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Abnormal neurological soft signs in babies born to smoking mothers were associated with lower breastfeeding for first three months

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Running Head: Maternal smoking and breastfeeding

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ABSTRACT

Aim: We examined associations between neurological alterations in infants born to smoking mothers and breastfeeding success at discharge and three months of age.

Methods: This 2016 study compared 35 normal weight infants born to smoking mothers at 37-41 weeks and 35 matched controls born to non-smoking mothers at the Maternity Hospital of Careggi University, Florence, Italy. Neonatal behaviour was evaluated using the neurological soft signs (NSS) component of the Graham-Rosenblith Scale. Breastfeeding variables were measured using the LATCH score that covers: breast latching, audible swallowing, type of nipple, mother's comfort and help they needed to hold their baby to their breast. A questionnaire on excessive crying and feeding was distributed at discharge and further data were collected during a three-month telephone interview.

Results: At discharge, the infants born to smoking mothers had a significantly lower LATCH score and significantly poorer performance on several items of the NSS component than the controls. The LATCH score and number of NSS were inversely proportional. At the three-month follow up only 57.1% of the smoking group infants were breastfeeding compared with 87.5% of the control infants ($p < 0.01$).

Conclusion: Infants with smoking mothers displayed altered neurobehavioural profiles and had a difficult start to breastfeeding.

Key Notes

- This study examined associations between neurological alterations in infants born to smoking mothers and breastfeeding success at discharge and three months of age.
- We recruited 35 full-term normal weight infants born to smoking mothers and 35 born to non-smoking mothers at an Italian university hospital.
- At three months, 57.1% of the smoking group and 87.5% of the controls were breastfeeding and the smoking group infants displayed altered neurobehavioural profiles.

Keywords: Breastfeeding, Maternal smoking, Neurobehavioural profile, Newborn infants, Pregnancy

INTRODUCTION

Tobacco smoke is the second leading cause of death in the world and the leading cause of preventable death, according to the World Health Organization (WHO) (1). Pregnancy provides women smokers and their partners with a valuable opportunity to alter poor lifestyle and health-related habits, including smoking.

Numerous studies have shown direct links between the number of cigarettes smoked during pregnancy and the risk of an adverse event occurring during gestation (2-5). In addition, studies have shown that the risk increases more and more rapidly with exposure to passive smoking, such as if the mother's partner smokes (6-7).

Several studies have also shown that exposure to smoking during pregnancy led to significant increases in perinatal and infant mortality and morbidity, with unfavourable short-term and long-term effects (8-12). In fact, neonatal outcomes have been

negatively correlated with smoking, which has been associated with intrauterine growth retardation, low birth weights and decreased anthropometric indices, in particular head circumference (13). Smoking cigarettes during pregnancy also seems to play a decisive role in the appearance of adverse neurobehavioral outcomes in newborn infants, which include increased muscle tone, increased irritability and alterations in crying (9,10). Several small controlled studies that used structured, neurobehavioural examinations, administered by clinicians, to investigate the effects of maternal smoking in newborn infants, found changes in crying behaviour and soothability and increased muscle tone (14-18).

Despite the evidence on the quantifiable damage that newborn infants experience due to exposure to nicotine through breastfeeding, these have not been sufficient to inhibit breastfeeding in smoking mothers. Although breastfeeding women are advised to stop smoking, breast milk is still the main source of nourishment, even for babies exposed to smoking. However, despite recommendations that encourage breastfeeding, studies show that women who smoke are less motivated to breastfeed and that nursing smokers are more likely to wean their infants off breast milk earlier than women who do not smoke (19,20).

Early weaning has been attributed to numerous other factors, in particular problems related to milk production or psychological motivation (21-22).

The aim of this study was to examine the association between behavioural alterations in infants exposed to maternal smoking during pregnancy and successful breastfeeding. Our hypothesis was that even mild neurological changes in newborn infants would cause difficulties in initiating breastfeeding and that this would subsequently lead to early weaning.

