

Relationship of Respiratory Symptoms and Signs with Hypoxemia in Infants Under 2 months of Age

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Abstract

Introduction: Hypoxemia is the most serious manifestation of any acute illness in infants less than two months and has shown to be a risk factor for mortality. Hypoxia can be detected using a pulse oxymeter or arterial blood gas analysis. However this facility is not available in most centers of Nepal. This study has correlated different signs and symptoms to predict hypoxia. **Methodology:** This hospital based prospective cross sectional study included 160 infant < 2 months, presenting to OPD or Emergency department with any acute illness A complete history was taken and weight, temperature, respiratory rate, heart rate and oxygen saturation was recorded. Presence or absence of nasal flaring, cyanosis, chest indrawing, head nodding, grunting, wheezing and crepitations on auscultation was recorded subsequently. Clinical signs of hypoxemic and non hypoxemic infants were compared and then analyzed. **Results:** 160 infants, 95 (59.4%) were male and 65 (40.6%) were female. Of the total population, 56(35%) were hypoxic where as 104(65%) were non hypoxic. Infants who presented with more than 3 symptoms, were lethargic, tachypneic or had chest indrawing had higher sensitivity(92.8%, 75%, 75% and 89.3 % respectively) where as infants with nasal flaring, grunting, head nodding or central cyanosis had high specificity (91.3%, 87.5%, 98% and 100%) respectively. **Conclusion:** Infants presenting with ≥ 3 symptoms, lethargy, respiratory rate of ≥ 70 /minute or chest indrawing can be used for screening purpose to detect hypoxia and infants showing signs like grunting, head nodding, nasal flaring or central cyanosis should be considered hypoxic and treated with supplemental oxygen.

Key words: Hypoxia, Respiratory rate, Chest indrawing, Nasal flaring

Introduction

Hypoxemia is the most serious manifestation of any acute illness in infants less than two months and has shown to be a risk factor for mortality. Hypoxic infants are 4.3 times more likely to die than non hypoxemic infants^{1,2}.

Infants are more prone to hypoxemia as their respiratory muscles are poorly equipped to sustain large work loads. They are more easily fatigued than those of older children, limiting their ability to maintain adequate ventilation in lung disease. They also have a very narrow airway leading to increased resistance (airway resistance is inversely proportional to its radius raised to the 4th power)³ and highly compliant chest wall making

it a major determinant of Functional Residual Capacity (FRC).

Clinical features like cyanosis, tachypnea, grunting, head nodding, inability to cry, no spontaneous movement during clinical examination and chest retractions have been identified as the best clinical predictors of hypoxemia^{1,2}. The Integrated Management of Childhood Illnesses (IMCI) also makes use of clinical features to classify pneumonia into various categories based on severity. However facility to measure oxygen saturation (SpO₂) is not available at peripheral hospitals of Nepal. This study was done to help find out a correlation between respiratory symptoms and signs with Arterial

Oxygenation (SpO₂) and thus help predict hypoxemia in infants with pneumonia or any other acute illness. Prompt oxygen supply then given can reduce mortality and morbidity.

Studies have been done to correlate clinical signs and symptoms of pneumonia with hypoxemia. These studies have been able to identify clinical predictors of hypoxemia in children with pneumonia or lower respiratory tract infections. However, very few studies have been done to correlate clinical signs and symptoms with hypoxemia in infants. Therefore this study was planned to study the prevalence of hypoxemia in infants less than two months with any acute illness and to identify its clinical predictors.

Methodology

This was a hospital based prospective cross sectional study conducted at Kanti Children Hospital, Maharajgunj, and Kathmandu, Nepal over a span of one year, August 2007 to July 2008.

160 infant < 2 months, presenting to Out Patients Department (OPD) or Emergency department with any acute illness were included in the study. Infants ≤ 24 hours of age, with major congenital malformations, referred cases after previous hospitalization, severely ill requiring intensive care and clinically suspected Cyanotic Congenital Heart Disease or found later on Echocardiography were excluded.

