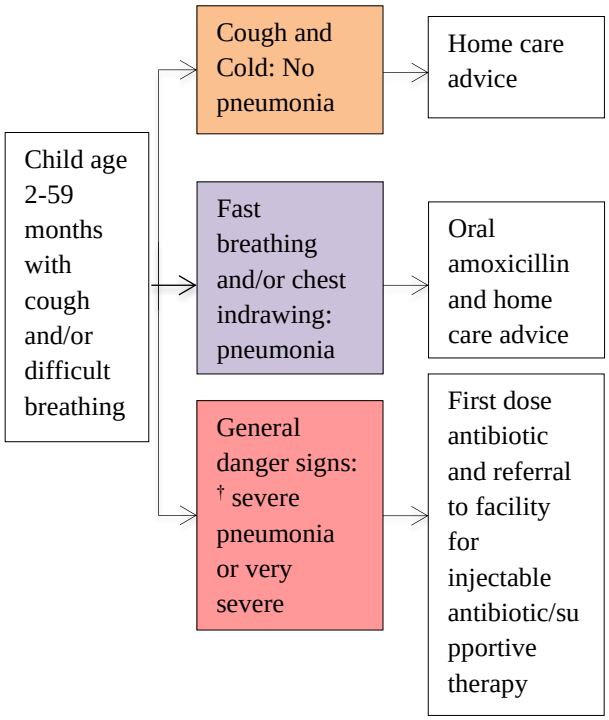

Figure 1: Revised WHO classification and treatment of childhood pneumonia.

Not able to drink, persistent vomiting, convulsions, lethargic or unconscious, stridor in a calm child or severe malnutrition.

For logistic reasons, the WHO recommended case management is structured towards treatment as pneumonia in preference to acute asthma. It is warned that wheezing can occur during pneumonia and therefore, care must be taken when treating wheezing not to miss treating pneumonia with an antibiotic.[4,5] Further, the need for bronchodilator therapy is guided by the presence of a wheeze which for paramedical personnel pertains to only an estimated one-third episodes in which the wheeze may be audible without the aid of a stethoscope. Thus, according to the current guidelines, in a child with cough and rapid breathing, there is a predilection for over-treatment for pneumonia with antibiotics and for under-treatment for asthma with bronchodilators. There is thus an urgent need for refining the available algorithm for case management to reliably differentiate pneumonia from acute asthma.[1,6]

Asthma

Asthma is a chronic inflammatory disorder of the airways characterized by an obstruction of airflow, which may be completely or partially reversed with or without specific therapy.[7] Airway inflammation is the result of interactions between various cells, cellular elements, and cytokines. In susceptible individuals, airway inflammation may cause recurrent or persistent bronchospasm, which causes symptoms including wheezing, breathlessness, chest tightness, and cough, particularly at night or after exercise.

Signs and symptoms

- Cough
- Fast breathing
- Retractions
- Decreased activity
- Grunt and wheeze (audible and auscultatory)
- Cyanosis, in extreme cases

Since signs and symptoms of asthma and pneumonia have considerable overlap, in current WHO ARI CASE MANAGEMENT guidelines, in a child presenting with cough and rapid breathing, there is a predilection for over -treatment of pneumonia and under treatment of asthma.

METHODS

Study Design was descriptive, Study Period was January 2017 to January 2019 at outpatient department in Sree Balaji Medical College and Hospital

Study population was 245 children (6 months to 5 years of age)

Inclusion criteria

Children (6 months-5years) presenting with

- H/O acute cough,

- Respiratory distress,
- Fever

Exclusion criteria

- Severe malnutrition
- foreign body inhalation
- chronic illness
- H/O prior treatment with antibiotics
- grunt
- stridor
- cyanosis
- unstable vitals
- Known asthmatic

