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ORIGINAL PAPER

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Risk Factors and Outcome of Neonatal Pneumothorax in Tuzla Canton

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ABSTRACT

Aim: The aim of this study was to analyze risk factors and outcome of neonatal pneumothorax in Tuzla Canton. **Methods:** Neonates with chest X-ray confirmed pneumothorax in University Clinical Center of Tuzla, within a three-year period, from January 2015 to December 2017, were retrospectively studied. Participants were evaluated for baseline characteristics, predisposing factors of neonatal pneumothorax, accompanying disorders and mortality. **Results:** During the observed three-year period 11425 neonates were born in Tuzla Canton, with 7.33 % of preterm births, and 604 neonates were treated in NICU, with 265 neonates who required mechanical ventilation. Neonatal pneumothorax (NP) was diagnosed in 22 patients (9 term, 13 preterm), 12 (54.5%) were male. The incidence was 0.20% of total births, respectively 3.64% of those treated in NICU. The mean gestational age were 35.1 ± 3.0 weeks and birth weight 2506.8 ± 727.7 grams. NP was mostly unilateral (72.7%) and right-sided. The most commonly associated diseases were: respiratory distress syndrome, intracranial haemorrhage, pneumonia, transient tachypnea and sepsis. In 8 (36.4%) neonates, the underlying cause of NP could be mechanical ventilation (secondary), whereas in 14 (63.6%) NP was spontaneous, without previous mechanical ventilation, although 11 of them required mechanical ventilation after pneumothorax. **Conclusion:** All perinatal risk factors were investigated, and significant differences in two observed groups related to mechanical ventilation were found for birth weight, gestational age, Caesarean section, length of mechanical ventilation, surfactant replacement therapy and outcome. Three (13.64%) neonates with NP died, and among risk factors with poor outcome, significant was only Apgar score in the first minute ≤ 5 .

Keywords: pneumothorax, neonates, risk factors, outcome, mortality.

1. INTRODUCTION

Pneumothorax is not a disease for itself, it is rather a complication, an urgent, undesirable state of air penetration into the virtual space between two layers of pleura. Smaller content of air can be tolerated by the body and be asymptomatic, while rapid penetration and increased air volume endanger life due to partial or complete lung collapse and require urgent treatment. Based on the size and gradation of lung collapse, it is named as partial or total, one-sided, or more rarely bilateral (1).

The clinical manifestation also depends on the size, from the asymptomatic to the image of a severe respiratory distress. The diagnosis should be quickly confirmed by the usual respiratory assessment methods. Although transillumination and lung ultrasound is increasingly used, chest radiograph is still a gold standard for diagnosis and monitoring of treatment effects. Treatment of small and partial pneumothorax is usually conservative, while larger and total require urgent surgical drainage of the chest (2, 3).

Pneumothorax can occur at anytime in life, but studies report more frequent occurrence in the neonatal age. Neonates, especially those who are very ill, often suffer from respiratory problems. Pneumothorax is a potential hazard for all neonates, especially premature infants, and especially those requiring mechanical ventilation (4). It is generally considered as a complication of resuscitation, positive pressure ventilation or mechanical ventilation, as a barotrauma or volume trauma (5).

But, pneumothorax occurs unexpectedly in term infants, with "mature" lungs, and without a previous lung trauma, as well (6). Pneumothorax significantly increases mortality and incidence is different according to the reports. Why does pneumothorax actually occur in some

neonates, and can we identify risk factors for this?

2. AIM

The aim of this study was to investigate epidemiological and clinical particularities and outcome of neonatal pneumothorax in our region and identify risk factors for the onset of pneumothorax in neonates.

3. METHODS

In a retrospective study, medical records of all neonates who were admitted to Department of intensive care, Pediatrics clinic of University Clinical Center of Tuzla during the three-year period (from January 2015 through December 2017), a total of 604 patients were screened, and we reviewed records of neonates with pneumothorax. All neonates hospitalized in three-year period, with chest X-ray confirmed pneumothorax, 22 of them, were included in this study.

Participants were evaluated for baseline characteristics, predisposing factors of neonatal pneumothorax, accompanying disorders, and mortality. We reviewed data for patients' demographics including gestational age (GA), birth weight (BW), gender and Apgar scores at the 1st and 5th minute, type of delivery, possible premature rupture of membrane, postnatal age at the time of admission, and time to manifest pneumothorax, inborn-outborn status. Characteristics of neonates admitted with pneumothorax (n = 22) are shown in Table 1.

Pneumothorax was divided into spontaneous pneumothorax (an intrapleural air collection in the absence of intubation, positive ventilation) and secondary pneumothorax (with mechanical ventilation). The pre-condition of lung health was analyzed through the first radiographic lung findings, made before the pneumothorax. We analyzed laboratory, microbiological and radiological findings, therapeutic procedures, length of stay in the Intensive Care Unit and outcome.