PATIENTS AND METHODS

The study was carried out at the Maternity Hospital of Careggi University, Florence, Italy, from January 2016 to September 2016. It comprised 70 postpartum mothers and their newborn infants and the mothers were interviewed before discharge, when their infants were three to four days of age. In our hospital it is standard procedure for mothers and infants to stay for 48 to 72 hours after a straightforward delivery.

Mothers were excluded if they had taken any illicit drugs, antidepressants, thyroid or steroid medication during their pregnancy or if they had consumed more than three alcoholic drinks per month during their pregnancy. They were also excluded if they developed either psychiatric or serious physical illnesses during their pregnancy.

The newborn infants who were included in the study were all singletons who were born at 37-41 weeks of gestation with an appropriate weight for their gestational age. Their gestational age, in weeks, was based on the mother's last menstrual period and confirmed by ultrasound.

Infants who had congenital anomalies, jaundice or serious medical complications were excluded from the study.

We interviewed the mothers and they were assigned to the smoking or non-smoking control group based on their self-reported cigarette use. Having selected 35 smoking mothers we then matched them with 35 controls by socioeconomic status, degree of education, maternal age, parity, normal pregnancy, type of delivery, placental weight and weight gain during pregnancy.

All the mothers who took part expressed their intention to breastfeed their infants. The hospital's infant feeding policies and procedures complied with The Ten Steps to Successful Breastfeeding, launched by the World Health Organization and UNICEF, which is widely regarded as the optimal standard for breastfeeding management in

hospitals. Routine practice in our unit included: placing the newborn infants skin-to-skin with their mothers at birth, keeping the babies in the mothers' rooms, helping the mothers to initiate breastfeeding within an hour of birth and not giving breastfed newborn infants any other drinks than breast milk.

Breastfeeding-specific variables were assessed according to the LATCH scale, which represents five different breastfeeding elements. L stands for how well the infant latches onto their mother's breast. A is for the amount of audible swallowing that is noted. T is for the mother's nipple type. C is for the mother's level of comfort. H is for the amount of help the mother needs to hold her infant to her breast (23). The LATCH scoring system has already been validated as a useful tool to predict the duration of breastfeeding (24,25). The following parameters were obtained on each newborn infant during the recruitment period and took place within the first few hours of delivery: weight, length, cranial circumference, Apgar score at one and five minutes, arterial umbilical pH, arterial umbilical partial pressure of carbon dioxide, partial pressure of oxygen and exposure to passive smoking.

All the neonatal neurological examinations were performed 48-72 hours after birth by the same paediatric neurologist, who was masked to the smoking exposure status of the newborn infants. All examinations took place in a quiet examination room under similar lighting and temperature conditions.

Only the neurological soft signs (NSS) component of the Graham-Rosenblith Scale was evaluated (26). This comprises six signs: abnormal crying, shaking, visual abnormalities, a marked change in state, hypersensitivity and tremors. The presence of one or more of these signs indicates poor performance and the absence of signs shows normal and adequate performance. The final score consists of the total number of abnormal NSS that are present.

A questionnaire that included information about excessive infant crying and feed modality was distributed to each mother at discharge from the hospital and then the results after the mothers had filled in during the first weeks were reported at the telephone interview. Excessive crying was defined as crying for more than three hours per day, for more than three days per week and for more than three weeks or crying for more than 1.5 hours per day for six or seven days (16).

Statistical analysis

The clinical characteristics of the two groups of infants were reported as means and standard deviations or rates and percentages. The Student t-test was used for continuous variables and Fisher's exact test was used for categorical variables. A p value of less than 0.05 was considered statistically significant. The scores for the NSS were correlated to the LATCH scores by linear regression analysis for all babies of smoking group and presented as coefficients of linear correlation (r), coefficients of determination (R^2) and 95% confidence intervals (95% CI). GraphPad Prism 6 Software (GraphPad Software Inc, California, USA) and Excel for Mac 2011 (Microsoft Corp, Washington, USA) were used for the statistical analysis.