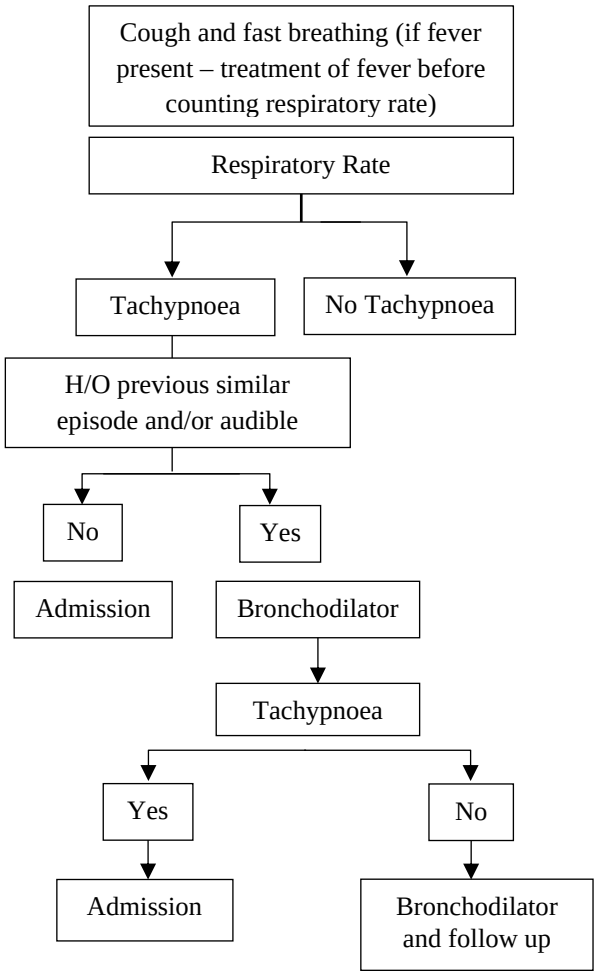

Figure 2: Flow paths of cases in the study.

Statistical analysis

Proportions of the children who had persistent tachypnoea following bronchodilator therapy and those in whom tachypnoea resolved were arrived at. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of the persistent tachypnoea following bronchodilator therapy, fever, chest indrawing in predicting pneumonia (infiltrates in the chest X ray) individually and in combination were arrived at among the entire study population. The same analysis was applied after excluding those children who had more than two previous similar episodes, family H/O asthma or allergy, previous nebulization either alone or in combination, presence of these would point more towards asthma as the cause of cough and fast breathing. $p < 0.05$ was considered to be statistically significant.

RESULTS

Table 1 shows 36 children with first episode of respiratory distress out of which 22 had pneumonia and 14 did not have pneumonia.

Table 1: First episode of respiratory distress (n=36).

Pneumonia	Male		Female		Total
	n	%	n	%	
Yes	12	50.0	10	27.7	22
No	10	27.7	4	11.1	14

According to Table 2, among the 36 children the predominant symptoms were cough, cold, fast breathing.

Table 2: Symptoms and History analysis of 36 children.

Symptoms + history	No. of children (n)	Percentage (%)
Fever	25	69.44
Cough+ cold	36	100
Fast breathing	36	100
Chest indrawing	24	66.66
Decreased feed intake	27	75
Lethargy	27	75
Running nose	26	72.22
Vomiting	19	52.77
Audible wheeze	13	36.12
Cyanosis	0	0
Family H/O allergy /asthma	0	0
Previous H/O nebulization	1	2.77
Previous similar episode	0	0

Table 3: Signs elicited in the 36 children.

Signs	No. of children (n)	Percentage (%)
Temperature> 37.4°C	29	80.55
Undernutrition	31	86.11
Wheeze	1	2.77
Crepitations	35	97.22

Table 4 shows, for the 205 children the predominant symptoms were cough, cold and fast breathing with all of them had previous history of respiratory distress.

According to Table 5, out of 205 children, 92% had crepitations and 80% had wheezing.

Table 6 shows that among 76 children who had infiltrates radiologically, 56 children had persistent tachypnoea after trial bronchodilator. In 20 children tachypnoea disappeared (Sensitivity: 73.68). Out of 129 children who had no infiltrates on chest x ray 115 children showed resolution of tachypnoea following bronchodilator. But 14 children continued to have persistent tachypnoea despite normal chest x ray (Specificity: 89.14%). Out of 70 children with persistent tachypnoea, 56 children had infiltrates on chest x ray. (PPV= 80%). Out of 135 children whose tachypnoea resolved following bronchodilator, 115 children had normal x ray. (NPV = 85.18%). p <0.05. Overall accuracy of persistent tachypnoea after bronchodilator in predicting pneumonia is 83.41%.

Table 4: Symptoms and History analysis of 205 children.