The study was approved by the institutional review board (Ethics Committee of the Institution).

Statistical analysis used by the standard methods of descriptive statistics. The significance of differences between samples was tested using parametric and nonparametric tests of significance and methods of linear correlation, using statistical program Arcus Quick Stat and Systat software.

4. RESULTS

During a three-year period, from January 2015 to the end of December 2017, in Tuzla Canton area 11425 neonates were born, 10588 full-term and 837 preterm (625 late preterm and 212 very preterm neonates). Percentage of premature births was 7.33%. During the study period, 604 neonates were admitted to the Neonatal intensive care unit: 237 term, 172 late premature and 195 very preterm infants, and 265 neonates during the research period required mechanical ventilation (215 premature and 50 term neonates).

Neonatal pneumothorax (NP) was diagnosed in 22 patients (9 term, and 13 preterm), with incidence of 0.20% of total births, respectively 3.64% of those treated in the neonatal intensive care unit. Three (13.64%) neonates admitted with pneumothorax died during the study period.

Out of total 22 neonates with pneumothorax, 10 (45.5%) were female and 12 (54.5%) were male. The mean gesta-

Variables	n (%)
Gender	
Male	12 (54.5)
Female	10 (45.5)
Birth weight, mean \pm SD, (minimum-maximum)	2629.5 \pm 875.09 (940 – 4240)
<2 500	12 (54.4)
\geq 2 500	10 (45.5)
Gestational age, weeks mean \pm SD, (minimum-maximum)	35.1 \pm 3.58 (27 – 40)
<37	13 (59.1)
34-36	5 (22.7)
<34	8 (36.4)
\geq 37	9 (40.9)
One minute Apgar score, mean \pm SD, (minimum-maximum)	7.1 \pm 2.62 (2 – 10)
7-10	15 (68.2)
4-6	4 (18.2)
0-3	3 (13.6)
Five minute Apgar score, mean \pm SD, (minimum-maximum)	8.1 \pm 1.70 (3 – 10)
7-10	18 (81.8)
4-6	3 (13.6)
0-3	1 (4.5)
Inborn/outborn status	
Inborn	14 (63.64)
Outborn	10 (45.45)
Postnatal age of admission, days; mean \pm SD, (minimum-maximum)	1.6 \pm 1.36 (1 – 7)
Postnatal age of occurrence, days; mean \pm SD, (minimum-maximum)	2.5 \pm 1.57 (1 – 7)
Pneumothorax type	
Spontaneous (without previous mechanical ventilation)	14 (63.6)
Secondary (with previous mechanical ventilation)	8 (36.4)

Table 1. Characteristics of neonates admitted with pneumothorax (n = 22)

tional age were 35.1 \pm 3.0 weeks and birth weight 2 506.8 \pm 727.7 grams. In 8 (36.4%) neonates, the underlying cause of NP could be mechanical ventilation (secondary), whereas in 14 (63.6%) NP was spontaneous, without previous mechanical ventilation, although 11 of them required mechanical ventilation after pneumothorax.

Pneumothorax was right-sided in 9 neonates left-sided in 7, and bilateral in 6 of them. The most commonly associated diseases in neonates with pneumothorax were: respiratory distress syndrome, intracranial haemorrhage, pneumonia and sepsis in preterm; and transient tachypnea, pneumonia, hypoxic ischemic encephalopathy and sepsis in full-term neonates (Table 3). There was no significant difference in the values of inflammatory markers in neonates with pneumothorax compared to others. The most commonly associated causative agents were Coagulase negative Staphylococcus (CoNS), Staphylococcus aureus, and Escherichia coli in full-term neonates; CoNS and En-

Neonates: n (%)	Total	Full-term	Preterm	Late preterm	Very preterm
Births in Tuzla Canton	11425 (100%)	10588 (92.67%)	837 (7.33%)	625 (5.47%)	212 (1.86%)
Treated in NICU	604 (100%)	237 (39.24%)	367 (60.76%)	172 (28.48%)	195 (32.28%)
Occurrence of pneumothorax	22 (100%)	9 (40.9%)	13 (59.1%)	5 (22.7%)	8 (36.4%)
Mortality	3	1	2	1	1

