

Causes of respiratory distress among neonates of gestational age 32 weeks and more

KREŠIMIR MILAS¹, HANA DOBRIĆ¹, MATEJ ŠAPINA¹, KRUNOSLAV MILAS², KATARINA POPOVIĆ², VESNA MILAS¹, KAROLINA KRAMARIĆ¹

¹ Department of Pediatrics, Clinical Hospital Centre Osijek, Faculty of Medicine Osijek, University of Josip Juraj Strossmayer, Osijek, Croatia

² Department for Emergency Medicine, Osijek, Croatia

Corresponding autor:

Vesna Milas

Department of Pediatrics, Clinical hospital Center Osijek

Hutlerova 4, 31000 Osijek, Croatia

Phone: 00 385 31 512 287

Fax: 00 385 31 512 287

e-mail: milas.vesna@kbo.hr

ABSTRACT

Respiratory distress (RD) is the commonest reason for admission in Neonatology intensive care units (NICU) and it is caused by respiratory and non-respiratory illnesses. The goal of the study is to find out most important causes of RD in preterm babies with 32 or more weeks of gestation, and to compare the etiology factors for RD in those preterm and in full term babies. Retrospective study in the NICU, Clinical Hospital Osijek, during the year 2016 was done. Almost 20% of admitted in NICU have RD, 34% of preterm babies of or older than 32 weeks, and 12% of terms babies. Among newborns with RD 61% were boys, and 39% girls. Among all live born 4% of boys and 2, 6% of girls had RD. Mother's illnesses as a cause of RD were found in 23, 2% and illnesses of the child in the other 60, 1%. Complications during delivery caused RD in the last 4% of newborns (some neonates have had more than one reason for RD). In 18, 9% of newborns the etiological factor was not found, and RD is probably genetically caused. The proportion of unknown causes is higher in preterm babies (22%). RD in term babies is mainly caused by illnesses of the child himself, and in preterm by mother's illnesses.

Key words: neonatal respiratory distress, sepsis, complications in pregnancy, gestational diabetes

INTRODUCTION

Respiratory distress is a challenging problem and one of the most common causes of admission in NICU. (1) It is the most contributing cause of morbidity and mor-

tality among preterm and term neonates. Symptoms of the condition are: sharp pulling in of the chest bellow and between the ribs with each breath, shallow breathing, flaring of the nostrils and grunting sounds and cyanosis. Neonates with RD are 2-4 times more likely to die than those without RD. (2) The manifestations of the disease are caused by diffuse alveolar atelectasis, edema and cell injury. Serum proteins that inhibit surfactant function leak into the alveoli. RD can be caused with respiratory and non-respiratory causes. The influenced factors are prematurity, cesarean section delivery, chorioamnionitis, male sex, different chronic or acute mother's diseases such as gestational diabetes or hypertension, different chronic or acute mother's diseases, and acute infections of the child, asphyxia, erythroblastosis fetalis and hydrops, meconium aspiration syndrome, some congenital anomalies of the respiratory (diaphragmatic hernia, tracheomalatia, thymus hyperplasia) and other systems (cardiac, renal, gastrointestinal) and systemic diseases. It can be caused with the mothers' acute or chronic illnesses or with the illnesses of the newborn himself, as well as by complications during the delivery (bleeding, polycitemia, knocked umbilical cord) and rare genetic mutation of surfactant protein. (3) These neonates develop RD because they have faulty genes that affect how their bodies make surfactant. Genetic disorders of surfactant protein metabolism comprise up to 10% of all childhood interstitial lung disorders. (4) These factors may impair surfactant production, release and function. Infants delivered before labor starts do not benefit from the adrenergic and steroid hormones released during labor. (5) Cause of RD stays unknown till today in some preterm

as well as in term babies. (6)

The study has been designed to point out the etiology of the RD separately in moderately preterm, late preterm and term babies. We want to see the differences between two groups. Goal is to find out in how many newborns (in both groups) the cause of RD stays uncovered despite our efforts.

