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Chest Radiography and Clinical Outcome of Congenital Diaphragmatic Hernia in Single Institution Experience

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Abstract

Background: This study aimed to evaluate findings on chest radiography (CXR) for clinical outcomes, persistent pulmonary hypertension (PPH) and pulmonary hypoplasia (PH) in congenital diaphragmatic hernia (CDH).

Method: 22 neonates with CDH were retrospectively reviewed for the patient demography, clinical, initial arterial blood gas and CXR, PPH, operative finding, treatment outcome and survival.

Result: The intrathoracic stomach (ITS) was found in 6/22 CXR, there were statistically significant differences in APGAR score at 1 minute and 5 minutes (1 minute; ITS 7 (6,8) versus non ITS 8 (8,9) p = 0.018, 5 minutes; ITS 7.8 (1.8) versus non ITS 9.2 (0.7) p = 0.035), initial arterial blood gas bicarbonate level (ITS 15.5 (14.7,19.2) versus non ITS 21.2 (20.2,23.4) p = 0.007) and PPH (50% ITS versus 6.2% non ITS, p = 0.046). Pulmonary hypoplasia (PH) was 2 shapes; apex 14/22 and hilar 8/22 CXR, there were no statistically significant differences in any clinical outcome and PPH. Regarding to severity of mediastinal shift on chest x ray, 17/22 CXR showed mediastinal shift more than mid clavicular line, there were no statistically significant differences in clinical outcome, hernia content, PPH, LOS, complication and survival.

Conclusion: Intrathoracic stomach finding in CXR were demonstrated as markers of poor clinical and possible PPH. Furthermore, pulmonary hypoplasia shape and severity of mediastinal shift were not correlated to any clinical outcome, hernia content, PPH, LOS, complication and survival.

Keywords: *Congenital Diaphragmatic Hernia; Pulmonary Hypoplasia; Persistent Pulmonary Hypertension of the Newborn; Intrathoracic Stomach; Lungthorax Ratio*

Introduction

Congenital diaphragmatic hernia (CDH) affects about 1 in 2000 - 3000 live births worldwide [1]. CDH is a challenging congenital anomaly to treat due to the combination of pulmonary hypoplasia (PH) with variable degrees of abnormal pulmonary vasculature causing respiratory insufficiency, persistent pulmonary hypertension (PPH) and right sided heart dysfunction after birth. Pulmonary hypoplasia was found to be the cause of mortality in neonates with CDH who developed symptoms of respiratory distress within a few hours after birth. Pulmonary hypoplasia was a poor postnatal prognostic factor that affected the survival of neonates with CDH including outcomes of

postnatal CDH treatment. A variety of methods to predict outcome have been proposed by chest radiographic findings [2-4]. Chest x-ray radiography (CXR) depicts lung volume in neonates with CDH. Newborns with hypoplastic lungs often show a small aerated lung area on chest x-rays [5]. Some studies have investigated the correlation between clinical outcome in neonates with CDH and specific chest radiographic parameters [6]. One group of investigators classified two patterns of hypoplastic lung in CDH chest x-rays as apex and hilar types. Survival rate of the apex group (81%) was significantly higher than the hilar group (33%) [2]. A correlation was demonstrated between CXR findings and survival rates for CDH patients in our institution.

Aim of the Study

The aims of this study were to compare initial CXR findings from the CDH neonates in the first 24 hours of life with outcome of postnatal treatment and survival rate in neonates with CDH.

Methods

Medical records from the pediatric surgical database in Songklanagarind Hospital from January 1987 to June 2017 were searched for all neonates with a proven diagnosis of congenital diaphragmatic hernia (CDH). This is a tertiary referral center for neonatal surgery and medicine. This audit was approved by the Songklanagarind Hospital Clinical Audit Support System and, it was not a research project, but informed parental consent were undertaken.