NICU: neonatal intensive care unit

Table 2. Incidence of neonatal pneumothorax in Tuzla Canton

Condition (n)	Full-term (n=9)	Late preterm (n= 5)	Very preterm (n=8)	Total (n=22)
Respiratory distress syndrome(hyposurfactose)	-	5	8	13
<i>Transient tachypnea of the newborn</i>	8	-	-	8
Intracranial haemorrhage	2	4	8	14
Hypoxic ischemic encephalopathy	8	2	-	10
Perinatal asphyxia	3	1	2	6
Pneumonia	8	1	4	13
Atelectasis	2	-	1	3
Pulmonary haemorrhage	1	-	1	2
Sepsis	7	2	5	14
Cholestatic jaundice	2	1	1	4

Table 3. Comorbidity in neonates with pneumothorax

Parameter	Spontaneous pneumo- thorax	Related to MV	P value
number	14/22	8/22	0,0704
Male	7/14	5/8	0,571
Birth weight,grams; mean \pm SD, (minumum-maximum)	2946.0 \pm 761.57 (1700 – 4240)	2075.0 \pm 817.28 (940 – 3450)	0,0206
<2 500	4/14	6/8	0,0354
\geq 2 500	10/14	2/8	0,0354
Gestational age, weeks mean \pm SD, (minumum-maximum)	36.5 \pm 2.59 (32 – 40)	32.7 \pm 3.95 (27 – 39)	0,0139
Caesarean section	3/14	6/8	0,0140
Days of mechanical ventilation	3.9 \pm 2.66 (0.0 – 8.0)	6.5 \pm 3.16 (2.0 – 11.0)	0,0488
Surfactant replacement therapy	2/14	7/8	0,0008
Outcome:			
survivors	14/14	5/8	0,0137
deaths	0/14	3/8	0,0137

MV: mechanical ventilation

Table 4. Risk factors for neonatal pneumothorax

terococcus species, in late preterm neonates; and Streptococcus agalactiae and Enterococcus species in very preterm neonates.

In all cases, the diagnosis was based on a clinical manifestation of a sudden worsening of the respiratory function, which was confirmed by radiography (chest x-ray).

Only one case of neonatal pneumothorax was treated conservatively, while the rest of the cases (21) required urgent thoracic drainage, 18 of them also required mechanical ventilation, and 11 of them required Surfactant replacement therapy. Persistence of thoracic drainage was 2-10 days, mechanical ventilation 1-11 days, and NICU stay 2-38 days.

Out of total amount 19 neonates with pneumothorax recovered completely, while 3 neonates died. One of them was

a full-term infant with severe post-asphyctic multi organ dysfunction; one late preterm infant with severe respiratory distress syndrome and bilateral pneumothorax; and one extremely immature with severe respiratory distress syndrome and pulmonary hemorrhage.

All perinatal risk factors were analyzed. Neonates with pneumothorax are classified into two groups, depending on the origin: a group with spontaneous pneumothorax (without previous mechanical ventilation) and a group with secondary pneumothorax (appeared during mechanical ventilation). Significant differences in two observed groups were found in birth weight, gestational age, Caesarean section, length of mechanical ventilation, surfactant replacement therapy and outcome (Table 4). Other risk factors

were not significantly different in the two observed groups.

Risk factors of neonatal pneumothorax were analyzed in two groups of neonates, depending on the outcome (survivors/died). A significant difference was found only in Apgar score in the first minute ≤ 5 , which was significantly more common in the group of deaths; and the length of NICU stay, which was significantly longer in survivors.

5. DISCUSSION

The incidence of neonatal pneumothorax (NP) varies depending on the area and the population. From the total population of live births, it's in a range from below 0.5% (7-9) to 3-7% (10, 11). Hospital incidence is higher and varies from 1.8% (12) to 9% (13). In our study, the incidence of neonatal pneumothorax from total live births was 0.2%, while the hospital incidence was 3.6%. Gender distribution, according to the reports, is mostly balanced, or mild preference is reported in male, as is the case in our results.

NP is more often seen in neonates with low birth weight and premature infants (11-13), while in our study, they were almost equally represented neonates who weighed less than 2500 g, versus those above that weight, and with a slight majority of premature infants.

NP in our patients, mostly occurred in the second day of life, which corresponded with literature (11). Mechanical ventilation increases incidence of neonatal pneumothorax, referring NP in ventilated neonates from 2-4% (12, 14) to nearly 25% (15), and commonly it is about 10% of total ventilated neonates (16, 17). In our study, from total 604 intensively treated neonates, 265 of them required mechanical ventilation, whereas 8 of them had a pneumothorax (3%). All those who had NP associated with mechanical ventilation were born prematurely, with gestational age less than 34 gestational weeks, while spontaneous pneumothorax was observed in term and late premature infants. It is interesting that a large number of neonates with NP (66.3%) in our study actually had spontaneous pneumothorax, without previous mechanical ventilation, although 78.5% of them, due to progression of respiratory failure, required mechanical ventilation after pneumothorax. These data partly fitted with some published reports (6, 9, 13, 18).