Symptoms + history	No. of children (n)	Percentage (%)
Fever	97	47.31
Cough + cold	205	100
Fast breathing	205	100
Chest indrawing	82	40
Decreased feed intake	123	60
Lethargy	44	21.46
Running nose	52	25.36
Vomiting	37	18.04
Audible wheeze	30	14.63
Cyanosis	0	0
Family H/0 allergy /asthma	47	22.92
Previous H/0 nebulization	80	30.92
Previous H/0 respiratory distress	205	100
One episode	133	64.87
More than two episodes	72	35.12

Table 5: Signs elicited in the 205 children.

Signs	No. of children (n)	Percentage (%)
Temperature >37.4°C	97	47.31
Undernutrition	123	60
Wheeze	164	80
Crepitations	189	92.19

Table 7 shows that evaluating fever as a sign in predicting pneumonia against the gold standard of radiological infiltrate, 60 children who had fever had infiltrate in chest x ray. 16 children who did not have fever had infiltrate (Sensitivity: 78.94%). Out of 129 children who had normal x ray 92 did not have fever (Specificity: 71.31%). p <0.05. Overall accuracy of fever in predicting pneumonia is 74.14%.

Table 6: Association between persistence of tachypnoea after bronchodilator challenge and pneumonia.

Tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	56	14	70
No	20	115	135
Total	76	129	205

Table 7: Association between fever and pneumonia.

Fever	X ray infiltrate		Total
	Yes	No	
Yes	60	37	97
No	16	92	108
Total	76	129	205

Table 8 explains that 70/76 who had chest indrawing showed x ray infiltrate (Sensitivity: 92.10%). Out of 129 children with normal chest x ray, 117 children had no chest indrawing (Specificity: 90.69). 82 children with chest indrawing, 70 children had x ray infiltrates (PPV: 85.36%). Of the 123 children who did not have chest indrawing, 117 children had normal chest x ray (NPV: 95.12%). p <0.05. The overall accuracy of chest indrawing in predicting pneumonia is 91.21%.

Table 8: Association between chest indrawing and pneumonia.

Chest indrawing	X ray infiltrate		Total
	Yes	No	
Yes	70	12	82
No	6	117	123
Total	76	129	205

Table 9 explains that 53/70 children who had fever at presentation and showed no response of tachypnoea to bronchodilator had infiltrate on chest x ray (PPV: 75.71%). 23/135 children who had neither fever nor persistent tachypnoea following bronchodilator had infiltrate on chest x ray. On the other hand, 17/70 children who had both fever and persistent tachypnoea after bronchodilator showed no infiltrate. 112/129 children were afebrile, and tachypnoea disappeared after bronchodilator had normal chest x ray. (Specificity: 86.82%). p <0.05. Accuracy of combined presence of

both fever and persistent tachypnoea in predicting pneumonia is 80.48%.

Table 10 shows that 61/76 children who had both chest indrawing and persistent tachypnoea following bronchodilator had infiltrate on chest x ray (Sensitivity:80.26%). 120/129 children who did not have chest indrawing and who showed good response to bronchodilator had normal chest ski gram (Specificity: 93.02%). p <0.05. Accuracy of the combined presence of chest indrawing and persistent tachypnoea in predicting pneumonia is 88.29%.

Table 9: Association between fever and persistence of tachypnoea and pneumonia.

Fever+ persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	53	17	70
No	23	112	135
Total	76	129	205

Table 10: Association between chest indrawing and persistence of tachypnoea and pneumonia.

Chest indrawing + persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	61	9	70
No	15	120	135
Total	76	129	205

Table 11 shows that 65/76 children who had combined presence of fever, chest indrawing and persistent tachypnoea showed x ray infiltrates (Sensitivity: 85.52%). 124/129 children who did not have all the three characteristics had normal x ray (Specificity: 96.12%). 65/70 children who had infiltrates in x ray had fever, chest indrawing with persistence of tachypnoea in combination (PPV: 92.85%). Out of 135 children who had neither of these characteristics,124 children were with normal chest ski gram (NPV: 91.85%). p <0.05. The combined presence of fever, chest indrawing and persistent tachypnoea following bronchodilator in predicting pneumonia has an excellent accuracy of 92.19%.

There were 72 children out of which 42 had more than two previous similar episodes and 13 had family history of asthma and 17 had previous history of nebulization.

Presence of these factors either single or in combination may more likely suggest that asthma may be the cause of cough and respiratory distress.