It was approved by The Biomedical Research Involving Human Subjects from Research Ethics Committee of Songklanagarind Hospital. Neonates with CDH must have presented with respiratory distress and had initial chest radiography within the first 24 hours of life. Seventy three neonates with CDH were found, while fifty one CDH neonates were excluded from our investigation. Reasons for exclusion included three cases from our diagnosis of hiatal hernia, two cases from diagnosis of traumatic diaphragmatic hernia, forty five cases from incomplete medical records since their initial 24 hours of life-postnatal chest x-ray radiology files could not be located in the database and one CDH neonate from death after admission to the Neonatal Intensive Care Unit (NICU). Each patient was either inborn or outborn delivery by including the referral system of patient care at the hospital. All CDH neonates were intubated at birth. They were initially started on conventional mechanical ventilation but transferred to high frequency oscillation ventilator (HFV) if they were difficult to ventilate/oxygenate. The CDH neonates must have presented with respiratory distress in the first 24 hours after birth and had initial chest x-ray radiology files. Thus, twenty two CDH neonates were included in the final study. Of this group, twelve patients were male and ten were female. Data retrieved from the medical records included sex, type of labour, inborn delivery, gestational age, prenatal diagnosis, maternal underlying disease, Apgar score at birth, birth weight, clinical presentation, association disease, immediate complication between admission, length of hospital stay (LOS), duration of mechanical ventilation and findings during the initial 24 hours after birth for arterial blood gas and chest x-rays. Persistent pulmonary hypertension (PPH), systolic blood pressure in the first 24 hours after birth, operative findings (the side of the hernia), treatment outcome and survival (clinical improved: hospital discharge to home or stable enough for back-transfer to an outside institution for continued convalescence) were also documented. Each chest x-ray was reviewed by 2 experienced pediatric surgeons. Conclusions regarding findings were made by prognostic criteria and definitions were included for aerated lung, mediastinal shift and hypoplastic lung. The reviewers were unaware of the clinical outcome of any of the patients. Two experienced pediatric radiologists were involved in the final review of each chest x-ray. To measurement the aerated lung area, all chest x-ray films were scanned into the Picture Archiving and Communication System (PACS) and cardiac, mediastinal, thymic and abdominal shadows within the thorax were subtracted from the thoracic area to calculate the aerated lung area. Bilateral lung areas were measured on postnatal period.

Initial chest x-ray findings of each subject were evaluated. Considerations were:

(1) The ratio of aerated ipsilateral lung area was graded by dividing the superior-to-inferior length of the visualised aerated lung, on the same side as the congenital diaphragmatic hernia, by the length of lung that would normally be expected (diaphragm positioned

at the 10th posterior rib). The length of visualised aerated lung was defined as the distance from the most superior point at which lung markings were visualised to the most inferior point at which lung markings were visualised. The lung was considered aerated even when lung markings were visualised through a shifted mediastinum. The lung/thorax ratio in the affected side (the same side as CDH) = C/A in figure 1.

(2) The ratio of aerated contralateral lung area was graded by dividing the superior to inferior length of the visualised aerated lung on the opposite side of the congenital diaphragmatic hernia. The lung/thorax ratio in the non-affected side (the opposite side to CDH) = B/A in figure 1.

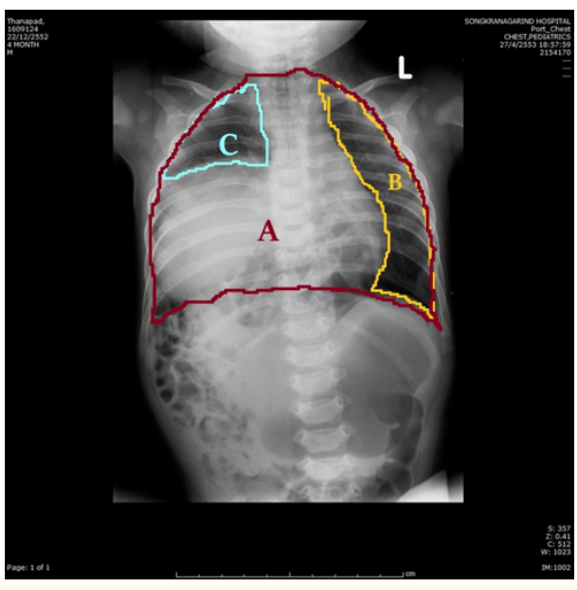

Figure 1: *Lung/thorax ratio in the affected side C/A and the non-affected side B/A.*