We notice a slight decrease in the incidence of pneumothorax in ventilated premature neonates, compared to some earlier studies from these regions (19,20), likely as a result of new gentle and protective ventilation strategy, in the context of forward shift in treatment of prematurity and respiratory distress syndrome.

Position of NP in our, as in most other studies, was mostly unilateral (72.7%) and right-sided. Right or left-sided NP was represented in the ratio 1.3:1. Bilateral NP was recorded in 6 neonates (27.7%), in four of them performed after birth, and in two neonates during mechanical ventilation. It seems to be a larger proportion than in other studies, but there are published similar experiences (21).

The challenge is to interpret these results, especially since we recorded during the study, during one summer month, a small group of four term neonates with a very similar clinical presentation of respiratory distress and spontaneous pneumothorax, as suspicious of a possible epidemic phenomenon, caused by a certain causative agent, but we could not confirm this by the obtained microbiological tests. Can spontaneous pneumotho-

rax, in mature and late premature infants, be partly affected by an infectious agent, to the newly started lung function?

Pathophysiology of interstitial emphysema as a central issue of air leak syndrome, and therefore pneumothorax, is very complex and still unclear. As already known, the risk factors for development of pneumothorax and all other phenomena from air leak syndrome, include prematurity, low Apgar score, respiratory distress syndrome and infection (neonatal sepsis, pneumonia), as well as some settings of mechanical ventilation (22, 23). In our study the most commonly associated diseases in neonates with pneumothorax were respiratory distress syndrome, pneumonia and sepsis, but there was no significant difference in the values of inflammatory markers in neonates with pneumothorax compared to others. In neonates with NP, it is surprising that gram positive isolates dominate, although the total sample had mixed isolates and even a slight predominance of gram negative pathogens. There is no sufficient data about possible correlation between specific pathogens and NP.

We analyzed all perinatal risk factors in group with spontaneous pneumothorax versus group with secondary pneumothorax in ventilated neonates. Significant differences in two observed groups were found in birth weight, gestational age, Caesarean section, length of mechanical ventilation, surfactant replacement therapy and the outcome. All these indicators were significantly worse in the group of neonates with NP generated during mechanical ventilation, so our study confirms that low birth weight, lower gestation, Caesarean section and surfactant therapy are risk factors for NP in neonates on mechanical ventilation. It is also significant that all three neonates with a poor outcome came from this group.

Crucial for a satisfactory outcome of the NP is timely recognition (there is no doubt about it in literature), and adequate treatment (there is still some difference). Commonly, conservative (expectant) approach is applied for small and asymptomatic NP, while complete NP requires surgical approach, needle aspiration or thoracic drainage (22, 23). Only one case of neonatal pneumothorax in our study, was treated conservatively, while the other 21 cases required urgent thoracic drainage. No complications of this procedure were recorded, and persistence of thoracic drainage was 2-10 days, mechanical ventilation 1-11 days, and NICU stay 2-38 days. Interpretation for almost no complication of thoracic drainage can be because of, in our clinic, this is performed by pediatric surgeons who are an integral part of NICU team.

NP endangers the newborn's life, complicates treatment, prolongs the stay in the NICU, increases costs and increases mortality. High mortality in neonates with NP, associated with another pathology, is reported in most studies, ranging from 13-36% (7, 12, 21). Outcome for 86.4% neonates with pneumothorax in our study was positive, and they recovered completely, without sequelae, while 13.6% died. Risk factors for neonatal pneumothorax were analyzed in two groups of neonates, depending on the outcome (survivors/died). A significant difference was found only in Apgar score in the first minute ≤ 5 , which was significantly more common in the group of deaths, and the length of NICU stay, which was significantly longer in survivors.

Our study had some limitations. On one hand, it was a single centre study, with relatively small study sample. On the other hand, the results identified risk factors for the development of NP in ventilated neonates. The risk factors for occurrence of NP spontaneously, without prior

mechanical ventilation, are not yet clear, and for this area of research, a prospective, well-designed study, with larger sample, would be required.

6. CONCLUSION

NP is an undesired emergency state, with risky clinical course and outcome and requires immediate and adequate action for recognition and treatment. All perinatal risk factors were analyzed, and significant differences in two observed groups of NP were found in birth weight, gestational age, Caesarean section, length of mechanical ventilation, surfactant replacement therapy and outcome. Three (13.64%) neonates with NP died, among risk factors for poor outcome, significant was only Apgar score in the first minute ≤ 5 . New information about possible risk factors and better understanding of total pathophysiological sequences in NP could improve treatment, survival and long-term outcome for all, especially for the most risky neonates.

- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms
- **Author's contribution:** Each author gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
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