MATERIALS AND METHODS

We conducted a retrospective study included patients (neonates) with respiratory distress with 32 weeks of gestation or older. Study covers all admitted neonates (inborn and out born) in the Neonatology intensive care unit in Osijek of University hospital Osijek in the period of one year, 2016. Very preterm babies (up to 32 weeks of gestation) were excluded from the study because the cause of RD among them seems clear. Medical records of the department and nursing lists were used as a source of data. The following parameters were analyzed: mother's chronic (hypertension, diabetes mellitus, hypothyreosis, infections) and acute illnesses (gestational diabetes mellitus, preeclampsia, infections), complications during labor (hemorrhage, stimulated or induced labor, complications with umbilical cord), neonatal illnesses (congenital heart and other anomalies, tracheomalation, thymus hyperplasia, meconium aspiration, asphyxia, sepsis, hydrops), gender of the neonate, gestation alter and birth weight, mode of delivery and Apgar score. In all newborns RD was seen in the first 24 hours. Incidence has been carrying out. Statistical analysis was performed using SPSS software system, along with the chosen level

of significance of $p=0.05$. Comparison of variables was tested by X2 test with Yates's correction.

RESULTS

The study included 69 neonates, 41 preterm and 28 full terms. Total number of admitted newborns of and older than 32 weeks of gestation during 2016 has been 348, 120 preterm and 228 term babies. Frequency among all admitted for RD has been 19, 8%. Almost 34% of admitted preterm and 12% term babies had RD. RD had 42 (61%) female and 27 (39%) male newborns. Among all live born males in 2016, 4% had RD. The percentage of RD among all live born female babies had been 2, 6%. Among preterm babies with RD 21 (51, 1%) has been born by cesarean section, and 20 (48, 9%) spontaneously. Full term babies 11 (39, 3%) has been born by cesarean section, and 17 (60, 7%) spontaneously. Among admitted newborns with RD there was statistically significant difference among the number of admitted pre terms and full terms. ($p<0, 05$). (Table 1)

We wanted to point out mother's chronic illnesses (hypertension, diabetes mellitus, hypothyroidism, and chronic infections) as well as illnesses during pregnancy (gestational diabetes mellitus and preeclampsia) as a cause of RD. Hypertension in mother has been more often cause of RD in preterm babies, almost two times oftener. It is the same with diabetes mel-

litus, and chronic mother's illnesses. But, it was not statistically significant. It means that mothers chronic illnesses and illnesses during pregnancy result with RD significantly oftener in preterm babies. Among newborns illnesses we have been looking for congenital anomalies of the heart and other anomalies. One preterm baby has artesian esophagi, and 3 neonates had anomalies of the genitourinary tract. Neonates had illnesses as a cause of RD more often than preterm babies. Among all newborns with RD newborn's illnesses were the most common cause of RD. Only term neonates had congenital heart anomalies. One of the causes of RD was tracheomalatia, and it is more often in term neonates. The same was with thyme hyperplasia. Among preterm babies with RD asphyxia has been the most common cause (22% of all causes). Sepsis has been responsible for the other 17, 1% RD in preterm babies. In terms sepsis was responsible for nearly 18% of RD. Some neonates had more than one cause of RD, because of that the number of causes was bigger than the number of neonates. In almost 22% of preterm and 14, 3% of term baby's cause stays unknown. Among all newborns with RD newborn's illnesses were mainly responsible for RD. Complications during the labor happened more often among term babies (bleeding, complications with umbilical cord). They were responsible for only 4, 3% of RD. (Table 2)

DISCUSSION

Respiratory distress lasts as the most frequent reason for admission in the NICU. The both preterm and term newborns are at risk. There are many reasons why neonates are vulnerable for RD. They stay in the mother's uterus for nine months and their mother's destiny is theirs. In this study we point out the incidence of RD among live born babies about 3, 4%, and among all admitted in NICU 19, 8%: 59,4% were preterm and 40,6% term babies. Among term newborns admitted in NICU 12, 3% had RD, and among preterm 34%. The same amount is mentioned in literature. (7, 8) In developing countries the percentage of RD among admitted term neonates is higher. Similar incidence as we pointed out is mentioned in the literature. (9, 10) Male newborns had RD more often, M: F ratio was 1, 6: 1. The proportion of our neonates with RD born by caesarian section and spontaneously was equal, preterm babies were born by caesarian section more often. If we look the total number of newborns born spontaneously, proportion of those with RD is 2, 6%. Different is if we look neonates born by caesarian section, percentage has been 5%. The similar is mentioned in the literature. (11) In our study RD has been mostly caused in both groups by newborn's illnesses and some special conditions among them (sepsis, asphyxia). Congenital anomalies were the third cause of RD among newborns illnesses. In our study (but we had small