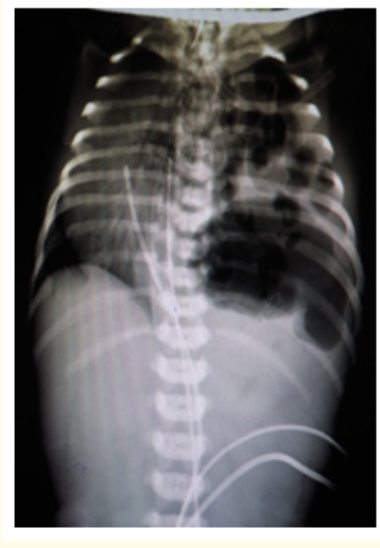

Figure 2.1: *Example of ABC measurement.*

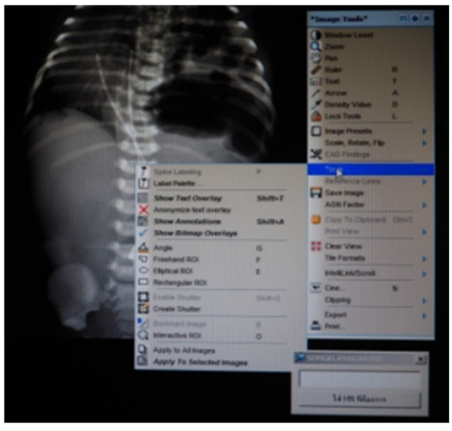

Figure 2.2: *Example of ABC measurement.*

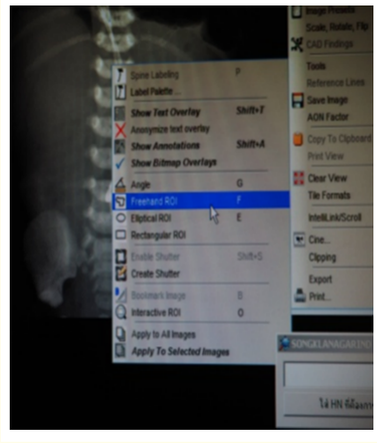

Figure 2.3: *Example of ABC measurement.*

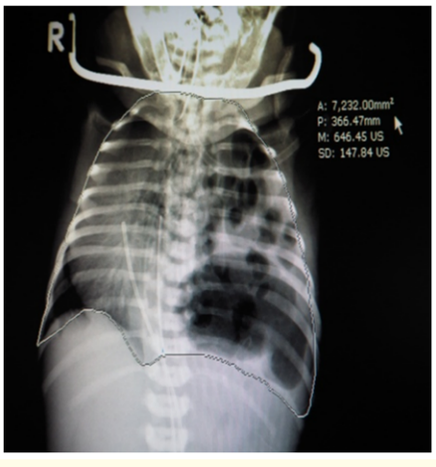

Figure 2.4: *Example of A measurement.*

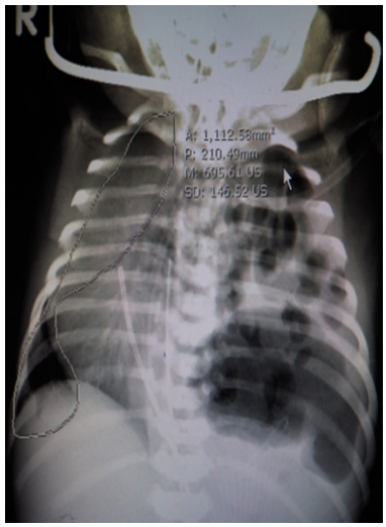

Figure 2.5: *Example of B measurement.*

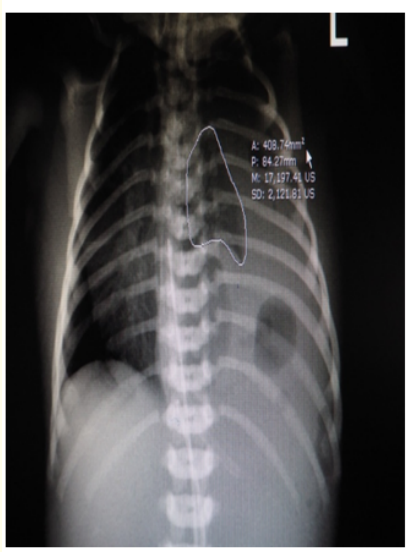

Figure 2.6: *Example of C measurement.*

Figure 2: *Example of A B C measurement.*

(3) Mediastinal shift was noted are being absent if displaced less than half the width of the hemithorax (mild mediastinal shift), displaced more than half the width of the hemithorax but not abutting the chest wall and abutting the chest wall (severe mediastinal shift). The width of the hemithorax was defined as the distance between the medial aspect of the lateral ribs and the ipsilateral