All infants, fulfilling the inclusion criteria, attending the OPD or Emergency department were attended on day-0 or day-1. A complete history and clinical examination was done.

Weight, temperature, respiratory rate, heart rate and oxygen saturation was recorded. Presence or absence of nasal flaring, cyanosis, chest indrawing, head nodding, grunting, wheezing and crepitations on auscultation was recorded subsequently.

SPO₂ was measured with a pulse oxymeter (9500 oxymeter, Nonim medical INC, USA) with the sensor placed at the finger or toe tip or the ear lobe. The reading that was stable for at least 30 seconds was recorded. The infant was labeled as hypoxic if his/her oxygen saturation was below 90%.

Based on age, the infants were grouped into three groups:

1. 24 hours to 7 days of life (Early Neonate)⁴
2. 8 days to 28 days of life (Late Neonate)⁴
3. 29 days to 60 days of life.(Early Infant)⁴

Based on pulse oximetry, they were divided into two groups:

1. Hypoxemic: Arterial oxygen saturation <90%.
2. Non Hypoxemic: Arterial oxygen saturation ≥90%.

Data was entered and analyzed using SPSS 11.5 software. A *p*-value of ≤ 0.05 was considered significant. Clinical signs were compared between hypoxemic and non hypoxemic infants using chi-square test or the Fischer Exact test. Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Values (NPV) were calculated for different signs and symptoms. Reciever Operating Characteristics (ROC) curve for different respiratory rates was also analyzed.

Results

This study included a total of 164 infants out of which 4 were excluded because they were diagnosed to have Congenital Heart Disease by Echocardiography. Out of remaining 160 infants, 95 (59.4%) were males and 65 (40.6%) were females. Of the total population, 56(35%) were hypoxic where as 104(65%) were not hypoxic.

Based on different symptoms (chief complaints), it was found that fever and decrease sucking were the two most common complaints in the age group of 1-7 days and 8-28 days followed by cough as the second common complaint. On the other hand, fever and cough were the main complaint in the age group of 29–60 days category followed by difficulty breathing as the next common complaint. History of convulsion was found to be the least common in all age categories. The data based on symptoms are shown below.

As already mentioned earlier, the most common symptoms were nearly the same for all age groups. It was seen that all symptoms except for irritable cry and convulsions had a high sensitivity but lacked specificity. It was also seen that only cough and difficulty in breathing was significantly associated with hypoxia.

None of the mothers presented with a single symptom. Since symptoms given by care takers are subjective and a positive response is often found on asking leading questions, symptoms were grouped into two categories as ≥3 symptoms and <3 symptoms and was then analyzed.128 (80%) cases on the whole presented with ≥3 symptoms with the majority in all the three groups. There was no significant association found between hypoxia and cases presenting with ≥3 symptoms in the age categories 1-7 days and 29 - 60 days although it was significantly associated in the

age category of 8-28 days. However, taking the whole population together, the association was found significant (p -value=0.003). This association also showed a high sensitivity (92.8%) but a poor specificity (26.9%).

Based on the different signs seen in different age groups: Out of 160 patients, 56 (35%) were hypoxemic. Although the respiratory rate cut off value for diagnosis of Pneumonia as given by World Health Organization is ≥ 60 /min in the age group of <2 months, a significant number of cases were found to be hypoxic at a rate ≥ 70 /min. The ROC (Receiver Operating Characteristics) curve, shown below, also shows the rate of ≥ 70 /min having the maximum sensitivity and specificity for diagnosing hypoxemia.

Chest Indrawing was seen in 91(56.8%) cases out of which 50(54.9% of cases with chest indrawing) were found to be hypoxic. Chest indrawing showed significant association with hypoxia in all the age categories (p -value=.036/.001/.001 respectively) and was also significantly associated when the whole population was taken together (p -value=0.001). Chest Indrawing showed a high sensitivity rate of 89.3% and can be used as a good screening test for hypoxia, but lacked specificity.

