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Original Articles

DISTURBANCES IN THE ACUTE CARDIORESPIRATORY ADAPTATION OF FULL-TERM NEONATES

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Summary

We studied the incidence and causes of transition disturbances in the first 30 minutes of life in full-term newborns. This one-year study was retrospective and included 1147 full-term live-born neonates without life-threatening congenital anomalies and surgical complications. They were divided into four groups: 0 (with normal transition), 1 (resuscitated without endotracheal intubation), and 2 (intubated); A (without underlying maternal, obstetric or fetal/neonatal problem, with adequate for GA eight and from single birth) and B (with one or more of following: underlying maternal, obstetric or fetal/neonatal problem, SGA or LGA, from multiple pregnancies).
Of the newborns, 9.1% of required resuscitation and 1.6% - extensive resuscitation with intubation. The groups significantly differed in the incidence of underlying maternal, obstetric, or fetal/neonatal problems. Resuscitated babies were born via Caesarean section (CS), in abnormal presentation (PaN) and by vacuum extraction or forceps (V/F) predominantly. The highest incidence of the small for gestational age (GA) babies – SGA, was detected in Group 2. Twins and large for GA (LGA) had prevalence in Group 1. Resuscitation was necessary for 18.1% of CS-delivered babies. V/F and PaN lead to the highest need for intubation.
According to our data, every 10th of the full-term neonates required assistance in the fetal-to-neonatal transition. The causes could be diseases of the mother or fetus/newborn, multiple births, SGA, or LGA. A compromised medical decision about the time and way of delivery may result in iatrogenic transition disturbances.
Key words: fetal-to-neonatal transition, way of delivery, newborns

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Introduction

The fetus-to-newborn transition is a critical process and the most complex physiological adaptation that occurs in human life [1].

The fetus must shift from reliance on the maternal heart, lungs, metabolic, and thermal systems (via the placenta) to being able to self-sufficiently deliver oxygenated blood to the tissues and regulate various body processes. The transition requires complex physiological changes that must occur in a relatively short time [1].

All organs and systems are involved at some level, but the major immediate adaptations are the establishment of air-breathing concurrently with changes in pressures and flow within the cardiovascular system. While the majority of term infants complete this process in a smooth and organized fashion, some infants experience a delay in transition. It could be due to the obstetric, maternal problems, or underlying fetal/neonatal disease. Hospital-based deliveries increase the transition difficulties for many fetuses because of the frequent use of elective Caesarean sections, medications (anesthetics and analgesics), rapid clamping of the cord [2].

The transition is a time of significant risk to the newborn and necessitates astute observations by the healthcare team.

We aimed to study the incidence and causes of disturbances in the acute cardiorespiratory adaptation (the first 30 minutes of life) in full-term newborns.

Material and Methods

The retrospective study was conducted at Georgi Stranski University Hospital, Pleven, Bulgaria, from 01.07.2014 to 30.06.2015. The inclusion criteria were as follows: full term (37 complete gestational weeks – GWs), live-born neonates. Neonates with congenital anomalies – life-incompatible or compromising the cardiorespiratory function, or requiring surgical intervention in the first postnatal days were not included in the study.

The patients were grouped as follows: group 0 (with healthy cardio-respiratory adaptation), group 1 (resuscitated without endotracheal intubation), and group 2 (intubated). All the indicators we studied may affect the fetus-to-newborn transition: maternal diseases (diabetes mellitus, hypertension, anemia etc.); obstetric history (pathology of placenta, hemorrhage, pelvic-fetal disproportion, prolonged and complicated labor); mode of delivery: partus normalis (PN), Caesarean section (CS), in abnormal presentation (breech presentation, occiput transverse position and persistent occiput posterior position) – partus anormalis (PaN), and by instrumental appliance – vacuum extraction or forceps (V/F); anthropometrics and gestational age (GA) at birth; neonatal diseases and conditions (infection, blood antigen isoimmunization, meconium or amniotic fluid aspiration, small for GA (SGA) or large for GA (LGA); number of fetuses in utero; clinical outcome (healthy, with residual problems, death); hospital stay.