edge of the vertebral bodies. In all neonates, the side of congenital diaphragmatic hernia was noted. Based on the gas and soft-tissue density pattern in the hernia content, stomach was considered to be present in the hernia when either a stomach bubble or a distal portion of the nasogastric tube was present in the thorax. Small bowel was considered to be in the hernia when bowel loops were too numerous in the hernia to be explained by colon alone. Colon was considered to be in the hernia when the bowel in the hernia was seen to directly communicate with the ascending or descending colon in the abdomen or when the bowel in the hernia showed haustral markings. Liver was considered to be in the hernia when prominent soft tissue was present in the hernia and umbilical venous catheters were deviated, suggesting an abnormal position of the liver.

Classified radiographic findings of pulmonary hypoplasia (PH) were considered as figure 3.1 Apical type was defined as the expansion of the lung on the affected side, starting at the pulmonary apex. Figure 3.2 Hilar type was defined as expansion starting at the hilum.

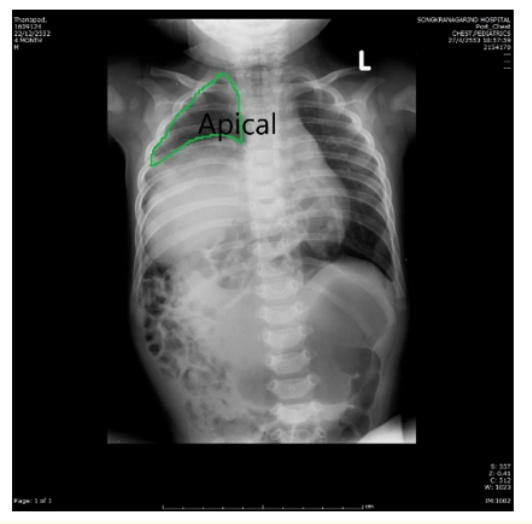

Figure 3.1: *Apical type.*

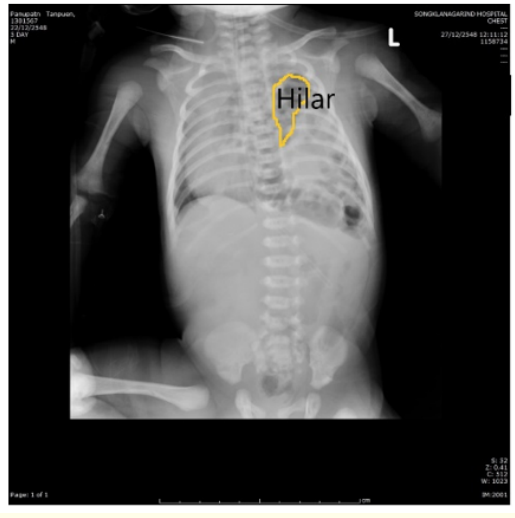

Figure 3.2: *Hilar type.*

Figure 3: *Classified radiographic findings pulmonary of hypoplasia.*

Each individual radiographic was compared with treatment outcome and survival. Interpretation of statistically significant data ($P < 0.001$ and $P < 0.05$) was analysed by Fisher's exact test and the Mantel-Haenszel chi-square test. Using EpiData version 3.1 (EpiData version 3.1, Christiansen TB., *et al*., EpiData Association, 2010). Data analysis suggested markers of unsatisfied treatment outcome and poor survival when certain radiographic criteria were present (intrathoracic stomach finding (ITS), pulmonary hypoplasia (PH) finding: hilar type, C/A less than 0.05, B/A less than 0.04 and severe mediastinal shift). Outcome and survival statistics were compiled for when zero to five of these factors were present. Additional clinical data were analysed to determine the relationship to treatment outcome. Survival included Apgar score at 1 and 5 minutes, initial arterial blood gas bicarbonate level, persistent pulmonary hypertension (PPH), hernia content findings from chest x-rays, length of hospital stay (LOS) and immediate complication.

