Immediate and late respiratory morbidity in children after elective cesarean section: comparison of early-term cesarean section (week 37-38+6) and full-term cesarean section

**Background:**
In the last decade there is a global tendency for an increase in the percentage of performed elective CS surgeries, in addition to the impact on maternal morbidity and mortality CS involves many risks to the neonate, in the last years there are more and more reports on the impact of CS on neonatal morbidity, especially the respiratory one, which is reflected in more specialized hospital care and prolonged neonatal hospital stay.[1, 2]

As already known, there is an inverse relationship between birth week and neonatal complications, including respiratory morbidity and mortality[3], in the other hand still there is no enough studies to show if there is a significant difference between children born by elective CS in early term (weeks 37-38+6) and those born by full term (weeks 39-40+6).[4]

**Objectives:**

To compare the immediate and late respiratory morbidity including performing respiratory function test in the two groups of children born by elective CS first group children born during gestational weeks 37-38 + 6 and the second group born during weeks 39-40+6.

**Methods:**

The study was performed in two parts, the first part, a retrospective cohort study, we collected data from pediatric cases born in French hospital of Nazareth whose ages at the time of the study were between 5-8 years, the second part included inviting randomly part of those children and their parents to fill out questionnaires and perform a pulmonary function test(spirometry).

**Results**

In the first part of the study - a significant correlation is observed between the week of birth and the APGAR score value in the first minute; In the second part, a clear correlation is observed between birth week of birth and respiratory function test values at the ages 5-8years.

**Conclusions:**

From our results we concluded that there is a definite relationship between week of birth and early and late respiratory morbidity - which was evident in better values ​​in 1-minute APGAR score and respiratory function in full term births compared to early term births.

**Abbreviations**

Cesarean section (CS), FVC (forced vital capacity), FEV1 (forced expiratory volume in one second), FEF (Forced expiratory flow)

## **What is known**

It is known that a premature birth involves many newborn complications including that of the respiratory system, especially when talking about the late, very and extremely preterm infants.

## **What is new**

One of the unique advantages in this study that it tested the late effect of early (37-38+6) elective CS in the respiratory function later in life at 6-8 years using a spirometry test which is considered gold standard method to assess respiratory function in this age, something which have not been tested in all the studies that we reviewed.

**Introduction**

In the last decade there is a global tendency for an increase in the rate of CSs despite the increased risk for neonatal respiratory complications compared with vaginal delivery; in Netherlands, the percentage of births by CS is 14.3%, in the UK and Canada between 22.8-26.8%, while in the US the percentage reaches 32.3% and the highest percentage is in Mexico which comes up to 43.9%.[5, 6] In Israel(the country in which this study was conducted) the percentage of CS in 2012 was 20.6% (9.5%-28.7%), 6% increase compared to the previous year, these figures were reported at an annual meeting of Israeli society for mother and fetus and relied on data from 26 centers in Israel. [7]

Cesarean section is indicated for maternal and fetal reasons and is divided into elective and emergency procedures, the maternal indications for Cesarean section include obstetric and maternal complications, such as multiple pregnancy, placenta previa and history of cardiac disease, while fetal indications include intrauterine growth retardation and nonreassuring fetal status. Elective CS may be indicated in cases of breech presentation and prior history of CS or uterine surgery, due to increased risk of neonatal brain injury, uterine rupture, or other complications.[6] Notably, it can be seen globally that the most common cause of CS have been changed from uterine or embryonic to psychosocial factors, defined as "maternal fear of giving birth" or "maternal demand" without the presence of medical reasons, and another cause is the decline in the rate of attempted vaginal birth after single cesarean delivery.[8-11]

WHO published a review about the risks associated with cesarean delivery during the years 2004-2008 in 24 countries, The conclusion of this review was that CS involves an increase in significant maternal and neonatal risk and recommended that CS should be performed only when there is an expectation of a particular benefit that exceeds the maternal and neonatal risks associated with this procedure.[12]