Ethics

The research protocol was approved by the hospital's institutional review board and the mothers provided written, informed consent for them and their infants to be included in the study.

RESULTS

This study comprised 35 neonates born to smoking mothers and 35 newborn infants born to non-smoking mothers. The characteristics of the two groups of infants are shown in Table 1. These were not significant, except for the fact that the infants born to smoking mothers had greater passive smoke exposure than the control infants (p= <0.01).

At discharge, the smoking group had more difficulty initiating breastfeeding than the non-smoking group (45.5% versus 20.0%, p= <0.01). The mean LATCH scores for the infants with smoking mothers were significantly lower than the controls (7.00 ±1.8 versus 8.45 ±1.8, respectively, p<0.01) (Table 2). The infants in the smoking group showed significantly worse performance for several NSS items (57.1% versus 8.6%, p <0.01) and 12 (34.3%) scored positive for more than NSS (Table 2).

Regression analysis found that the LATCH score was inversely proportional to the NSS score (r -0.81; R^2 0.69, 95% CI -0.90 to -0.69) (Fig. 1). However, the NSS score did not correlate well with the numbers of cigarettes smoked by pregnant mothers (r 0.26; R^2 0.07, 95% CI -0.07 to 0.54) (Fig. 2).

At three months after discharge, none of the 35 dyads in the smoking group and three of the 35 controls had been lost to follow up. The difference in the proportions of babies with excessive crying was not significant between the smoking and non-smoking groups (31.4% versus 18.7%, respectively, p = 0.12), but the differences between modes of feeding were significant. A much higher percentage of the non-smoking mothers were still exclusively breastfeeding than the smoking mothers (87.5% versus 57.1%, p = <0.01) and 22.9% of babies from smoking mothers were exclusively receiving formula compared to none of the babies born to the non-smoking controls (p = <0.01) (Table 2). The remainder were receiving a combination

of breast milk and formula. All newborn infants fed with formula were weaned from the breast by their mothers within the first month of life. Just over a third (34.3%) of the smoking mothers reported that they stopped smoking during breastfeeding, but the difference in breastfeeding rates between the mothers who quit (50.0%) and the mothers who continued to smoke (60.9%) was not significant (Table 3).

DISCUSSION

Maternal smoking during pregnancy remains a major public health issue, even though the rates have decreased over the last few decades. Our study investigated the effects of maternal smoking during pregnancy on infant neurobehaviour and the LATCH scores showed that the babies born to smoking mothers had a significantly more difficult start to breastfeeding and had a significantly lower LATCH score than the newborn infants born to the non-smoking controls. Furthermore, our data showed a strong inverse correlation between the LATCH scores and the NSS scores, which indicated neurobehavioural issues among the infants born to smoking mothers.

Several studies have found a relationship between impaired neonatal neurobehaviour and maternal tobacco use during pregnancy (14-18). In particular, Mansi et al (15) showed that women who smoked throughout their entire pregnancy were associated with irritable newborn infants, who were less interactive with their environment. The authors evaluated the behaviour of the newborn infants with the Brazelton Neonatal Behavioral Assessment Scale, which comprises 28 behavioural items scored on a nine-point scale and 18 reflex items scored on a three-point scale. The scale can be used to analyse clusters of items, such as habituation, orientation, motor performance, ranges of state, autonomic regulation and reflexes. Mansi et al observed a strong correlation between irritability and urinary cotinine levels in

newborn infants born to smoking mothers. There was also a correlation with the number of cigarettes smoked each day and the intake of maternal nicotine in those infants exposed to active maternal smoking. Linear regression analysis showed that urinary cotinine was the best predictor of infant irritability.