Results

Demographic data

From our results, female CDH neonates were found in 10 of the 22 cases (45.5%). In regard to type of labour, caesarean sections were found in 7 of the 22 cases (31.8%). Most of the CDH neonates were inborn delivery at 21 of the 22 cases (95.5%). Gestational ages of CDH neonates were mostly between the 37th and 40th week (15/22, 68.2%) whereas gestational age at less than the 37th week was found in 5 cases (22.7%). Mean gestational age of the CDH neonates was at the 39th week. Prenatal diagnosis by foetomaternal ultrasonography was found in 3 of the 22 cases (13.6%) with no overall maternal underlying disease in CDH neonates. Median of Apgar scores at 1 and 5 minutes were 8. Overall mean birth weight of the CDH neonates was (mean ± SD) 3023.8 ± 392.4g. The most clinical presentation of the CDH neonates was respiratory distress in the first 24 hours of life in 20 of the 22 cases (90.9%). Associated diseases were found in 12 of the 22 cases (54.5%) and classified into 2 categories as syndromic diseases: Goldenhar syndrome (1/12, 8.3%) and non-syndromic diseases: pneumonia, Patent Ductus Arteriosus (PDA), G6PD deficiency, undescended testis, indirect inguinal hernia, neonatal jaundice, neonatal sepsis, lung atelectasis, eventration of the diaphragm, neonatal anaemia and thrombophlebitis (11/12, 91.7%). Immediate complications between admission were found in 8 of the 22 cases (36.4%) as arrhythmia (supraventricular tachycardia, premature ventricular contraction), hypotension, infected surgical wound, pneumothorax, pleural effusion, intraoperative complication: accidental tear visceral organ (liver capsule), lower gastrointestinal bleeding and cardiac arrest. Median of the length of hospital stay was 13 days with interquartile length (IQR) of 9,20. Mechanical ventilators were used in 17 cases (77.2%). Duration of mechanical ventilation was (mean ± SD) 6.2 ± 5.6 days for conventional mechanical ventilators used in 16 cases (72.7%) and a high frequency ventilator was used in 1 case (4.5%) for persistent pulmonary hypertension (PPH). For data retrieved from operative findings, the side of defect was mostly on the left (19/22, 86.4%), posterior site of defect was found in 20 of the 22 cases (90.9%) and size of defect was (mean ± SD) 4.9 ± 1.8 centimetres (cm). Initial arterial blood gas recorded in the first 24 hours after birth on the PaO_2 chart (mean ± SD) was 109.2 ± 59 mmHg, $PaCO_2$ (mean ± SD) was 39.3 ± 12.7 mmHg and median of HCO_3 level was 20.6 with IQR between (18 and 21.6) mmol/L. From chart records in the first 24 hours after birth, systolic blood pressure was (mean ± SD) 77.8 ± 14 mmHg. Persistent pulmonary hypertension (PPH) was found in 4 of the 22 cases (18.2%) and 21 CDH neonates were clinically improved after discharge from the hospital (95.5%) with death between admission at NICU for 1 case (4.5%). From chest x-rays, pulmonary hypoplasia was found in all 22 cases and classified into 2 categories. Apical type was found in 14 cases (63.6%) whereas hilar type was found in 8 cases (36.4%). From the results, survival rates in the apical group (100%) were more than the hilar group (87.5%). Visceral organ herniation from chest x-rays gave liver (3/22,13.6%), stomach (7/22, 31.8%), spleen (9/22, 40.9%) and bowel (21/22, 95.5%). Severe mediastinal shift from chest x-ray findings was found in 17 of the 22 cases (77.3%) whereas mild mediastinal shift was found in 5 cases (22.7%). Measurements of aerated lung area from initial chest x-rays were made in the first 24 hours of life. As previously described, ipsilateral aerated lung area was represented as C (mm^2). Median of C (IQR) was 264.2 (186.3, 574.1). Contralateral aerated lung area was represented as B (mm^2). Median of B (IQR) was 118.4 (69.6, 466.4). Total thorax area was represented as A (mm^2). Median of A (IQR) was 6471.1 (5567.3, 7451.6). When the calculation was performed as the ratio of ipsilateral aerated lung area divided by total thorax area (CA ratio), the median of CA ratio (IQR) was 0.05 (0,0.1). The esti-