There are many contradictory reports in the literature about increasing morbidity and mortality as a result of CS, and this is due to different reviews and due to the mixing of elective and emergent CSs together; In addition there are more and more reports about the effect of CS on neonatal morbidity, primarily in the respiratory system, which is reflected in prolonged hospital stay after delivery and higher rates of hospital admissions.[1, 2]

It is also known about an inverse relationship between birth week and newborn complications and morbidity, in which as the baby born closer to full term as the chances for complications decreases.[13] and it is also important to note that there are also recent reports that newborns born in week 37-38+6 (early term) have higher developmental disorders and learning difficulties compared to those born on week 39-40+6(full term).[14]

To reduce the mainly respiratory complications in neonates born in elective CS it have been recommended by the American college of Obstetrics and Gynecology in 2007 to postpone CS until 39 weeks pregnancy [4]On the other hand despite this recommendation still there are no enough evidence in the literature to prove that there is a significant difference in respiratory complications between births at early term (weeks 37-38+6) and those born at full term (weeks 39-40+6); In 2009 Tita A et al. found that the rates of adverse respiratory outcomes, mechanical ventilation, newborn sepsis, hypoglycemia, admission to the neonatal ICU, and hospitalization for 5 days or more were increased by a factor of 1.8 to 4.2 for births at 37 weeks and 1.3 to 2.1 for births at 38 weeks compared to full term births[15], in 2012, Nir V et al. compared in retrospective study the differences between these two groups and showed that there are more morbidity in the early term group compared to full term. [16]

Study population and Methods:

**Study population:**

Our study included children who were born in elective CS between the years 2003-2007 in French hospital of Nazareth which were divided into two groups, the first group (study group) included children born between weeks 37-38+6, And the second group (control group) included children born between 39-40+6 weeks.

**Methods:**

The study was conducted in two parts:

In the first part we reviewed the birth files for both groups collecting relative information including APGAR score, neonatal respiratory complications after delivery, Mother age at birth, birth week, gender, pregnancy type (spontaneous, IVF), birth season, place of residence.

In the second part we invited randomly part of the parents to fill questionnaire and their children to pass a Spirometry test checking FVC, FEV1, FEV1/FVC.

later on, the data were summarized and we compared the variables between the two groups, Chi-square test was used to assess categorical variables between groups, and t-test was applied for continuous variables, p value < 0.05 was considered significant, Statistical analyses were performed using IBM SPSS statistics 22.0 for Windows.

**Results:**

The results also have been divided into 2 parts, the first part describes the results around birth, and the second part describes the results at 5-8 years.

First part:

This part included 118 participants, the information was collected from the files at French hospital database, and this group divided into two groups, first group included 62 neonates born in elective CS at early term (37-38+6 weeks) and second group included 56 neonates born at full term (39-40+6 weeks).

N=118

 Group 1 Group 2

 Group 1 Group2

N=62

N=56

Statistical analysis showed significant difference (P=0.022) in APGAR 1 between the two groups, which showed that the first subgroup was lower than that of the second subgroup; In contrast, no statistically significant difference (P=0.22) was observed between the two groups in the APGAR 5 (table 1), regarding the data of respiratory distress and the need for oxygen support after birth no statistically significant difference was observed between the two groups according to chi-square test, results of the correlation tests between the two groups are described in table 4, in the other hand it is worth noting that four newborns from the first group(early term) needed oxygen support after delivery, but this number was very small to demonstrate any statistically significant difference.

When other data were examined including mother's age at birth, illness during pregnancy, spontaneous pregnancy versus pregnancy after fertility treatments etc., no significant difference was found between the two groups (table 3).

Second part:

This part describes the group of children aged 6-8 years who performed the breath function test(Spirometry) by experienced respiratory technician, a total of 41 children participated and we divided them into two groups by week of birth, Group 1(birth week 37-38+6) included 24 children, Group 2(birth week 39-40+6) included 17 children.