Table 12 shows that after excluding children who were more likely to be asthmatics, 54/70 children showed infiltrates on chest x ray had persistent tachypnoea. 16/70 children in whom tachypnoea resolved had infiltrates. (Sensitivity: 77.14%). 57/63 children in whom tachypnoea disappeared following bronchodilator had normal x ray. (Specificity: 90.46% an increase from 89.14%). p <0.05.

Table 13 shows that sensitivity of fever in predicting pneumonia is 88.57%. On excluding the population of children in whom the cause of tachypnoea was likely to be asthma the specificity of fever in predicting pneumonia increased from 71.31% to 82.53%. p <0.05.

Table 11: Fever, chest indrawing and persistence of tachypnoea in combination, in predicting pneumonia.

Fever + Chest indrawing + Persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	65	5	70
No	11	124	135
Total	76	129	205

Table 12: Association between persistence of tachypnoea after bronchodilator challenge and pneumonia.

Tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	54	6	60
No	16	57	73
Total	70	63	133

Table 13: Association between fever and pneumonia.

Fever	X ray infiltrate		Total
	Yes	No	
Yes	62	11	73
No	8	52	60
Total	70	63	133

Table 14: Association between chest indrawing and pneumonia.

Chest indrawing	X ray infiltrate		Total
	Yes	No	
Yes	65	5	70
No	5	58	63
Total	70	63	133

Table 14 shows that 65/70 children, who had infiltrate presented with chest indrawing. 58/63 who did not have chest indrawing had normal chest x ray. Specificity has increased from 90.69% to 92.06% in these children. p <0.05. Table 15 explains that the combined presence of both fever and persistent tachypnoea in these children whose etiology for tachypnoea were more likely to be asthma has got a specificity of 92.06. There is an increase from 86.82% to 92.06% in these children when compared to the entire study population. p <0.05.

Table 15: Association between fever and persistence of tachypnoea and pneumonia.

Fever+ persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	53	5	60
No	17	58	73
Total	70	63	133

Table 16: Association between chest indrawing and persistence of tachypnoea and pneumonia.

Chest indrawing + persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	57	3	60
No	13	60	73
Total	70	63	133

Table 17: Association between fever, chest indrawing and persistence of tachypnoea and pneumonia.

Fever + Chest indrawing + persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	58	2	60
No	12	61	73
Total	70	63	133

Table 18: Association of pneumonia with the signs.

Association of pneumonia with the following	Sensitivity (%)		Specificity (%)	
	n1= 205	n2= 133	n1= 205	n2= 133
Persistent tachypnoea	73.68	77.14	89.14	90.46
Fever	78.94	88.57	71.31	82.53
Chest indrawing	92.10	92.85	90.69	92.06
Fever + Pers istent tachypnoea	69.73	75.71	86.82	92.06
Chest indrawing + Persistent tachypnoea	80.26	81.42	93.02	95.23
Fever+ Chest indrawing + Persistent tachypnoea	85.52	82.85	96.12	96.82

n1: Entire study population
n2: excluding likely asthmatics

Table 16 explains that the combined presence of both chest indrawing and Tachypnoea also showed increase in specificity from 93.02% to 95.23% in diagnosing pneumonia. p <0.05. Table 17 explains that the simultaneous presence of fever, chest indrawing and persistent tachypnoea after bronchodilator in predicting pneumonia is highly specific for pneumonia. Specificity: 96.82% There is no significant increase in specificity in this study group when compared to the entire study population.

DISCUSSION

At the time of conception of case management of WHO guidelines for case management of childhood pneumonia in early eighties, pneumonia was assumed to be the predominant condition presenting with cough, cold and fast breathing.[1,2] Up to this time enough data has been accumulated to highlight the increasing prevalence and severity of asthma globally.[8-10] There is a considerable overlap in clinical presentation of pneumonia and asthma. It is also important to emphasis that asthma related fatalities do occur.[7,11] and can be effectively prevented by accurate diagnosis and early institution of treatment with bronchodilators.