mated cut off value was derived at 0.05 and the ratio of contralateral aerated lung divided by total thorax area (BA ratio) as the median of BA ratio (IQR) was 0.04 (0,0.1). The estimated cut off value was derived at 0.04. Cut off value of CA ratio was less than 0.05 in 15 of the 22 cases (65.2%) and cut off value of BA ratio was less than 0.04 in 14 of the 22 cases (60.9%). Both cut off values were used in the retrieved data. The hypothesised optimal CA ratio and BA ratio cutoff levels were subject to scrutiny in relation to patch use to determine if smaller ipsilateral aerated lung area and contralateral aerated lung area were associated with inability to achieve the cutoff.

	Apical type	Hilar type	P value
	n=14	n=8	
Size of defect (cm) Median (IQR)	4 (3,5)	8 (7,8)	0.022
Site of defect			0.031
-Anterior %, (n)	7.1% (1/14)	12.5% (1/8)	
-Posterior %, (n)	92.9% (13/14)	87.5% (7/8)	
Complication %, (n)	0% (0/14)	100% (8/8)	< 0.001

Table 1: *Correlation between demographic data and type of pulmonary hypoplasia from CXR findings.*

From table 1, sizes of the defect in the hilar group (median 8 cm IQR (7,8)) were significantly more than those of the apical group (median 4 cm IQR (3,5)) (P = 0.022). With regard to site of defect, posterior defects in the apical group (13/14, 92.9%) were found to be significantly higher than in the hilar group (7/8, 87.5%) (P = 0.031). Complications of the hilar group (100%) were significantly more than those of the apical group (0%) (P < 0.001). Term gestational age, birth weight, Apgar score at 1 and 5 minutes, persistent pulmonary hypertension of newborn (PPH), arterial blood gas, associated disease, LOS and survival did not differ significantly between the two groups.

	Mild group	Severe group	P value
	n=5	n=17	
Systolic blood pressure (mmHg) Mean ± SD	92.3±10.8	74.4±12.6	0.04

Table 2: *Correlation between systolic blood pressure and degree of mediastinal shift.*

From table 2, systolic blood pressure of the severe group (74.4 ± 12.6 mmHg) was significantly less than the mild group (92.3 ± 10.8 mmHg) (P value = 0.04). Results in table 2 demonstrated severe mediastinal shift from chest x-rays related to decreasing systolic blood pressure.

	Non ITS	ITS	P value
	n = 16	n = 6	
Bicarbonate level from initial arterial blood gas (mmol/L) Median (IQR)	21.2 (20.2,23.4)	15.5 (14.7,19.2)	0.007
PPH %, (n)	6.2% (1/16)	50% (3/6)	0.046

Table 3: *Correlation between intrathoracic stomach (ITS) findings from chest x-rays with demographic data.*

Results in table 3 show the relationship between intrathoracic stomach (ITS) from chest x-rays, bicarbonate level from initial arterial blood gas and PPH. ITS from chest x-rays was found in 6 of the 22 cases (bicarbonate level from initial arterial blood gas (mmol/L) 15.5 IQR (14.7, 19.2), PPH 3/6 (50%)) whereas 16 cases showed non ITS (bicarbonate level from initial arterial blood gas 21.2 (mmol/L) IQR (20.2, 23.4), PPH 1/16 (6.2%)).

Bicarbonate levels from initial arterial blood gas of the ITS group were significantly less than those of the non ITS group (P = 0.007) whereas PPH outcomes of the ITS group were found significantly more than those of the non ITS group (P = 0.046). Metabolic acidosis from initial arterial blood gas including PPH related to ITS from chest x-rays affected the clinical outcome of CDH infants.