Because of the proven negative effect of some factors (underlying maternal, obstetric, fetal/neonatal problems, adequacy of birth weight to the GA, twin pregnancy) on the transition, we decided to further divide all the patients in two groups: Group A (without underlying maternal, obstetric or fetal/neonatal problem, with adequate for GA weight and from single birth) and Group B (with one or more of following: with underlying maternal, obstetric or fetal/neonatal problem, SGA or LGA, from multiple pregnancy).

Adequacy of birth weight to the GA was determined by the Fenton growth chart 2013 for girls and boys [3]. The WHO Guidelines on Basic Newborn Resuscitation 2012 [4] was applied.

The study data were processed using software statistical packages Statgraphics v. 4.0; SPSS v. 13.0 and Microsoft Office 2016 for Windows 10.

The results were described by tables, graphics, and numeric values (frequency coefficients, mean values, correlation coefficients, etc.).

We used parametric tests to verify hypotheses under normal distribution – t-test of Student and Analysis of Variance (ANOVA) with posthoc tests of LCD, Tukey HSD, Scheffe, Bonferroni, Newman-Keuls, Duncan, and non-parametric tests in cases of difference from a normal distribution - χ^2-test of Pearson, H-test of Kruskal-Wallis, etc. Various types of regression models were used to present relationships between variables.

The significance of the findings and conclusions was fixed as $p<0.05$.

Results

One thousand one hundred and forty-seven (100%) live-born term infants were evaluated. Of these, 1042 (90.9%) did not need assistance for the transition. The rest 105 (9.1%) were resuscitated, and 18 of them (1.6%) were intubated before the 30th postnatal minute (Table 1).

Table 1. Demographic data of Groups 0, 1 and 2

Characteristics	Groups			
	0	1	2	p
n (% of all)	1042 (90.9%)	87 (7.5%)	18 (1.6%)	-
Maternal age (years)	26±6 (14-53)	27±6 (15-40)	26±7 (15-38)	NS
GA (GWs)	38.9±1.2	38.7±1.3	38.5±1.3	NS
Birth weight (g)	3242±434	3224±613	2887±403	0.004†
SGA*	6.9	10.3	16.7	0.019‡
LGA*	6.1	13.8	5.6	
Twins*	0.7	5.8	0	<0.001
Hospital stay (days)	3.9±1.6	5.9±2.4	8.9±3.1	<0.001

* % of the all in the group; † significant difference between groups 0-2 and 1-2; ‡ significant difference between groups 0-1; §significant difference between groups 0 and 2

The incidence of underlying maternal, obstetric, or fetal/neonatal problems significantly differed between the groups (markedly increasing in Group 2, as compared to Group 0, p<0.001 for all the indices). (Figure 1).

The second main difference was the adequacy of the birth weight to the GA – the rate of SGA -babies was highest in Group 2, in Group 1 the LGA -babies and twins predominated (Table 1).

The third difference between the groups was the mode of delivery: the babies on Group 0 were born predominantly via PN, unlike the babies in Group 1 and 2 – via CS, PaN, and V/F (Figure 2).

Other traits of the resuscitated groups (1 and 2) were pathologic blood gas analyses with biochemical evidence of asphyxia (Figure 3), increased incidence of residual problems at discharge (Figure 4), and prolonged hospital stay (Table 1).

Comparing A- and B-groups (Table 2), we established that the babies of Group A were predominantly PN-delivered (Figure 5) and were healthy on discharge. The patients of Group B were more immature, more often born via CS, PaN, or V/F, and 19.5% of them needed resuscitation (Figure 6).

Despite the absence of aggravating factors in Group A, 30 of these patients (3.9%) were resuscitated. Analyzing the characteristics of the non-resuscitated and resuscitated patients of Group A (Table 3), we found a significant difference in the delivery mode - the resuscitated patients were more often born via CS, PaN, and V/F (Figure 7).

The above observations made us consider evaluating the need for resuscitation according to the delivery way (Figure 8).

The highest incidence of resuscitation need was determined in Subgroup V/F and the highest incidence of intubation – in the Subgroup PaN.