These data further support the hypothesis that nicotine and cigarette smoke compounds inhaled by the mother during smoking act directly on the developing fetal nervous system. In fact, fetuses have been shown to experience hypoxia-ischaemia during each cigarette their pregnant mother smokes, due to the vasoconstrictor effect of nicotine (9,10). An animal model showed that the nicotine itself was a neuroteratogen, which caused cell damage, reduced cell numbers and impaired synaptic activity (27). Another study reported that these mechanisms were receptor-mediated and involved brain regions and the transmitter system, which have prominent cholinergic inputs (28). When receptors are stimulated they induce premature cell differentiation and initiate the programme for apoptosis. However, relating the neurobehavioural disturbance found in animal studies to changes in human behavioural performance is far more difficult, because genetic and environmental factors contribute to cognitive performance. Nevertheless, babies born to smoking mothers may exhibit behavioural characteristics that are different to other newborn infants.

Stroud et al (14) investigated the affect of prospectively measured smoking during pregnancy on aspects of neonatal behaviour in a large community sample and found that exposure to maternal smoking was associated with increased irritability and hypertonicity in neonates. In particular, neonates who were exposed to heavy maternal smoking, defined in that study as one pack of 20 cigarettes or more per day, showed greater irritability than neonates exposed to moderate maternal smoking, of

less than one pack, or unexposed neonates. Neonates exposed to both heavy and moderate maternal smoking were also more hypertonic than unexposed neonates. Exposure to maternal smoking did not affect the neonatal responses to respiratory challenges (14).

Given the associations between both maternal smoking and infant irritability and later behavioural dysregulation, the results of our study have important implications for our original hypothesis. We hypothesised that NSS in infants born to smoking mothers would cause difficulties in initiating breastfeeding and lead to milk formula being substituted for breast milk. To our knowledge, this was the first study to find a correlation between abnormal NSS in babies born to smoking mothers and early weaning from breastfeeding.

The amount of nicotine that is transferred into breast milk is more than double the amount that is transferred to maternal serum. Although lactating women who smoke are advised to stop smoking, breast milk still remains the ideal food for infants, even if the mother does not stop smoking. Despite recommendations that encourage breastfeeding, studies have found that women who smoke wean their infants from the breast earlier than those who do not smoke (19,20). Possible explanations have been put forward to account for this phenomenon, which do not necessarily conflict with each other. First, smoking has been found to have an adverse affect on the lactational process by decreasing milk production and altering the composition of the mother's breast milk (21). Second, infants can develop colic or display excessive crying if their mothers smoke during breastfeeding and this might promote early weaning (16). Finally, mothers who smoke are less motivated to breastfeed. In

addition, our results showed a strong correlation between smoking during pregnancy, abnormal newborn infant behaviour, difficulty in initiating breastfeeding and early weaning from breastfeeding (22).

When we carried out a telephone-based questionnaire interview with the mothers to ask how they fed their infants at three months of age, we found that the proportion of breastfed babies born to smoking mothers was significantly lower than the proportion born to non- smokers. A fifth (20.0%) of the smoking mothers had already initiated mixed feeding and just under a quarter (22.9%) were only giving their infants formula. None of the non-smoking mothers had stopped breastfeeding their babies. Furthermore, all the newborn infants who were fed with milk formula at three months of life were weaned from the breast by their mothers during the first month of life, suggesting that the initial difficulties they experienced when they started breastfeeding affected their ability to continue breastfeeding.

In addition, the mothers who stopped smoking during breastfeeding did not obtain better results than the mothers who continued to smoke. Therefore, we can hypothesise that the substances contained in the breast milk of smoking mothers may be a contributory factor to early weaning from the breast. We can also speculate that the behavioural disorders in infants born to mothers who smoked during pregnancy, which were associated with difficulties in initiating breastfeeding, played a very important role in breastfeeding failure. Although the hormonal mechanisms underlying such changes, and the effects of smoking on the lactation process, remain unknown, the mechanisms that lead to the start of the lactation process are well known. The appropriate approach to the maternal breast by newborn infants, and how frequently they feed, are certainly the most important stimuli for initiating breastfeeding. Therefore, a newborn infant who shows poor performance, such as

abnormal crying, shaking, visual abnormalities, marked changes in states, hypersensitivity, and tremors, will probably fail to perform the appropriate manoeuvres to initiate the lactation process.