Table 1. Mode of delivery and gender of newborns (N) with RD in 2016

N with RD		preterm	term	total	live born	% RD
		N %	N %	N %		
gender	male	27 (39,2)	15 (21,8)	42 (61)	1004	4,2
	female	14 (20,3)	13 (18,7)	27 (39)	1029	2,6
total		41 (59,5)	28 (40,5)	69 (100)		
Mode of						
delivery	spontaneously	20 (54,1)	17 (45,9)	37 (53,6)	1414	2,6
	Cesarean section	21 (65,6)	11 (34,4)	31 (46,4)	619	5,0
N with RD		41 (59,2)	28 (40,8)	69 (100)		
admitted in NICU		120 (34,5)	228 (65,5)	348 (100)		19,8

$P<0, 05$ among admitted preterm and full term newborns with RD

$P<0, 05$ among preterm and full term babies according to mode of delivery

$P>0, 05$ according to the gender of neonates with RD

N, newborns

NICU, neonatology intensive care units

RD, respiratory distress

Table 2. Causes of respiratory distress in newborns

Causes of RD	Preterm	Neonate	All (%)
	N (%)	N (%)	
	hypertension	2 (7,1)	8 (11,6)
Mother's illnesses	DM (GDM)	1 (3,6)	4 (5,8)
	Chronic illnesses	1 (3,6)	4 (5,8)
Total N of mother's illnesses	12 (29,3)	4 (14,3)	16 (23,2)
	CA of the heart	3 (10,7)	3 (4,3)
Newborn's illnesses	Other CA	3 (10,7)	4 (5,8)
	tracheomalatia	2 (7,1)	3 (4,3)
	Thyme hyperplasia	2 (7,1)	3 (4,3)
	sepsis	5 (17,9)	12 (17,4)
	asphyxia	3 (10,7)	12 (17,4)
	aspiration	1 (3,6)	1 (1,4)
	systemic	1 (3,6)	4 (5,8)
Total N of Newborn's illnesses	22 (53,7)	20 (71,4)	42 (60,1)
Complications during late pregnancy and labor	1 (2,4)	2 (7,1)	3 (4,3)
Known causes	35 (85,4)	26 (92,9)	61 (88,4)
N of newborns with known causes	32 (78)	24 (85,7)	56 (81,1)
Unknown	9 (22)	4 (14,3)	13 (18,9)
N of newborns	41 (100)	28 (100)	69 (100)

CA, congenital anomalies

DM, diabetes mellitus

GDM, gestational diabetes mellitus

N, number

RD, respiratory distress

number of cases) we found higher percentage in term newborns. These anomalies were: congenital heart, gastro-intestinal and anomalies of the kidney. There are some different dates from the literature. (11) Complications during the late pregnancy or labor have been the rarest cause of RD among the study groups. These included placental abruption and complications with umbilical cord. Mother's illnesses have been the cause of RD in 23, 2% of newborns, more common in preterm babies (one third of the whole number). The most frequent cause has been mother's hypertension. It was highly connected with RD, especially in preterm older than 32 weeks of gestation. Many dates from literature agreed with the fact. (12) Second cause among mother's illnesses has been diabetes mellitus or gestational diabetes mellitus (GDM). It has been responsible for RD in 5, 8% of all newborns. It seems that the association is closer in late preterm babies. We found in literature that GDM is not a major contributor to RDS in late