Grunting, was seen among 29 (18.1%) patients out of which 16 (55.1%) were hypoxic. Grunting with hypoxia was seen more in the age group of 1-7 days (100%) and was found to be statistically significant with hypoxia (p - value =.013). However, there was no significant association in the age groups 8-28 days (p -value=.178) and 29 – 60 days (p - value=.341). Taking the whole population together, it was however found that grunting was significantly associated with hypoxia (p -value=.012). Grunting had a high specificity of 87.5% with a low sensitivity of 28.5 %.

Out of 160 patients, 39 (24.4%) patients had nasal flaring. Among 39 patients, 30 (76.9%) had hypoxia where as 26 (21.5%) were hypoxic in patients without nasal flaring. Nasal flaring association with hypoxia was very significant in all age groups. Nasal flaring also had a high specificity rate (91.3%) with a low sensitivity (53.6%) like grunting. Both, grunting and nasal flaring cannot be considered as good screening markers.

Head nodding was observed only in 14 (8.7%) cases out of which 12 (85.7% of patients with head nodding) were found to be hypoxic. 9 cases in the neonate category had head nodding and all had hypoxia. Head nodding showed a significant association with hypoxia in age groups 1-7 days (p - value=.001) and 8-28 days (p - value=.003) but lacked significance in the age group 29–60 days (p -value=.355). However, head nodding was found significantly associated with hypoxia (p - value=.001) when the whole population was taken into account.

Among the patients in which head nodding was absent, 44 (30.1%) were found to be hypoxic. Head nodding showed a sensitivity of 21.4% and a specificity of 98% respectively.

Central Cyanosis was observed in 4 patients and was due to non cardiac causes. All 4 patients were hypoxic and thus had a specificity of 100%. Central Cyanosis was not found to be significantly associated with hypoxia in any age groups. This could be due to the low number of cases presenting with central cyanosis. However, on taking the whole population, it is found to be statistically significant (p -value=.014). Central Cyanosis is a very specific tool (specificity – 100%) for assessing hypoxia but a very poor sensitive marker (7%).

Table 1: Showing distribution of different symptoms in different age groups of the study population according to the mother / care taker.

Age Groups >>	1-7 days (n=22)	8-28 days (n=60)	29 – 60 days (n=78)	Total (160) n (%)
Symptoms	Present n(%)	Present n(%)	Present n(%)	
Fever	18 (82%)	54 (90%)	68 (87.2%)	140 (87.5%)
Cough	12 (54.5%)	43 (71.6%)	58 (74.4%)	113 (70.6%)
Difficult Breathing	6 (27.2%)	39 (65%)	55 (70.5%)	100 (62.5%)
Irritable Cry	9 (40.9%)	15 (25%)	11 (14.1%)	35 (21.8%)
Poor Sucking	19 (86.4%)	49 (81.6%)	45 (57.7%)	113 (70.6%)
Convulsion	1 (4.5%)	0 (0%)	5 (6.4%)	6 (3.75%)
≥ 3 Symptoms	16 (72.7%)	51 (85%)	61 (78.2%)	128 (80%)

Table 2: Showing, Sensitivity, Specificity, PPV and NPV of different symptoms of the study population as a whole.

S.N.	Clinical Features	SpO ₂ <90% n(%)	SpO ₂ >90% n(%)	P Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	Fever (n=140)	51 (36.4%)	89 (63.6%)	0.316	91	14.4	36.4	75
2	Cough (n=113)	47 (41.6%)	66 (58.4%)	0.007	83.9	36.5	41.6	80.8
3	Difficult Breathing (n=100)	46 (46%)	54 (54%)	0.001	82.1	48	46	83.3
4	Irritable/ Inconsolable cry (n=35)	11 (31.4%)	24 (68.6%)	0.616	19.6	76.9	31.4	64
5	Poor Sucking (n=113)	44 (38.9%)	69 (61.1)	0.105	78.5	33.6	38.9	74.4
6	Convulsion (n=6)	3 (50 %)	3 (50%)	0.423	5.3	33.6	50	65.5
7	≥ 3 symptoms (n=128)	52 (40.6%)	76 (59.4%)	0.003	92.8	26.9	40.6	87.5

Table 3: Showing, Sensitivity, Specificity, PPV and NPV of different signs of the study population as a whole.