An impressive fact was the high incidence of resuscitation in the Subgroup CS – 18.1%. It should be emphasized that CS may be indicated because of the underlying maternal, obstetric, or fetal problem. Therefore, we decided to compare the babies born via PN and CS without a history of such problems (from group A only – elective CS) (Table 4). The patients delivered via elective CS were significantly more immature, required resuscitation eight times more often and longer hospital stay than PN-delivered.

The reason for all the cases of transition disturbances (105) remained unexplained only in six neonates (6%) – no maternal, obstetric, or fetal/neonatal complication, PN-delivered. In 74 babies (71%), an underlying problem was present, in nine (8%) – an unrecognized obstetric problem, and in 16 (15%), the problem was associated with the elective CS only.

Severe transition disturbances were registered in 18 babies: one with unexplained reason, 14 with an aggravated medical history, and three with an unrecognized obstetric problem.

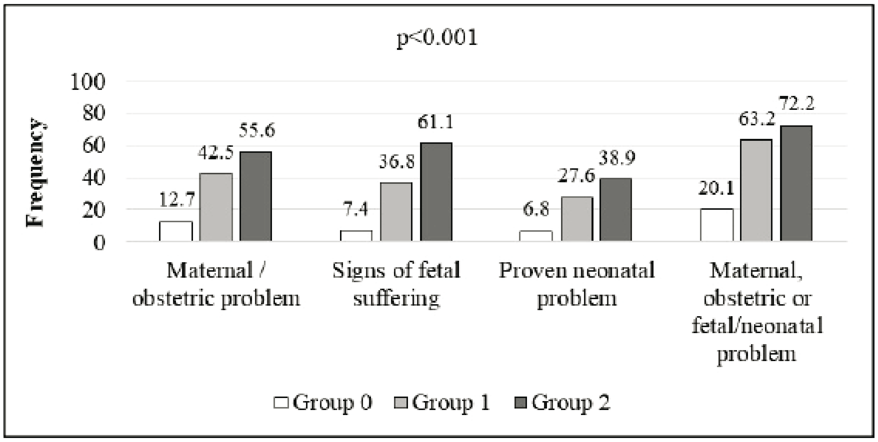

Figure 1. Maternal and fetal/neonatal morbidity in the groups (%)

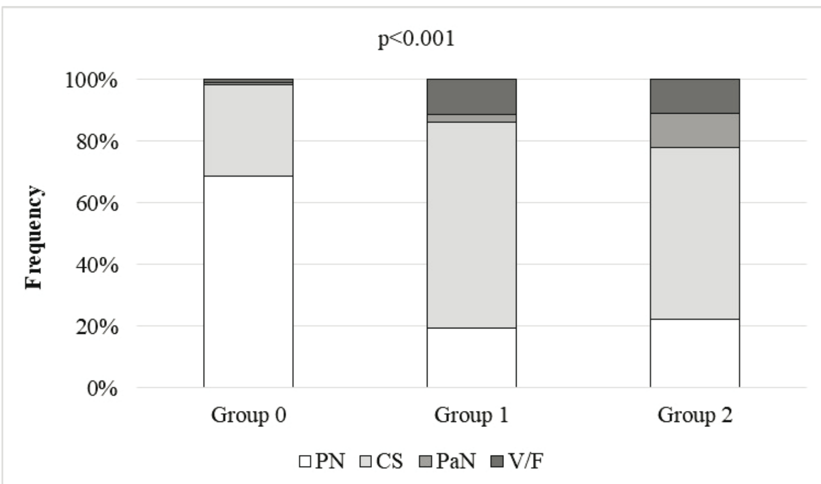

Figure 2. Delivery mode distribution in the groups (%)