This study had a number of limitations. First, we did not obtain cotinine samples to validate whether the mothers smoked or not and they were assigned to their respective groups based on self-reported cigarette use during their pre-discharge interview. However, assessing smoking levels in the immediate post partum period, of days one to four, would probably have led to smokers with negative cotinine results as they were still in hospital. Second, the effects of any withdrawal syndrome in the infants could have been superimposed on the persistent neurotoxic effects they suffered as a result of their mothers smoking during pregnancy.

However the newborn infants in our study were tested between 48 and 72 hours of life, which was considered to be long enough to rule out nicotine withdrawal syndrome, which usually appears early after birth when mothers are heavy smokers (29). Studies by Law et al (30) and Godding et al (18) reported that nicotine withdrawal syndrome was characterised by an early onset, within 12 to 24 hours of life, and rapid resolution within 36 hours. Finally, 35 smoking mothers was a small sample size and the results should be considered as preliminary.

CONCLUSION

Exposure to maternal smoking during pregnancy was associated with infant neurobehavioural disturbances and with difficulties initiating and continuing breastfeeding. Future studies are needed test this hypothesis in numerous populations of smoking mothers.

NSS, neurological soft signs; LATCH, Latching onto the breast. Amount of audible swallowing, Type of nipple. Comfort of mother, Help needed by mother to hold baby to breast; WHO, World Health Organization

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

FINANCE

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REFERENCES

1. World Health Organization (WHO). *Tobacco fact sheet n°339*, 2015.(Cited 2015 June 8). Available from: URL:
2. www.who.int/mediacentre/factsheets/fs339/en/
3. Mattison DR, Plowchalk DR, Meadows MJ, Miler MN, Malek A, London S. The effect of smoking on oogenesis, fertilization and implantation. *Semin Reprod Endocrinol*, 1989; 7(4): 291–304
4. Pineles BL, Park E, Samet JM. Systematic Review and Meta-Analysis of Miscarriage and Maternal Exposure to Tobacco Smoke During Pregnancy. *Am J Epidemiol*, 2013; 179 (7): 807-823
5. Cnattingius S, Mills JL, Yuen J, Eriksson O, Salonen H. The paradoxical effect of smoking in preeclamptic pregnancies: smoking reduces the incidence but increases the rates of perinatal mortality, abruptio placentae, and intrauterine growth restriction. *Am J Obstetr Gynecol*, 1997; 177(1) : 156–161

6. England L, Zhang J. Smoking and risk of preeclampsia: a systematic review. *Front Biosci*, 2007; 12 (7): 2471-2483
7. Jaddoe VW, Troe EJ, Hoffam A, Mackenbach JP, Moll HA, Steegers EA et al. Active and passive maternal smoking during pregnancy and the risks of low birthweight and preterm birth: the Generation R Study. *Paediatric Perinat Epidemiol*, 2008; 22 (2): 162-171
8. Windham GC, Hopkins B, Fenster L, Swan SH. Prenatal active or passive tobacco smoke exposure and the risk of preterm delivery or low birth weight. *Epidemiology*, 2000; 11(4): 427-433
9. Horta BL, Victora BG, Menezes AM, Halpern R, Barros FC. Low birthweight preterm births and intrauterine growth retardation in relation to maternal smoking. *Paediatric Perinat Epidemiol,* 1997; 11(2): 140-151
10. Cornelius MD, Day NL. Developmental consequences of prenatal tobacco exposure. *Curr Opin Neurol*, 2009; 22 (2): 121-125
11. Verhagen EA, Ter Horst HJ, Kooi EM, Keating P, van den Berg PP, Bos AF. Prenatal tobacco exposure influences cerebral oxygenation in preterm infants. *Early Hum Dev*, 2011; 87(6): 401-406
12. Andres RL, Day MC. Perinatal complications associated with maternal tobacco
use. *Semin Neonatol 2000*; 5:231–241
13. Cnattingius S. The epidemiology of smoking during pregnancy: smoking prevalence, maternal characteristics and pregnancy outcome. *Niotine Tob Res 2004*; 6 (2): S125-S140
14. Cliver SP, Goldenberg RL, Cutter GR, Hoffman HJ, Davis RO, Nelson KG. The effect of cigarette smoking on neonatal anthropometric measurements.