S.N.	Clinical Features	SpO ₂ < 90% n(%)	SpO ₂ >90% n(%)	P Value	Sensiti vity (%)	Specifi city (%)	PPV (%)	NPV (%)
1	Lethargy (n=83)	42 (50.6%)	41 (49.4%)	.001	75	60.5	50.6	81.8
2	Tachypnea ≥ 60/min (n=78)	42 (53.8%)	36 (46.2%)	.001	75	65.4	53.8	82.9
3	Tachypnea ≥ 70/min (n=29)	25 (86.2%)	4 (13.8%)	.001	44.6	96	86.2	76.3
4	Grunting (n=29)	16 (55.2%)	13 (44.8%)	.012	28.5	87.5	55.1	69.5
5	Indrawing (n=91)	50 (54.9%)	41 (45.1%)	.001	89.3	60.8	54.9	91.3
6	Nasal Flaring (n=39)	30 (76.9%)	9 (23.1%)	.001	53.6	91.3	76.9	78.5
7	Cyanosis (n=4)	4 (100%)	0 (0%)	.006	7	100	100	66.7
8	Head Nodding (n=14)	12 (85.7%)	2 (14.3%)	.001	21.4	98	85.7	69.8

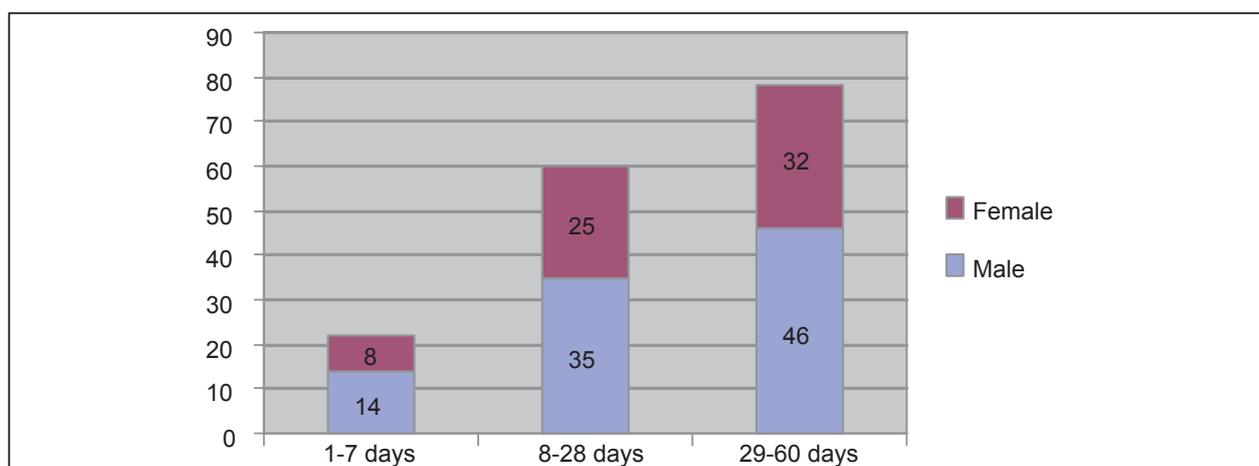


Fig 1: Showing distribution of study population according to age and sex.