	Non PPH	PPH	P value
	n=18	n=4	
Period of using ventilators (days) mean ± SD	4.6±3.8	13.2±7.5	<0.001
Ventilator group			
Conventional ventilator % , (n)	66.7% (12/18)	0% (0/4)	0.003
HFV %, (n)	33.3% (6/18)	100% (4/4)	0.029

Abbreviation: HFV, High Frequency Ventilator
PPH, Persistent pulmonary hypertension

Table 4: *Correlation between PPH and demographic data.*

PPH was found in 4 out of 22 cases (period of using ventilators (mean ± SD) 13.2 ± 7.5 days, conventional mechanical ventilator 0/4 (0%), high frequency ventilator 4/4 (100%)) whereas 18 cases showed non PPH (period of using ventilators 4.6 ± 3.8 days, conventional mechanical ventilator 12/18 (66.7%) high frequency ventilator 6/18 (33.3%)).

From table 4, periods of using ventilator of the PPH group were significantly more than those of non PPH group. Those using a high frequency mechanical ventilator in the PPH group (4/4 (100%)) were significantly more than those of the non PPH group (6/18, (33.3%)) whereas those using a conventional mechanical ventilator in the PPH group (0/4 (0%)) were significantly less than those of the non PPH group (12/18 (66.7%)). The PPH group was dependent on conventional mechanical ventilators whereas the non PPH group was dependent mainly on high frequency mechanical ventilators.

Discussion

Several studies have proposed using chest x-ray findings that reflected pulmonary hypoplasia as predictors of survival. Shimono., *et al*. divided pulmonary hypoplasia into two groups: apical and hilar. They reported that expansion of the lung on both sides of the hilar type was significantly less than that in the apical type after birth. They found that the prognosis of CDH neonates in the hilar type was significantly poorer than in the apical type. Shimono., *et al*. identified chest x-ray patterns in CDH neonates by 2 categories. They found no statistically significant differences in any outcomes and PPH. Donnelly., *et al*. defined the percentage of aerated lung by the superior-to-inferior length of visualised aerated lung (lung markings visualised) divided by the expected lung volumes (apex on 10^{th} posterior rib). The degree of mediastinal shift was defined by more quantitative criteria using the medial half of the hemithorax, lateral half of the hemithorax or mediastinum abutting the chest wall. In our study, we graded the degree of mediastinal shift following Shimono., *et al*. by using the lung markings visualised as Donnelly's determination. We divided the degree of mediastinal shift into absent, less than half of hemithorax (mild) and more than half of hemithorax (severe). Severe mediastinal shift showed no statistically significant differences in any clinical outcome, hernia content, PPH, LOS, complication and survival. Donnelly., *et al*. determined the relationship between percentage of aerated ipsilateral lung as greater than or equal to 10%, percentage of aerated contralateral lung greater than or equal to 50% and the mediastinum was displaced by less than half the width of the hemithorax; these were all statistically significant in increasing survival rate. Touloukian and Markowitz found that right sided CDH was associated with increased mortality but in our study results showed no correlation between side of hernia and survival. Identification of the intrathoracic stomach on chest x-rays has been emphasised as a predictor of decreased survival [7-9]. From our results in table 3, PPH related to ITS significantly less than PPH related to non ITS. ITS was demonstrated as a poor clinical marker predictor of PPH in CDH neonates. Results in table 4 indicate differences between periods of data collection so the high frequency ventilator was just to be used in the recently, so the numbers of using high frequency mechanical ventilators was a small number. In our retrospective descriptive study, there were limiting factors because of the small number of CDH neonates in our institution.

Conclusion

In conclusion, chest x-ray findings provided available prognostic information with regard to clinical outcome of CDH neonates. Intrathoracic stomach findings showed statistically significant correlation with poor clinical outcome and PPH. Our results identified a value marker making therapeutic decisions for CDH neonates.

Disclosure of Potential Conflicts of Interest

The author declare no conflict of interest.

Research Involving Human Participants

It was approved by The Biomedical Research Involving Human Subjects from Research Ethics Committee of Songklanagarind Hospital.

Informed Consent

This audit was approved by the Songklanagarind Hospital Clinical Audit Support System and it was not a research project, but informed parental consent were undertaken.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institution and national research committee and with the 1964 Helsinki declaration and its later amendments or operable with ethical standards.

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