Obstet Gynecol, 1995; 85(4): 625-630

15. Stroud LR, Paster RL, Goodwin MS, Shenassa E, Buca S, Niaura S et al. Maternal smoking during pregnancy and neonatal behavior: a large-scale community study. *Pediatrics*, 2009; 123(5): 842-848
16. Mansi G, Raimondi F, Pichini S, Capasso L, Sarno M, Zuccaro P et al. Neonatal urinary cotinine correlates with behavioral alterations in newborns prenatally exposed to tobacco smoke. *Pediatr Res*, 2007; 61(2): 257-261
17. Reijneveld SA, Lanting CI, Crone MR, Van Wouwe JP. Exposure to tobacco smoke and infant crying. *Acta Paediatr*, 2005; 94, (2): 217-221
18. Stroud LR, Paster RL, Papandonatos GD, Niaura R, Salisbury Al, Battle C et al. Maternal Smoking during Pregnancy and Newborn Neurobehavior: Effects at 10 to 27 Days. *J Pediatr 2009*;154:10-6
19. Godding V, Bonnier C, Fiasse L, Michel M, Longueville E, Lebecque P et al. Does In Utero Exposure to Heavy Maternal Smoking Induce Nicotine Withdrawal Symptoms in Neonates? *Pediatr Res* 55: 645–651, 2004
20. Villar M, Santa-Marina L, Murcia M, Amiano P, Gimeno S, Ballester F et al. Social factors associated with non-initiation and cessation of predominant breastfeeding in a mother-child cohort in Spain. *Maternal Child Healt J* 2018; 22: 725-734
21. Bertini G, Perugi S, Dani C, Pezzati M, Tronchin M, Rubaltelli FF. Maternal education and habitual behavior in the incidence and duration of breastfeeding: a prospective study. *JPGN* 2003; 37: 447-52
22. Hopkinson JM, Schanler RJ, Fraley JK, Garza C. Milk production by mothers of premature infants: influence of cigarette smoking. *Pediatrics* 1992;90:934–938.

23. Donath SM, Amir LH. The relationship between maternal smoking and breastfeeding duration after adjustment for maternal infant feeding intention. *Acta Paediatr* 2004;93:1514–1518.

24. Jensen D, Wallace S, Kelsay P. LATCH: a breasfeeding charting system and documentation tool. *J Obstet Gynecol Neonatal Nurs* 1994; 23: 27-32

25. Kumar SP, Mooney R, Wieser LJ, Havstad S. The LATCH scoring system and prediction of breastfeeding duration. *J Hum Lact* 2006; 22, 391–397.

26. Altuntas N, Kocak M, Akkurt S, Razi HC, Kislal MF. LATCH scores and milk intake in preterm and term infants: a prospective comparative study. *Breastfeed Med 2015*; 10: 96–101.

27. Bahena-Medina LA, Torres-Sanchez L, Schnaas L, Cebrian ME, Chaves CH, Osorio_Valencia E et al. Neonatal neurodevelopment and prenatal exposure to dichlorodiphenyldichloroethylene (DDE): a cohort study in Mexico. *J Expo Sci Environ Epidemiol* 2011; 21, 609-14.