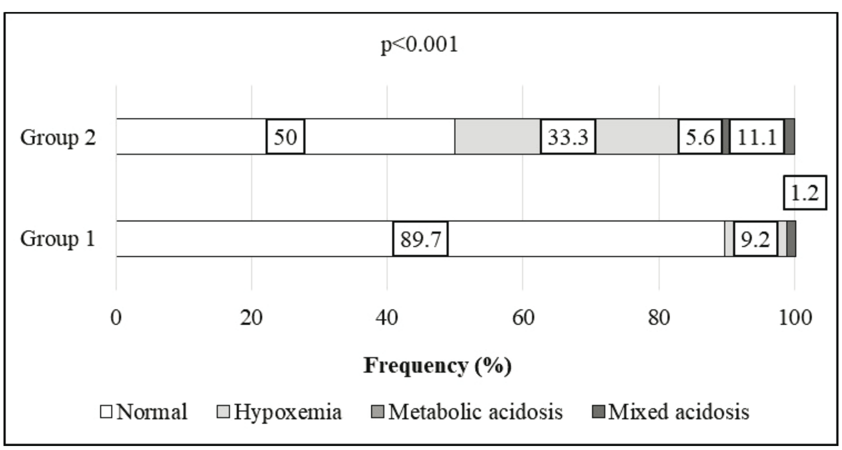

Figure 3. Blood gas analysis on admission (%)

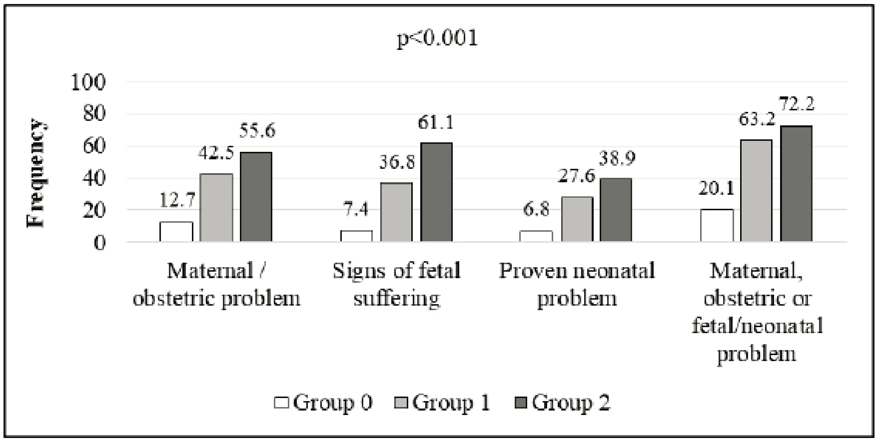

Figure 4. Status on discharge of the patients in the groups (%)

Table 2. Demographic data of the Groups A and B

Characteristics	**Groups**		
	A	**B**	**p**
n	763	384	-
Maternal age (years)	26.0±5.9	26.6±6.4	NS
GA (GWs)	39.0±1.1	38.7±1.3	0.002
Birth weight (g)	3251±347	3203±608	NS
Status on discharge (%) Healthy / With residual problems / Dead	100 / 0 / 0	96.9 / 2.9 / 0.2	<0.001

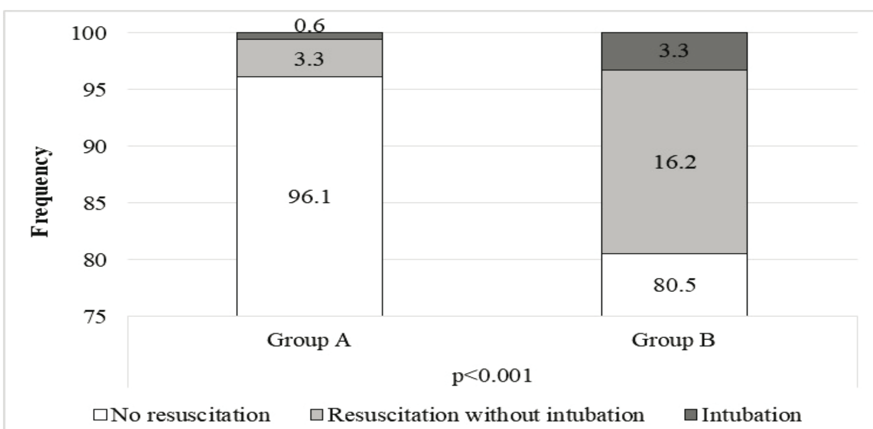

Figure 5. Delivery mode distribution in Group A and B (%)