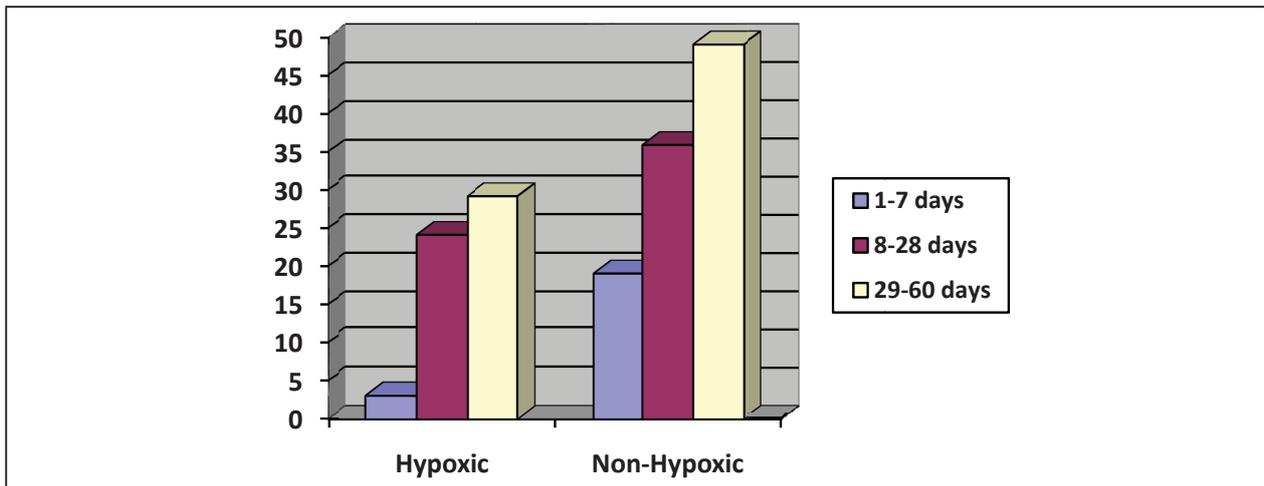


Fig 2: Distribution of hypoxic patients according to age

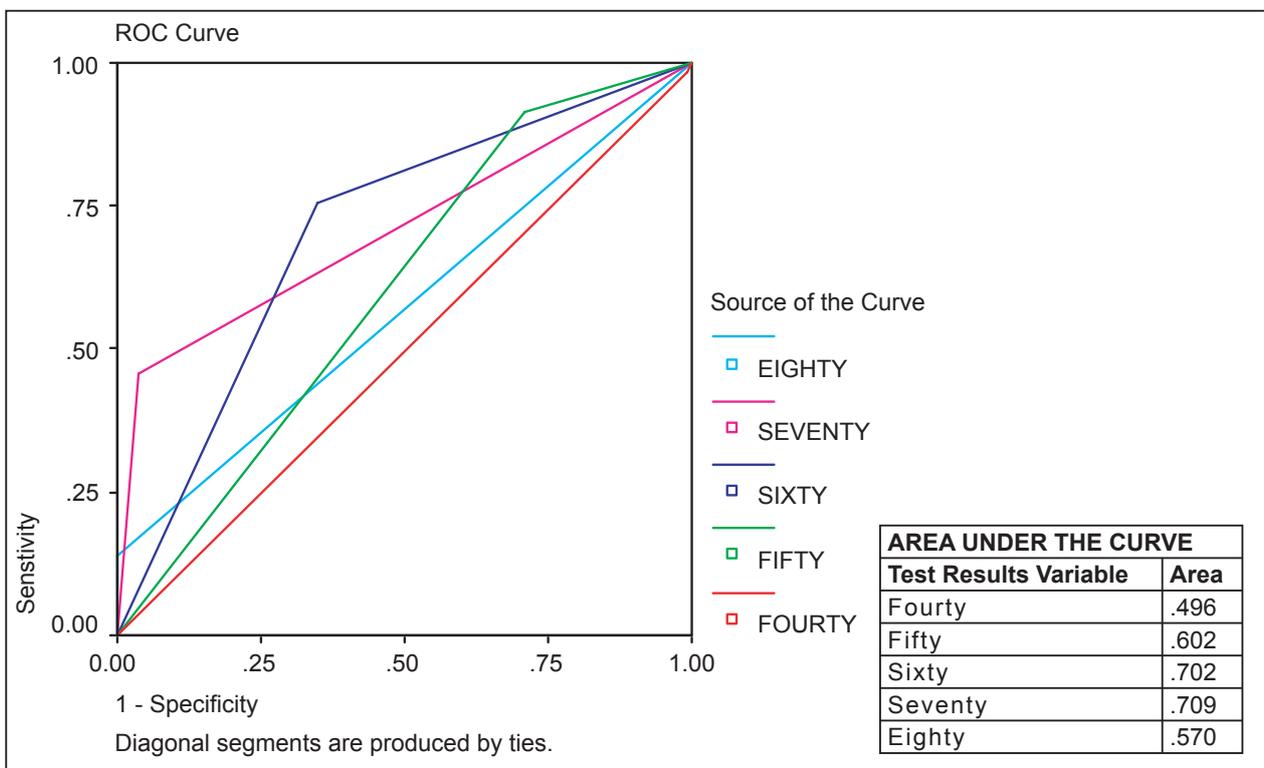


Fig 3: ROC curve of different respiratory rate with hypoxemia.

Taking the whole study population together, symptoms like fever, cough, difficulty breathing, poor feeding, irritability and convulsion and signs like tachypnea, conscious level, nasal flaring, chest indrawing, grunting, head nodding and central cyanosis were individually correlated with hypoxia although combination of these signs and symptoms were present in each patient. Individually it was seen that patients who presented with more than 3 symptoms, were lethargic, tachypneic or had chest indrawing had higher sensitivity (92.8%, 75%, 75% and 89.3 % respectively) and therefore had higher Negative Predictive Value (87.5%, 81.8%, 82.9%, and 91.3% respectively). So combination of these markers can be used as a good

screening tool to detect hypoxia. On the other hand, patients who had nasal flaring, grunting, head nodding and central cyanosis or a combination of any of the above should be considered hypoxic as they had high specificity (91.3%, 87.5%, 98% and 100% respectively).

Discussion

Hypoxia is a serious condition and prolonged hypoxia can lead to death of number of cells leading to dysfunction of various systems⁵. Prompt identification of hypoxia is possible with the help of a pulse oxymeter but unfortunately this is not available in most centers in this country.

The aim of this study was to find out the relationship between respiratory symptoms and signs with percentage of hemoglobin in arterial blood that is saturated with oxygen (SpO₂) and was considered hypoxia if it was less than 90 %.

The detection and effective management of hypoxia is an important aspect of the clinical management of acutely ill infants. Published data on the subject are not clear about whether there is a reliable co-relation between the respiratory rate or any other respiratory signs and presence of hypoxia in very young infants with acute symptoms. Using a pulse oxymeter various studies have been conducted to find the co-relation between respiratory rate or other respiratory signs and hypoxia in older children.