pre-term infants; more possibly is that the combination of prematurity and cesarean birth act independently to increase risk of respiratory morbidity. (13) The same percentage of causes has been caused with mother's chronic illnesses (diseases of the lungs, endocrine and kidney diseases). This was much more visible in preterm babies. Asphyxia is much more often cause of RD in preterm babies, and aspiration in term. Tracheomatia and thyme hyperplasia can be seen especially in the first days of admission in the NICU. There are much more often in full term newborns. Statistically significant difference between some causes of RD hasn't been found because of the small number of analyzed newborns. In almost 18, 9% of newborns cause of RD stays unknown (almost double often in late preterm babies than in term). The fact that RD is more often in boys speaks according the possibility of genetic origin of the disease. It is recognized that genetic risk for respiratory distress in infancy has been recognized with increasing frequency

in NICU. There are many mutations that can alter composition and function of the surfactant. (14) Further investigations are needed if we want to develop more rational strategies for treatment of RD, and if we want to counsel families whose infants are at the genetic risk for the disease at birth.

CONCLUSION

RD stays one of the major problems among newborns. Mother's illnesses, especially hypertension are very strong risk factor for RD in preterm babies. Sepsis and asphyxia are strong risk factors in both preterm and full term neonates. Cesarean delivery, especially in preterm babies and male gender stays other important risk factors for RD. Further advances in our understanding of genetic origin of the disease will help many newborns with RD. Discovery of risk alleles can be important for the further prognoses and treatment of neonates with RD.

REFERENCES

1. Swarnakar K, Swarnakar M. Neonatal respiratory distress in early neonatal period and its outcome. *Int J Biomed Adv Res.* 2015; 6:643-7.
2. Singh M. *Care of the Newborn.* 7th ed. Delhi: Sagar Publication; 2010. Respiratory disorder; 275-285.
3. Joseph KS. The natural history of pregnancy: diseases of early and late gestation. *Br J Obstet Gynecol.* 2011; 118(13): 1617-29.
4. Deutsch GH, Young LR, Deterding RR, Fan LL, Dell SD, Bean JA, Brody AS, Noguee LM, Trapnell BC, Langston C, et al. Diffuse lung disease in young children: application of a novel classification scheme. *Am J Respir Crit Care Med* 2007; 176:1120–1128.
5. Kushai Y, Bhakta. Respiratory distress syndrome. In: Cloherty JP, Eichenwald EC, Stark AR. *Manual of Neonatal care*, 6th ed. Lippincott Williams & Wilkins; 2004. p. 323.
6. Rimar Ž, Milas V, Mesić I, Medimurec M. Respiratory distress syndrome in Newborns of gestational age of over 32 weeks. *Coll Antropol.* 2014;38(2):621-626.
7. Rao GC, Rao MSP. Etiological profile of respiratory distress in first day of life of a newborn baby. *Int J Contemp Pediatr.* 2017; 4(1):210-214.
8. Metha A, Pratap D, Kushwaha KP, Singh A, Sharma A, Mittal M. A study of respiratory distress in neonates presenting within 72 hours. *Int J Ped Res.* 2017;5(1):24-30.
9. Santosh S, Kumar K, Adarsha E. Clinical study of Respiratory Distress in Newborns and its outcome. *Ind J Neonatal Res.* 2013; 1(1):2-4.
10. Dutta A, Sinhamahapatra KT. Spectrum of respiratory distress in newborn: a study from a tertiary care hospital in Kolkata. *The Child and newborn.* 2011; 15(2):45-48.
11. Mehrabadi A, Lisonkova S, Joseph KS. Heterogeneity of respiratory distress syndrome: risk factors and morbidity associated with early and late gestation disease. *BMC Pregnancy and Childbirth.* 2016; 16:281 Available <http://creativecommons.org/publicdomain/zero/1.0/>
12. Joseph KS. Theory of obstetrics: the fetus-at-risk approach as a causal paradigm. *J Obstet Gynaecol Can.* 2004; 26(11):953-60.
13. Bricelj K, Tul N, Lucovnik M, Kornhauser-Cerar L, Steblovnik L, Verdenik I. Neonatal respiratory morbidity in late-preterm births in pregnancies with and without gestational diabetes mellitus. *J of Matern Fetal Neonatal Med.* 2017; 30(4):377-379.
14. Cole SF, Hamvas A, Noguee ML. Genetic disorders of neonatal respiratory function. *Ped Res.* 2001; 50:157-162.