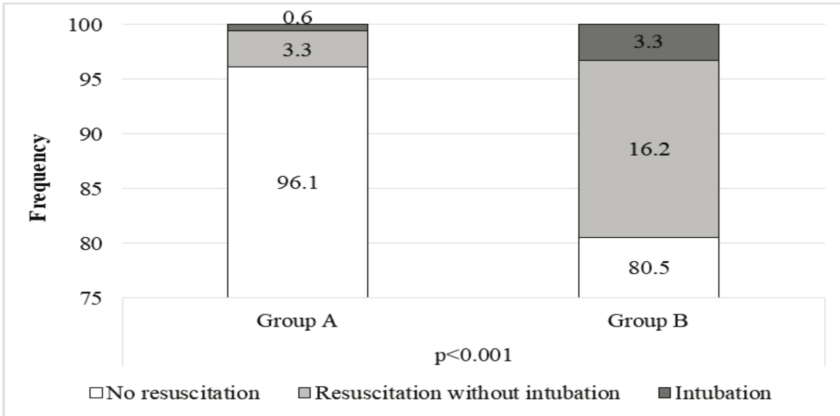

Figure 6. Resuscitation need in Group A and B (%)

Table 3. Characteristics of the non-resuscitated and resuscitated patients of Group A

Indices	Patients' categories		
	Non-resuscitated	**Resuscitated**	**p**
n	733	30	-
Age of the mother *(years)*	26.0±5.8	26.3±7.2	NS
GA *(GWs)*	39.0±1.1	38.7±1.1	NS
Birth weight *(g)*	3254±343	3189±438	NS

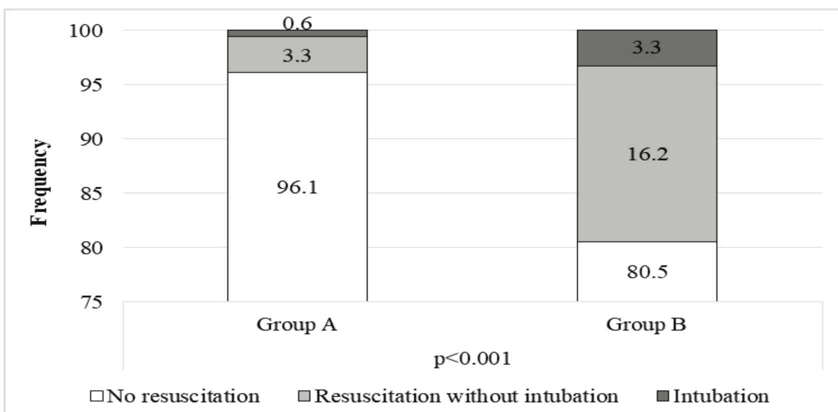

Figure 7. Delivery mode distribution in Group A - resuscitated and non-resuscitated subgroups (%)

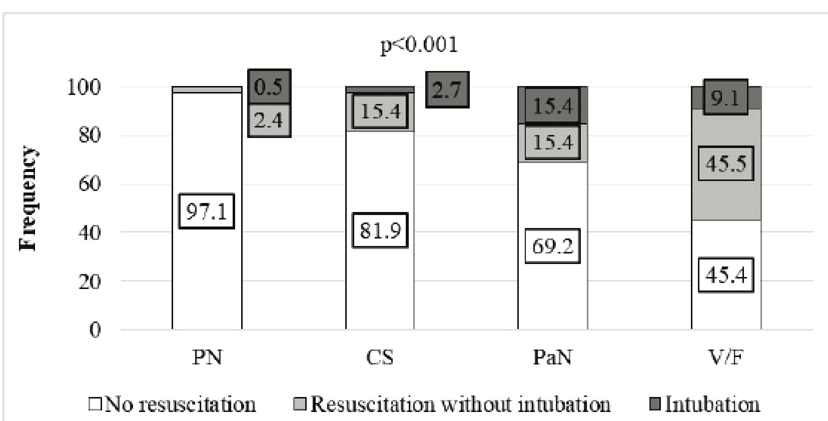

Figure 8. Resuscitation need rate according to delivery mode (%)

Table 4. Comparing the newborns of the Group A born via PN and CS

Characteristics	Patients' categories		
	PN	CS	p
n	553	187	-
GA *(GWs)*	39.1±1.1	38.7±1.2	<0.001
Maternal age *(years)*	25.4±5.6	28.0±6.1	<0.001
Birth weight *(g)*	3272±338	3220±351	NS
Resuscitated, including intubated* *(n)*	0.9 (5)	7.9 (15)	<0.001
Intubated* *(n)*	0.2 (1)	0.5 (1)	NS
Status on discharge* **(Healthy / With residual problems / Dead)**	100 / 0 / 0	100 / 0 / 0	NS
Hospital stay *(days)*	3.3±0.9	4.2±0.7	0.0000

* % of all in the group

Discussion

First inspiration and birth cord are clamping mark the beginning of the transition from intra- to extra-uterine life. The initiation of breathing is a complex process that involves many biochemical, neural, and mechanical factors [1]. Decreased O_2-concentration, increased CO_2-concentration, and a pH-decrease stimulate fetal aortic and carotid chemoreceptors, triggering the respiratory center in the medulla to initiate respiration. Mechanical compression of the chest creates negative pressure, and drawing air into the lungs as the lungs reexpand.

Further expansion and distribution of air throughout the alveoli occur when the newborn cries. To establish adequate ventilation and tissue oxygenation, a neonate must clear the fetal lung fluid, establish a regular pattern of breathing, and match pulmonary perfusion to ventilation. A vital role in this process is that of sodium reabsorption and catecholamine surge that occurs just before the onset of labor. Infants who do not experience normal labor are more likely to have residual lung fluid and subsequent respiratory problems. Other factors influencing transition are pulmonary blood flow, surfactant production, and respiratory musculature. Gas exchange is stabilized by the 2nd minute in most babies after vaginal delivery, and improvement in heart rate is the best clinical indicator of successful ventilation [1, 5].

In newborns with a healthy transition, lung aeration and partial liquid clearance are achieved on the first postnatal minutes, and liquid completely disappears by the 4th hour [6]. The acute hemodynamic-respiratory adaptation reflects the changes in circulation and breathing in the first 30 minutes.

Factors that place the neonate at risk of transition problems are [7]: maternal (diabetes, hypertension, cardiac or respiratory disease, severe anemia, shock, infection, drugs), obstetric pathology (pathology of placenta, hemorrhage, malpresentation, multiple gestation, chorioamnionitis, prolapsed cord, prolonged rupture of membranes, narcotic or magnesium sulphate administration, pelvic-fetal disproportion, V/F or CS, meconium-stained amniotic fluid), and fetal/neonatal problems (intrauterine growth restriction, fetal distress, pre-/postmaturity, congenital malformations, birth trauma, infections).

Many standard care practices may impact the transition: suctioning protocols, strategies to prevent heat loss, umbilical cord clamping, 100% oxygen use for resuscitation.

No definite conclusions can be drawn from studies on maternal analgesia effects on the newborn; thus, judicious use of medications in labor is recommended with further study of better bio-behavioral assessment tools to differentiate outcomes [8].

Some excess risk of a low Apgar score may be associated with repeat CS procedures [9]. The oxygen saturation and heart rate are significantly lower in CS-delivered infants [10].

The risks of perinatal asphyxia-related complications increase with higher maternal BMI in the term newborns [11].

Infants with underlying pathology may initially exhibit the same symptoms as those with mild transition problems. However, these infants deteriorate over time and may require increasing levels of support to maintain stability [7].

Approximately 10% of newborns require some assistance to begin breathing at birth. Less than 1% require extensive resuscitation measures [12].

It is crucial to distinguish cardiorespiratory depression (depressed vital functions against the background of normocarbia) from the perinatal asphyxia (peripartum hypoxic-ischemic event accompanied by hypoxia, hypercapnia, and metabolic acidosis). Whereas the perinatal asphyxia is a well evaluated and discussed problem, the cardiorespiratory depression is often neglected by the specialists, and there is no officially published statistics yet [13].

How can these results be explained? We found a statistically significant increased number of complicated pregnancies, fetal distress, and SGA in Group 2 (intubated neonates). In Group 1, we found similar problems like in Group 2, but the rate of the LGA and twins was the highest. Resuscitation of the PaN- and V/F-delivered neonates and those with inadequate to the GA weight proved an undiagnosed or neglected obstetric problem – a wrong medical decision about the optimal mode of delivery in these cases. Twin births are associated with both protective (earlier than in single birth maturation) and complicating factors (worsened condition of the second twin). Blood gas analyses revealed patients born in asphyxia who were part of both resuscitated groups only.

The patients of Group B were less mature, and half of them were CS-delivered. Pathologic predisposition resulted in about 20% resuscitation rate. Pathologic blood gas analyzes, and more unsatisfactory outcome were logical consequences.

Despite the absence of aggravating factors in Group A, 30 patients were resuscitated without data for asphyxia. These patients differed from the non-resuscitated in the delivery mode only: 30% of them were born via PaN and V/F (these were unrecognized obstetric problems), but more than half of them were born via CS (elective).

CS is an independent risk factor for transition complications because of disturbed stimulation of surfactant secretion and clearance of fetal lung fluid [2, 5], early umbilical cord clamping (compromising cardiovascular stabilization) [14, 15]. What is more, elective CS compared to PN and emergency CS increases the risk of respiratory complications [16], persistent pulmonary hypertension [17], and near-term respiratory distress syndrome [18].

Our data confirmed a higher risk of transition disturbances in CS-delivered newborns – 18.1% resuscitated of all the 376 CS-delivered babies. It is important to note that all CS in this period were performed under general anesthesia. Anesthetic medications used before extracting the baby from the uterus (according to the adopted protocol) were Lysthenon, Atracurium besylate, Propofol, and inhaled anesthesia with Sevorane. Each one of these medications has its depressive effect on the respiratory center in the fetal/neonatal brain. So the anesthesia given to anesthesia given to mothers was recognized as another important risk factor of transition disturbances in our study.

The incidence of CS in our hospital was very high at the time of our study. CS may indeed be a result of an obstetric decision because of specific indications, but 187 cases of CS in our study had no history of maternal, obstetric, or fetal/neonatal disease – elective CS. These neonates were more immature, and the resuscitation rate in this group was eight times higher than that in the PN-delivered babies as a result of the wrong medical decision on the time of CS delivery.

We confirmed a purely iatrogenic cause in 25 newborns (23.8% of all resuscitated babies) – 16 born via elective CS under general anesthesia, and 9 with unrecognized obstetric problems, born in a pathologic presentation. Three of these 25 newborns were intubated because of the severe disturbances of transition because of undiagnosed obstetric problems.

There are limitations to our study. It is retrospective, and there were unpreventable impacts of social, economic, personal, and ethnic factors on our results. The effect of cord clamping time was not examined because of the lack of data in this regard. The impact of the gender and the mode of conception (by assisted reproductive technologies or via natural conception) were not examined. Furthermore, this data reflects the experience of a single institution.

Conclusions

According to our data, 9.1% of full-term neonates required assistance in fetal-to-neonatal transition, and 1.6% suffered from severe cardio-respiratory disturbances. The causes could be those confirmed in the literature: maternal, obstetric, or fetal/neonatal complications, multiple birth or inadequacy of the birth weight to the GA. The highest risk of transition disturbances was found in the cases of an unrecognized obstetric problem, which led to labor in an abnormal presentation or the need for vacuum extraction or forceps. The transition disturbance risk was eight times higher in healthy babies from uncomplicated pregnancies delivered via elective CS, as compared to those born in a vaginal delivery. We proved a purely iatrogenic cause in nearly a quarter of resuscitated babies in our center.

Pregnancy monitoring is crucial to avoid or manage maternal, obstetric, and fetal problems. The mode of delivery and specifying the indications and time of the CS is the leading medical decision that may decrease the iatrogenic consequences. Close collaboration between obstetricians, anesthesiologists, and neonatologists is needed.

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