28. Slotkin TA. Fetal nicotine or Cocaine exposure: which one is worse? *JPET* 1998; 285: 931-945

29. Slotkin TA, Cho H, Whitmore WL. Effects of prenatal nicotine exposure on neuronal development: selective actions on central and peripheral catecholaminergies patways. *Brain Res Bull* 1987; 18: 601-11

30. Pichini S, Garcia-Algar O. In utero exposure to smoking and newborn neurobehavior. How to assess neonatal withdrawal syndrome?. *Ther Drug Monit* 2006; 28: 288-290

31. Law KL, Stroud LR, LaGasse LL, Niaura R, Liu J, Lester BM. Smoking during pregnancy and newborn neurobehavior. *Pediatrics.* 2003;111:1318–1323.

LEGEND

Fig. 1: The correlation between the LATCH score and the NSS

(r -0.81; R^2 0.69, 95% CI -0.90 to -0.69)

Fig. 2: The correlation between the numbers of cigarettes smoked by pregnant mothers and the NSS

(r 0.26; R^2 0.07, 95% CI -0.07 to 0.54)

Table 1. Demographic characteristics of the two study groups

	Smoking group (n=35)	**Non-smoking group (n = 35)**	**p value**
Gestational age, weeks (mean, SD)	39.3 ±1.1	39.3 ±1.1	0.50
Birth weight, grams (mean, SD)	3,286.5 ±457.4	3,318.2 ±474.9	0.39
Head circumference, cm (mean, SD)	34.2 ±1.4	34.6 ±1.1	0.15
Length, cm (mean, SD)	48.5 ±4.1	49.6 ± 2.3	0.10
Female, n (%)	20 (57.1%)	20 (57.1%)	1
Cesarean delivery, n (%)	12 (34.3%)	12 (34.3%)	1
One-minute Apgar, (mean, SD)	8.8 ±0.7	9.2 ±0.5	0.02
Five-minute Apgar, (mean, SD)	9.7 ±0.5	9.8 ±0.4	0.30
pH umbilical artery, (mean, SD)	7.28 ±0.1	7.27 ±0.1	0.38
pO2 umbilical artery, (mean, SD)	24.2 ±10.1	21.8 ±10.1	0.16
pCO2 umbilical artery, (mean, SD)	46.9 ±9.6	50.1 ±9.1	0.09
Passive smoke	21 (60%)	9 (25.7%)	<0.01

Abbreviations: pO2, partial pressure of oxygen; pCO2, partial pressure of carbon dioxide.

Table 2. Neonatal outcome of the study populations at the discharge from hospital and at three months of life

Discharge from hospital			
	Smoking group (n=35)	**No smoking group (n=35)**	**p value**
Breastfeeding Started Difficult	 19 (54.2%) 16 (45.8%)	 28 (80.0%) 7 (20.0%)	 0.04 0.04
LATCH score	7.00 ±1.8	8.45 ±1.8	<0.01
Newborn infants with poor performance, n (%)	20 (57.1%)	3 (8.6%)	<0.01
Newborns with NSS, n (%): **none** **1** **≥ 1**	 15 (42.9%) 8 (22.8%) 12 (34.3%)	 32 (91.4%) 0 (0%) 3 (8.6%)	 < 0.01 <0.01 0.01
Three months of life			
	Smoking group (n=35)	**No smoking group (n=32)**	**p value**
Days of life (mean, SD)	92.1 ±1.1	92.2 ±1.8	0.15
Infants with excessive crying, n (%)	11 (31.4%)	5 (18.7%)	0.12
Type of feeding • **Breastfeeding** • **Mixed feeding** • **Formula feeding**	 20 (57.1%) 7 (20.0%) 8 (22.9%)	 28 (87.5%) 4 (12.5%) 0 (0%)	 <0.01 0.51 <0.01

Table 3. Newborn infants born to smoking mothers and type of feeding at three months of life

	Stop smoking during breastfeeding (n =12)	Smoking during breastfeeding (n = 23)	p value
Type of feeding			
• **Breastfeeding**	6 (50.0%)	14 (60.9%)	p= 0.80
• **Mixed feeding**	3 (25.0%)	4 (17.4%)	p= 0.60
• **Formula feeding**	3 (25.0%)	5 (21.7%)	p= 0.70