It has been seen that most parents or caretakers are not able to explain their baby's problem properly and has the usual tendency to agree to any leading question put forward. It has been seen a number of times that the usual mechanism of breast feeding with rapid sucking followed by a pause is usually misinterpreted as decrease sucking, jitteriness as convulsions, regurgitation as vomiting or a normal warm body as fever. In this study, it was seen that 140(87.5%) of all cases were said to have fever but only 46(28.8%) actually showed a temperature >100.4°F. This difference could be due to absence of fever at the time of examination or misinterpreting normal warm body as fever as mentioned above. In the same manner other symptoms seen were cough in 113(70.6%), difficulty in breathing in 100(62.5%), decrease sucking in 113(70.6%) and convulsion in 6(3.8%) of the study population.

Since symptoms related to these small babies were usually subjective, this study grouped the symptoms in 2 categories as <3 symptoms and ≥3 symptoms, irrespective of types of symptoms. It was seen that parents or caretakers usually complained of more than 3 symptoms as seen in 128(80%) cases. Among 128, 52 (40.6%) were found to be hypoxic but no significant association was found with hypoxia (p -value=<0.05), except in the age category of 8-28 days (p -value=0.008). The reason for this could be that this is the period when the baby is totally under his/her mother's care directly and the mother could be more observant about the baby's symptoms. It is seen that during the first 7 days, mothers are usually facing some obstetrical related problems and the baby is under the care of some caretakers or family members who show much concern and interpret normal physiology as symptoms as mentioned earlier. In the same manner beyond 28 days baby are usually handled by caretakers or family members. However, the

association between ≥3 symptoms and hypoxia was found to be very sensitive (92.8%) but very less specific (26.9%).