N= 41

 Group 1 Group 2

N=24

N=17

The respiratory function test results demonstrated a significant statistic difference between the two groups as described in Table 6 in which the children in the first group (early term) demonstrated lower values mainly in these three parameters FEV1 (P = 0.02), FVC (P = 0.001), FEF (P =0.035), the other respiratory function test parameters were not statistically significantly different.

**Discussion:**

In this study, we examined differences between neonates born in elective CS on week 37-38+6 and neonates born in elective CS on week 39-40+6, We compared the APGAR values between the two groups around birth according to data from medical record, and later on we invited them for respiratory function test and for filling out questionnaires by their parents.

The first part of the study included 118 newborns, 62 in the first group (37-38+6) and 56 newborns in the second group (39-40+6), the data showed that there was a significant statistic difference in the first minute APGAR score in favor to the second group (those born after week 39); It also have been shown that there is a higher percentage of neonates in early term group that needed oxygen support after delivery and those who suffered from respiratory distress compared to the second group, but this difference did not reach statistical significance.

In the second part of the study which included 41 children ages 6-8 years, 24 in the first group(37-38+6) and 17 in the second group(39-40+6), it was evident that respiratory function values ​​mainly FEV1, FVC, FEF were statistically significant lower in the early term group compared to children in the full term group, the remaining parameters of respiratory function and other data collected in questionnaires did not show a statistically significant difference.

By looking at the results of the first part of the research, we can see that the significant difference was mainly in Apgar minute 1 which is known as a measure for assessing the general status of the fetus in the immediate postpartum period and is a useful screening test for clinically significant birth asphyxia and the risk of developing later on several neurological and psychiatric disorders, including cerebral palsy and intellectual disability [17-19], this important information highlights more the importance to strive for full term delivery; Another issue that we also looked at in the first part of our study is the immediate respiratory distress and the need for oxygen support, in this part the results analysis was very borderline(P = 0.051) in the first group and to prove this statistically perhaps we need a larger sample size.

After a broad and wide scan in the literature we found that this research is the first one to test the late morbidity in respiratory function in accordance to week of birth in *term* children, and is it known that spirometry considered the gold standard technique to measure lung function in children ≥6 years [20], this fact strengthen more the results we observed in the second part of our study which showed a statistically significant difference between the two groups in the FEV1, FVC, FEF value in favor to group 2 (full term) compared with group 1(early term) reflecting a better lung function in the second full term group, perhaps one of the explanations for this result that the lungs continue to grow even after 38+6 weeks pregnancy and the birth at week 39 and after results in better maturation of the lungs[21], therefore and according to this fact it is recommended to follow the recent guidelines and to schedule elective cesarean sections at week 39 and up[15, 22].

One of the limitations of this study is the relatively small number of participants in the second part of our study and it also it was not possible to perform this study with a blinded placebo control group.

In conclusion, it is known that a premature birth involves many newborn complications, both respiratory and other morbidities, looking at the results of our study we can show that even *early term* children born during gestational weeks 37-38+6 had higher risk for respiratory morbidity expressed in lower APGAR 1 minute score, the need for primary resuscitation immediately after birth and later on a worst pulmonary function test compared to full term children; Accordingly, we recommend that elective CSs be per-formed after 39 weeks’ gestation if there are no compelling medical reasons to perform them earlier.

Table 1- APGAR score

|  |  |  |  |
| --- | --- | --- | --- |
| p | GROUP 1 | GROUP 2 |  |
| P=0.022 | 8.82±0.64 | 9.02±1.34 | APGAR 1 |
| P=0.22 | 0.65±9.87 | 0.134±9.98 | APGAR 5 |
| P=0.60 | 1.4±5.87 | 0.64±5.76 | Admission days |

Table 2

|  |  |  |  |
| --- | --- | --- | --- |
| p | Group 1 | Group 2 |  |
| 0.358 | 30.69±5.99 | 29.63±5.7 | