



## Original Article

### Risk Factors for Pneumothorax in Ventilated Neonates in Neonates Admitted to Neonatal Intensive Care Unit



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#### Abstract

**Background:** Pneumothorax (PTX) is a common complication and potentially life threatening condition for neonates in the neonatal intensive care unit (NICU). The use of ventilatory support and neonatal resuscitation procedures with positive pressure is deemed necessary. **Aim of work:** The aim of this study is to identify the risk factors which predispose or relate to pneumothorax in neonates admitted in NICU of AL-Azhar Assuit University Hospital and the outcome of this problem. **Patients and Methods:** This is a retrospective descriptive study was carried out on mechanically ventilated neonates admitted to NICU of AL-Azhar Assuit University Hospital during the period from 1<sup>st</sup> January 2018 to 1<sup>st</sup> January 2020. **Results:** On studying the demographic and clinical characteristics of cases and risk factors implicated in incidence of pneumothorax, it's reported that 41.7% of cases were males, 75% born by caesarean section, most of cases with gestational age < 34 weeks, with birth weight < 2 kilogram. Respiratory distress syndrome (RDS) was the most prevalent underlying lung disease, as 75% of pneumothorax patients were having RDS, probably being the most common cause of admission and need for ventilatory support. During admission, 4 patients died with mortality rate 33.3% of all patients presenting with pneumothorax. **Conclusion:** The incidence of PTX was high due to positive pressure ventilation. It was higher in neonates on synchronized intermittent mechanical ventilation (SIMV) than on continuous positive airway pressure (CPAP) in preterm infants, in those of elective CS and neonates with low birth weight. Respiratory distress syndrome was the most prevalent underlying lung disease. Mortality was high due to lower birth weight and gestational age, the need of these patients to mechanical ventilation and more severe chest condition than other patients. **Recommendation:** Intensive care for neonates who develop pneumothorax is necessary as they have higher mortality rates. **Key words:** Pneumothorax; ventilator, SIMV; CPAP; PIP; PEEP; NICU.

## **Introduction**

Pneumothorax is defined as an abnormal accumulation of gas between the visceral and parietal pleura [1]. It can result in clinically important complications such as hypoxemia, increased work of breathing, hypercapnea, need for evacuation, obstructive shock, hypotension, and even death [2]. A pneumothorax must be considered in mechanically ventilated infants who develop unexplained alterations in hemodynamics, pulmonary compliance or oxygenation and ventilation [3]. Pneumothorax in an infant can be virtually asymptomatic or may be associated with severe circulatory disturbances including hypotension and hypoperfusion [4]. The risk factors for development of pneumothorax include prematurity, low Apgar score, respiratory distress syndrome and infection (neonatal sepsis, pneumonia), as well as some settings of mechanical ventilation [5]. The risk of pneumothorax is also increase in elective cesarean delivery

before 39 weeks [6]. The highest incidence of pneumothorax was in neonates with a gestational age of less than 32 weeks [7]. The early diagnosis and treatment of neonatal pneumothorax are essential to reduce morbidity, mortality, and complications [8]. Diagnosis of Pneumothorax can be achieved by chest X-ray (CXR) or computed tomography (CT). Despite CT being considered the gold standard for the diagnosis of Pneumothorax in adults, neonatologists always try to avoid CT because it requires infant transportation and exposure to excessive radiation. On the other hand, it has been shown that supine chest x-ray fails to identify a significant number of Pneumothorax, especially small and medium Pneumothorax [9]. Lung ultrasonography (LUS) has been successfully used in the diagnosis of Pneumothorax, as a radiation-free, inexpensive, point-of-care tool that the clinician can use at the bedside [10]. Treatment options for pneumothorax include expectant

management, needle aspiration (NA), and chest drain (CD) insertion [11].

## **Methods**

This retrospective descriptive study was performed throughout 24 months from 1<sup>st</sup> January 2018 to 1<sup>st</sup> January 2020, at NICU at AL-Azhar Assuit University Hospital. It was carried out on ventilated neonates that develop pneumothorax during their admission. Age and sex matched mechanically ventilated newborn that did not develop pneumothorax were recorded as controls. Data retrieved from records included gestational age, birth weight, gender, mode of delivery, underlying disease (necessitating ventilation) and may be contributing to the developing of pneumothorax as respiratory distress syndrome (RDS), neonatal pneumonias, meconium aspiration syndrome (MAS) and others ventilating mode & sitting, mortalities recorded as well.

Inclusion criteria: Neonates suspected clinically of having pneumothorax by sudden deterioration of patient condition

of ventilated neonate, diminished bilateral air entry confirmed by appearance of accumulation of air in pleural cavity by chest x-ray , Blood gases. Subsequent changes in ventilator sitting will be recorded up to being of developing of pneumothorax, other risk factors as vigorous sitting, Malposition of endotracheal tube will be recorded if present. The initial ventilator modes either continuous positive air way pressure or synchronized intermittent mechanical ventilation and changeable design making will be recorded.

Exclusion criteria: Cases who develop pneumothorax prior to or after mechanical ventilation (MV) or those with incomplete records will be excluded from our study.

## **Ethical consideration**

Approval of Al-Azhar Assuit Faculty of Medicine Committee (AAFMC) was taken. Oral and written consents were taken from parents or guardians of the patients and the aim of the study was explained to the parents before collection

of the data. The privacy of all data collected was assured.

### **Statistical analysis**

The collected data were revised, organized, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 25.0 for windows. Data are presented as the Mean  $\pm$  standard deviation (SD), frequency, and percentage. Chi-Square test ( $X^2$ ) and independent sample t test were used for comparison between different diagnostic methods and findings. A 5% level was chosen as a level of significance in all statistical tests used in the study.

### **Results**

This study included 70 neonates receiving ventilatory support (MV and CPAP) during the period of the study, 10 cases were excluded from the study due to incomplete documentation of their ventilatory settings prior to occurrence of pneumothorax or uncertainty of the development of pneumothorax, and hence a total of 60 cases were included in the study. The most common indication

for mechanical ventilation in the study population was respiratory distress syndrome (RDS) in 40%, as it detected by diminished bilateral air entry and confirmed by chest roentgenogram. Twelve cases were developed pneumothorax on mechanical ventilation (20%), about (75%) of cases that develop pneumothorax having RDS. Thus RDS is the most frequently encountered underlying respiratory disorder associated with pneumothorax, but it is not the direct cause. The most common ventilator mode associated with pneumothorax was synchronized intermittent mandatory ventilation (SIMV) (22%), on the other hand Continuous positive airway pressure (CPAP) showed a significantly lower incidence of air leak (10%). In multivariate regression model high PEEP was found to be one of the factors significantly associated with pneumothorax and seemed to be hazardous when associated with other pressure parameters as high PIP and rate.

Table (1) showed the demographic characteristics studied ventilated neonates. Table (2) showed the indication for mechanical ventilation in studied neonates. Table (3) showed the risk factors according to presence or absence of pneumothorax in studied neonates. Table (4) showed the mode of ventilation and selected ventilator settings In 60 studied neonates on mechanical ventilation. Table (5) showed the outcome according to presence or absence of pneumothorax in studied neonates. Figure (1) showed the indication of ventilation in studied neonates. Figure (2) showed the RDS in studied neonates with and without pneumothorax. Figure (3) showed the mode of ventilation in studied neonates with and without pneumothorax.

## **Discussion**

The most common indication for mechanical ventilation in the study population was respiratory distress syndrome (RDS) in 40%, as it detected by diminished bilateral air entry and

confirmed by chest roentgenogram. In the present study cases the most common indication for mechanical ventilation was RDS as it represent 40%, while cases of sever sepsis was 20 cases (33.3%), MAS was 6 cases (10%), and cases of PPHT was 5 (8.3%), both cases of hypoxic ischemic encephalopathy and diaphragmatic hernia was 2 cases (3.3%), and only 1 case of congenital pneumonia necessitate mechanical ventilation (1.67%). These results coincide with the result of Hadzic and coworker's [12] study in which the main co-morbid conditions associated with pneumothorax were RDS, MAS, TTN, and Pneumonia. The incidence of PTX in the current study was 20%, mostly due to that most of patients in this study were under positive pressure ventilation. The majority of our patients were females and caesarian section was the mode of delivery in most of them. The incidence of pneumothorax was higher at neonates with gestational age < 32 weeks and birth weight < 2 kg. RDS was the most

common diagnosis. The mortality in the current study was higher than some other reports due to lower birth weight and gestational age, the need of these patients to mechanical ventilation and more severe chest condition than other patients. Twelve out of sixty mechanically ventilated neonates were experienced pneumothorax with a percentage of 20% among ventilated neonates. Abdellatif and Abdellatif [13] reported in their study that the incidence of PTX was 9.1% which is lower than the results in our studies. The incidence in this study was much higher than Lim et al [4] who reported 1.3% of NICU patients got pneumothorax at a period of 10 years. While Navaei et al [14] reported that 5.8% of NICU patients who had PTX which was much lower than our results. The incidence quoted in related literature varied between 1.5% and 7.6% by Vibede et al [15] and Trevisanuto et al [16]. Other studies however showed lower incidences as the results of Wilinska et al [17] probably due to

diversity of ventilator protocols and modes in different centers .The high incidence of pneumothorax in this study was mostly due to more accessibility of x-rays in our department which helps in early diagnosis of pneumothorax. Among 12 patients with pneumothorax included in our study, 5 (41.7%) patients were males and 7 (58.3%) were females. Gender did not affect the incidence of occurrence of pneumothorax in our work. Several studies have different observation and considered male gender as a risk factor for the development of pneumothorax. Abdellatif and Abdellatif [13] reported that PTX was more common in males; 62.7% of cases, Apiliogullari et al [18] reported that 77% of their patients were males, as well as different studies showed that neonatal pneumothorax occurs more often in males than in females [19] However, a local study by Ali et al [20] found a higher incidence in term and post-term female neonates with low-birth weight. The risk of pneumothorax is also

increase in elective cesarean delivery before 39 weeks [6]. The mode of delivery was vaginal in 25% and caesarian section in 75%. Caesarian section was reported to be the more common mode of delivery in affected neonates, and it was reported by Abdellatif and Abdellatif [13] that caesarian section was the mode of delivery in 61% of cases. and it was 52% by Malek et al [21].

Apiliogullari et al [18] reported that caesarian section was another risk factor in PTX as it was the mode of delivery in 67% of cases and Benterud et al [22] explained it as after elective caesarean section, the baby is not stressed and often has 'wet lungs' followed by forced respiration that may lead to pneumothorax.

In the present study, the incidence of pneumothorax was higher in preterm infants and low birth weight (LBW) babies. This was observed in several studies as studies [14&23] and can be attributed to their higher risk for

developing lung pathology as RDS and for their greater need for ventilatory support. Abdellatif and Abdellatif [13] in a result of study observed the incidence of pneumothorax in preterms were 95.75% of pneumothorax patients, and cases with LBW were 93.98% of cases. The highest incidence of pneumothorax was reported in neonates with a gestational age of less than 32 weeks [7]. RDS was the most common diagnosis in our neonates suffering from pneumothorax, as 75% of pneumothorax patients were having RDS, probably being the most common cause of admission in our NICU and need for ventilatory support. This is in agreement with many other studies [14]. The results of the present study were higher than Lim et al [4] as neonates with RDS were 38% of pneumothorax patients, and Apiliogullari [18] as reported that RDS was in 43% of pneumothorax patients. Abdellatif and Abdellatif [13] reported that 61% of PTX cases were having RDS. In our cases, 60 Case were on

positive pressure ventilation, 12 of them developed pneumothorax. Synchronous intermittent mandatory ventilation was the mode of ventilation in (22%) of cases that develop pneumothorax, while cases that develop pneumothorax on CPAP were (10%). Thus there was a significant lower incidence of pneumothorax on CPAP (10%) than on SIMV (22%). Morley et al [24] reported the incidence of pneumothorax after CPAP was 9% , and even higher incidence reaching about 16% in patients on CPAP were also found by some authors as Greenough, Millner [25]. The latter also stated an incidence of pneumothorax in 34% of mechanically ventilated infants which is comparable to our results in which 20% of cases on mechanical ventilation developed pneumothorax. Similarly, positive pressure ventilation was reported in 93.22% of PTX patients by Abdellatif and Abdellatif [13] and ventilator settings were close to our results, while Apiliogullari et al [18] reported that 60% of all cases received mechanical

ventilation develops pneumothorax. High peak inspiratory pressure, high positive end-expiratory pressure application, and ventilator nonconformity are among the factors that can induce PTX during mechanical ventilation [18].

Though high PEEP was one of the factors significantly associated with pneumothorax in multivariate regression model in the present study, it seems to be hazardous when combined with other pressure parameters as high PIP and rate .This augments our assumption that aggressive ventilation is a leading cause for pneumothorax which should be diverted to less invasive techniques whenever possible. In the present study, high PIP was an independent risk factor for pneumothorax in multivariate regression model. This association was similarly detected in other studies of Klinger et al [26] where over ventilated newborns were at higher risk of developing pneumothorax.

Yellanthoor and Ramdas [27] also found that air leaks were more evident with PIP

>20 cmH<sub>2</sub>O, though did not reach statistical significance. Our results showed no significant difference in inspiratory time between neonates that developed pneumothorax and those who did not, probably due to the narrow range of change in this ventilator parameters in our NICU. The mean ( $\pm$  SD) of PIP, PEEP, and IT of the mechanically ventilated neonates with pneumothorax at which pneumothorax occurred was  $21.12 \pm 2.85$  cmH<sub>2</sub>O,  $5.90 \pm 1.357$  cmH<sub>2</sub>O and  $0.378 \pm 0.072$  respectively. These were relatively not high settings but probably were high after improving lung compliance of preterm neonates with RDS which were the majority of our cases.

Decreasing the risk of pneumothorax requires intensive control of ventilation, including optimizing PEEP and minimizing PIP and MAP. The mortality in our study reached (33.3%) in the neonates with pneumothorax ( $P < 0.001$ ). This has been reported in several studies [17,23, 27]. This percent is lower than

reported by Abdellatif and Abdellatif [13] as mortality rate was 62.7% and lower than the percent was reported by Navaei et al [14] (65%).

However, Malek et al [21] reported the mortality rate in their study was 40.8%, while Esme et al [28] observed much lower mortality (23%). The mortality rates are high, ranging from 46% to 77% if barotrauma is a complication of mechanical ventilation [29]. Others found no significant difference in mortality rate between those with and without pneumothorax [21]. Increased mortality might be attributed to lower gestational age, severity of underlying lung disease and hemodynamic instability caused by pneumothorax.

### **Conclusions**

Our results suggested that the incidence of pneumothorax was high due to positive pressure ventilation. It was higher in neonates on SIMV than on CPAP, in preterm infants and in those of elective CS and neonates with low birth weight. Respiratory distress syndrome

was the most prevalent underlying lung disease. Mortality was high due to lower birth weight and gestational age, the need of these patients to mechanical ventilation and more severe chest condition than other patients.

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### **Author's contributions**

HE and MA: Conceptualization; Investigation and writing the original draft. DM: Data curation; validation; software writing, review & editing. HE and MY: Supervision and visualization, Writing - review & editing. All authors have read and approved the final manuscript.

### **Conflict of interest**

Authors declare they have no conflict of interest

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**Table (1): Demographic characteristics of 60 studied ventilated neonates.**

<b>Variable</b>		<b>Number (%)</b>
<b>Mode of delivery</b>	Normal vaginal delivery	15 (25%)
	Caesarean section	45(75%)
<b>Premature rupture of membrane</b>	No	37 (61.7%)
	Yes	23 (38.3%)
<b>Consanguinity</b>	Negative	38(63.3%)
	Positive	22(36.7%)
<b>Gender</b>	Males	30 (50.0%)
	Females	30 (50.0%)
<b>Birth weight in kg</b>	Mean + SD	1.86+0.59
	Median (range)	1.9 (0.9-3.6)
<b>Gestational age in weeks</b>	Mean + SD	32.65+3.02
	Median (range)	34 (28-41)
<b>Previous ICU admission</b>	No	49 (81.7%)
	Yes	11 (18.3%)
<b>RDS</b>	No	36 (60%)
	Yes	24 (40%)
<b>Mortality</b>	No	50 (83.3%)
	Yes	10 (16.7%)

**Table (2): Indication for mechanical ventilation in 60 studied neonates .**

<b>Disease</b>	<b>Number (%)</b>
<b>RDS</b>	24 (40.0%)
<b>Severe sepsis</b>	20 (33.3%)
<b>MAS</b>	6 (10.0%)
<b>PPH</b>	5(8.3%)
<b>HIE</b>	2 (3.3%)
<b>Diaphragmatic hernia</b>	2 (3.3%)
<b>Congenital pneumonia</b>	1 (1.67%)

**Table (3): Risk factors according to presence or absence of pneumothorax in 60 studied neonates**

<b>Risk factors</b>	<b>Cases with pneumothorax N = 12 (20%)</b>	<b>Cases without pneumothorax N = 48 (80%)</b>	<b>P- value</b>
<b>Gestational age in weeks</b>	31.35±3.24	33.95±2.86	0.02*
<b>Birth weight in kg</b>	1.64±0.52	2.08±0.65	0.013*
<b>Gender</b>			0.62
Male	5 (41.7%)	25 (52.1%)	
Female	7 (58.3%)	23 (47.9%)	
<b>Mode of delivery</b>			0.32
NVD	3 (25%)	12 (25%)	
CS	9 (75%)	36 (75%)	
<b>RDS</b>			0.001*
Yes	9 (75%)	15 (31.25%)	
No	3 (25%)	33 (68.75%)	

\*Significant

**Table (4): Mode of ventilation and selected ventilator settings in 60 studied neonates on mechanical ventilation**

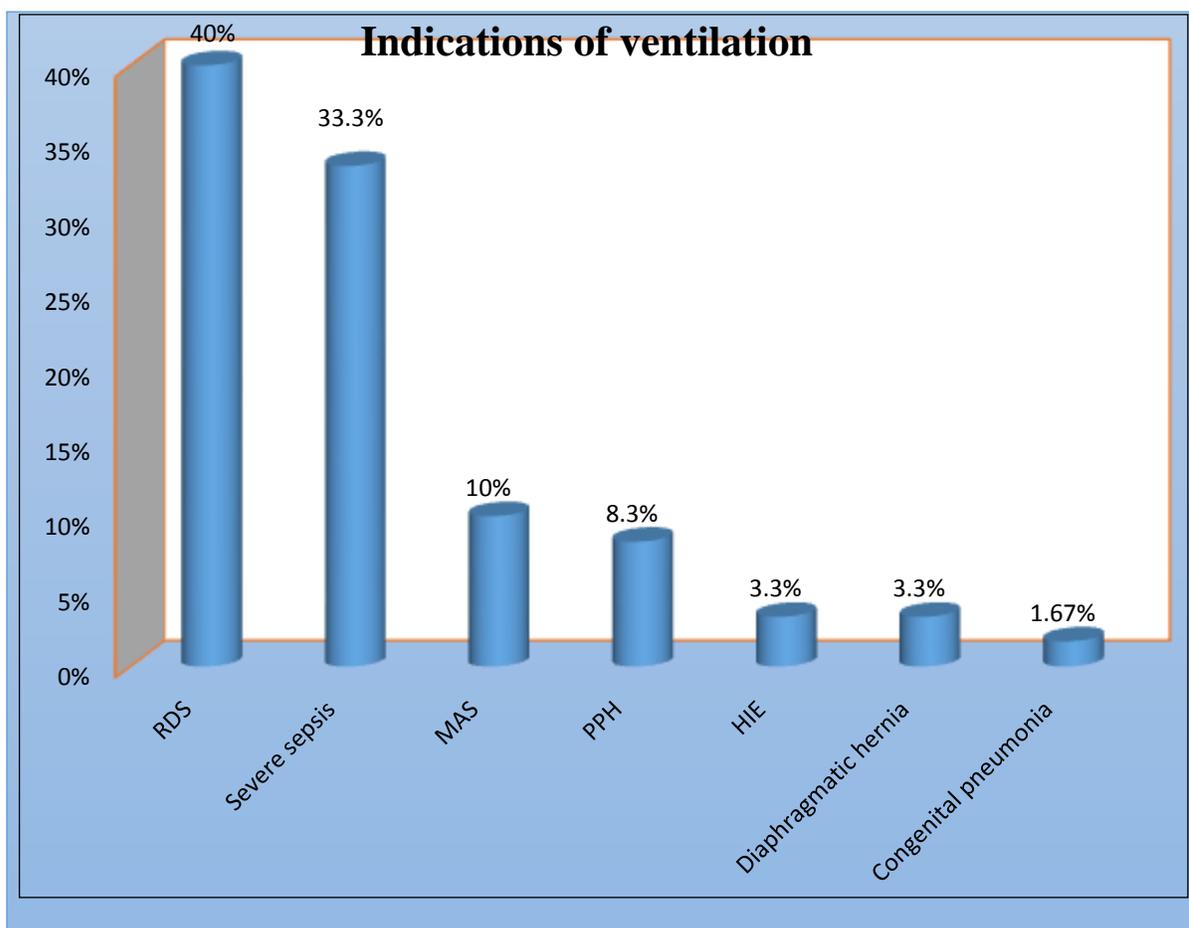
<b>Item</b>	<b>Cases with pneumothorax (N= 12)</b>	<b>Cases without pneumothorax (N= 48)</b>	<b>P- value</b>
<b>Mode of ventilation:</b>			0.001*
<b>CPAP (N-10) (no) (%)</b>	1/10 (10%)	9/10 (90%)	
<b>SIMV (N=50) (no) (%)</b>	11/50 (22%)	39/50 (78%)	
<b>SIMV settings</b>			
<b>PIP (mean± SD)</b>	21.12 ± 2.85	17.95 ± 2.102	0.001*
<b>PEEP(mean± SD)</b>	5.90 ± 1.357	5.0 ± 0.450	0.001*
<b>Rate (mean± SD)</b>	62.86 ±12.935	56.15 ± 5.065	0.001*
<b>IT (mean± SD)</b>	0.378 ± 0.072	0.365 ± 0.036	0.69

\*Significant, PIP: Peak Inspiratory Pressure, PEEP: Peak End Expiratory Pressure, IT: Inspiratory time