In a study conducted by Rajesh VT et al, where they evaluated the respiratory rate as an indicator of hypoxia in infants <2 months of age found out that a respiratory rate of ≥60/min predicted hypoxia with 80 % sensitivity and 68% specificity.⁶ These values were quite similar to this study where a respiratory rate ≥ 60/min predicted hypoxia with 75% sensitivity and 65.3% specificity.

Another study conducted by Lodha R et al to see whether clinical signs and symptoms could accurately predict hypoxia in children with Acute Lower Respiratory Tract Infections found that a respiratory rate ≥70/min in infants ≤3 months of age had a sensitivity of 89.2% and specificity of 51.8% for detecting hypoxia⁷ which was found to be in contrast with this study where Respiratory Rate ≥70/min could predict hypoxia with 44.6% sensitivity and 96% specificity. This difference could be due to the inclusion of only <2 months of age in this study. However the ROC curve (Figure 5) shows that a respiratory rate of ≥70/min covers maximum area under the curve (0.709) and this can predict hypoxemia with most accurate sensitivity and specificity combined altogether.

Onyango and colleagues included 45 infants less than 2 months of age in their study. They found no significant relation between the presence of hypoxia and a respiratory rate ≥70/min¹. Sensitivity was very similar to the present study (48% vs. 44.6%), but there was a vast difference in predicting specificity (70% vs. 96%). The reason for this could be due to the high altitude where the previous study was conducted.

Lodha R et al conducted a study in different age groups and found that chest wall indrawing had a sensitivity of 78.5% and a specificity of 66.7% for detecting hypoxemia⁷. Similarly a study conducted by Singhi S et al in children >2 months up to 59 months found chest wall indrawing having a sensitivity of 90 % and PV 98%⁸. Study done by Onyango FE et al in age group 3-11 months found association of chest indrawing with hypoxia with a sensitivity of 97% and specificity of 29%¹. However in this study, association between chest indrawing and hypoxia was found highly significant with a sensitivity of 89.3% and specificity of 60.8%. The sensitivity pattern was quite similar to the studies done above. The reason for decreased specificity could be due to the presence of decreased compliance of the chest wall in this age groups leading to the presence

of minimal chest wall indrawing even in normal infants³. Although studies on age <2 months have been done less, sensitivity pattern was very similar in most studies^{1,7,8}.

Very few studies have been conducted to show the association between nasal flaring and hypoxemia. Studies done by Weber M et al⁹, Laman M et al¹⁰ and Singhi S et al⁸ found nasal flaring to have a good balance of sensitivity and specificity. However our study showed a sensitivity of 53.6% and specificity of 91.3% and a positive predictive value of 76.9 %. This difference could be accounted due to study population comprising different age groups, with 2 months–59 months in the previous study and < 2 months in this study.

Conclusion

Hypoxia is a serious condition and if severe enough, can cause death of the cells leading to depressed mental activity, sometimes culminating to coma and also reducing work capacity of the muscles. Hypoxia can be best determined by the use of a pulse oxymeter but in many centers this may not be available. This study has helped in identifying certain symptoms and signs that can predict hypoxia and hence provide necessary treatment.

This study has used simple clinical signs which can be taught to health workers to identify hypoxic infants and provide them with oxygen therapy. Since oxygen supply may not be sufficient in all centers, this study can help health workers to identify infants who are at risk of hypoxia. Infants presenting with ≥ 3 symptoms, lethargy, respiratory rate of ≥ 70 /minute or chest indrawing can be used for screening purpose to detect hypoxia and infants showing signs like grunting, head nodding, nasal flaring or central cyanosis should be considered hypoxic and treated with supplemental oxygen.

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Conflict of Interest: This article is based on the final thesis (part of compulsory thesis submission) report submitted to Department of Paediatrics, National Academy of Medical Sciences (NAMS), Bir Hospital, Mahabaudhha, Kathmandu, Nepal.

Permission from IRB: Yes

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