WHO-IMNCI case management of ARI was developed in order to assist the field workers to reliably identify children with ARI and to institute treatment. It also enables them to identify those children who need to be immediately referred to hospital.[2,12] It has also been advocated to treat the children presenting with recurrent wheeze (audible) with trial of bronchodilators.[13,14]

Further, the need for bronchodilator therapy is guided by the presence of a wheeze which for paramedical personnel pertains to only an estimated one-third episodes in which the wheeze may be audible without the aid of a stethoscope.[14]

Thus, according to the current guidelines, in a child with cough and rapid breathing, there is a predilection for over-treatment for pneumonia with antibiotics and for under-treatment for asthma with bronchodilators.[15-17]

In this study, there were 205 children between 6 months to 59 months age group presented with acute cough and respiratory distress with previous history of similar episode. These children received trial nebulization with careful monitoring. The response of tachypnoea to nebulization was then assessed. 135/205 children showed good response to nebulization and their tachypnoea resolved. 115/135 children had a normal chest ski gram (NPV: 89.14%). Fever, defined as temperature of >37.4°C, has specificity of 71.31% in predicting pneumonia. Chest indrawing had an excellent specificity of 90.69%. However, the combined presence of fever, chest indrawing and persistent tachypnoea in predicting the presence of infiltrates on chest x ray has a very high sensitivity of 85.52% and specificity of 96.12%. There were 72 children, who either had more than two similar episodes and/or family H/O asthma and/or previous H/O nebulization; in these children acute cough and respiratory distress may have been due to asthma. Excluding these 72 children the same analysis was done in the rest 133 children. As expected, the specificities of fever, chest indrawing and persistent tachypnoea either

alone or in combination showed an increase from the entire study population indicating the clinical picture could have been due to asthma.

In short, pneumonia (presence of infiltrates on chest x ray) was diagnosed only in 76/205 children (37.07%) which is in accordance with the great importance of asthma as a cause of respiratory distress.

There are similar such studies which also found a low prevalence of pneumonia in children presenting with cough and rapid breathing. Study conducted by A.V Castro et al in Brazil.[17] showed that pneumonia was radiologically diagnosed in only 15.8% of the children who presented with cough and rapid breathing. Another study conducted by H.P.S. Sachdev et al in New Delhi also showed only 10% of x ray showing infiltrate in similar children.[15,16]

This study demonstrated association between persistent tachypnoea after bronchodilator in children with previous H/0 respiratory distress and presence of pulmonary infiltrate (p= 0.0001). By employing this algorithm, 85.18% of children did not receive unnecessary antibiotics.

This is in accordance with the study conducted by A.V. Castro et al where the NPV of resolution of tachypnoea after trial with bronchodilator was 87.3%.[17] The response to bronchodilator in children with previous history of respiratory distress could reduce the use of antibiotics in regions where there is an increasing prevalence of asthma. This would also prevent the problem of development of antimicrobial resistance by unnecessary use of antibiotics.[18-20]

Presence of fever at the onset, has a good specificity in diagnosis of pneumonia. This is not in accordance with the study by A.V. Castro which showed no significant association between fever and pneumonia.[17] But our Indian study conducted in New Delhi in 1995 showed absence of fever is associated with asthma rather pneumonia.[15]

The presence of chest indrawing is significantly associated with pneumonia, with a very high specificity of 90.69%. This is not in accordance with the result of the study conducted in Brazil by A.V. Castro where the presence of chest indrawing has a poor correlation with pneumonia.[17] The presence of fever, chest indrawing and persistent tachypnoea has a significant association with the presence of infiltrate in chest x ray with the highest specificity of 96.12%.

On excluding 72 children who either had previous H/O nebulization and/or family H/O asthma, and/or more than two episodes in whom asthma may be a cause of cough and respiratory distress the specificity of fever, chest indrawing, persistent tachypnoea either alone or in combination in diagnosis of pneumonia (presence of infiltrate) increased.

This is in accordance with the result of the study conducted by H.P.S Sachdev 1994 which showed that the best predictor for asthma was two or more earlier similar episodes (sensitivity84%, specificity84%) followed by temperature <37.6°C (sensitivity 73% and specificity 84%). Absence of fever, audible wheeze and a family history of asthma had excellent specificities (98-100%) but low sensitivities (20-34%). It is concluded that these simple clinical predictors can differentiate acute asthma and ARI.[15,16]

CONCLUSION

In a child presenting with cough and fast breathing with a previous similar episode, trial nebulisations can be given before investigating further for pneumonia.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Manikumar K, Pradeep P, Somasekar R. Simple predictors to differentiate acute respiratory infections from acute asthma in children 6 months to 5 years. Int J Contemp Pediatr 2019;6:2610-7.