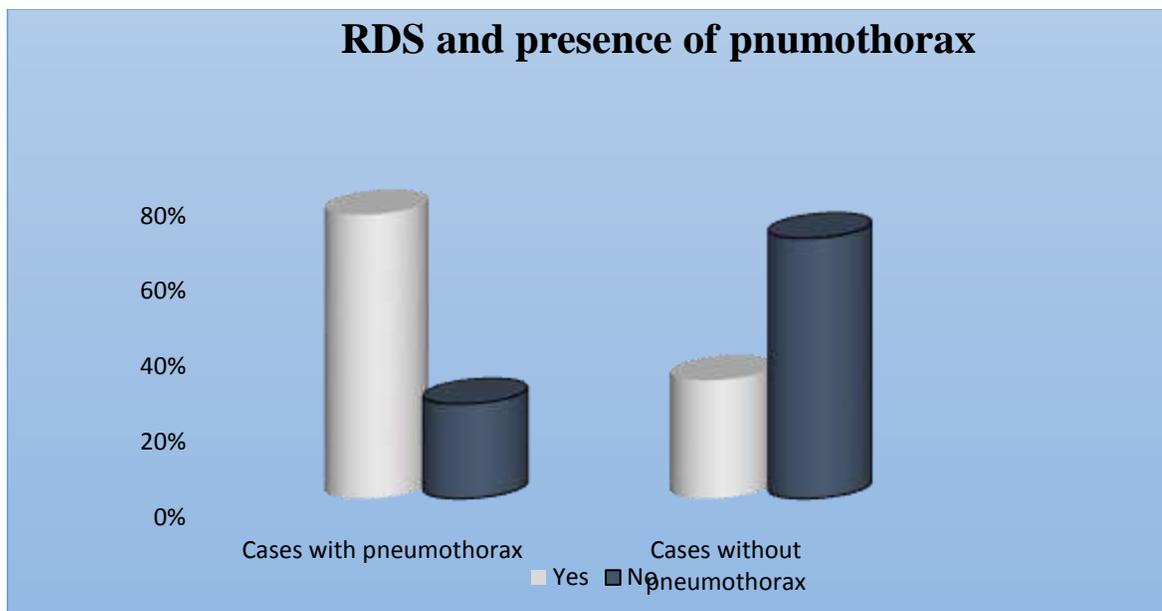
**Table (5): The outcome according to the presence or absence of pneumothorax in 60 studied neonates.**

Item	Cases with pneumothorax (N= 12)	Cases without pneumothorax (N= 48)	P-value
<b>Mortality</b>			0.001*
Yes	4 (33.3%)	6 (12.5%)	
No	8 (66.7%)	42 (87.5%)	

\*Significant,



**Figure (1): Indication of ventilation in studied neonates.**



**Figure (2): RDS in studied neonates with and without pneumothorax.**

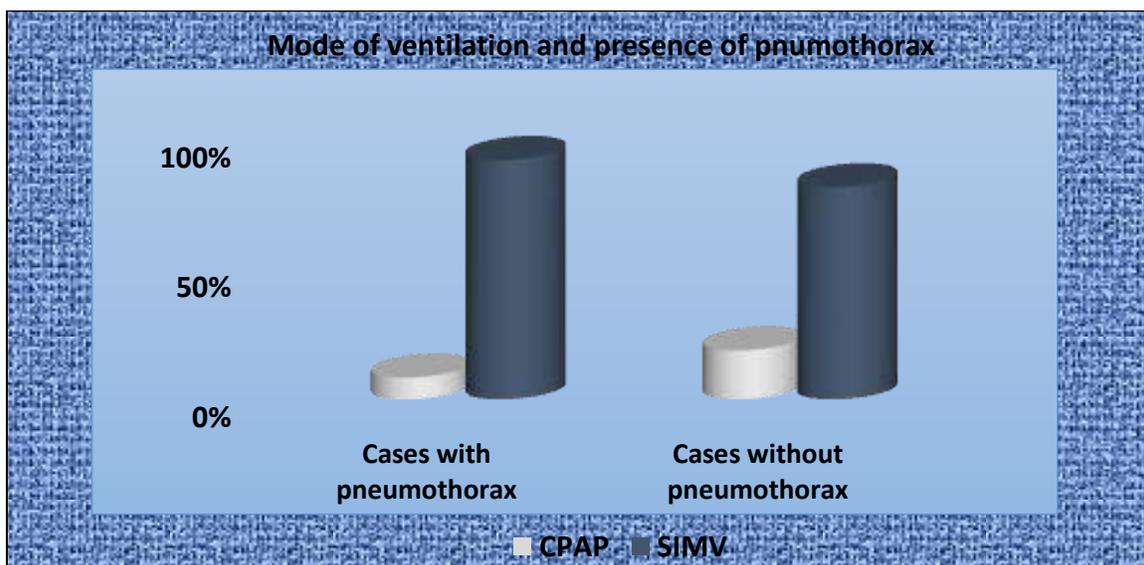


Figure (3): Mode of ventilation in studied neonates with and without pneumothorax.

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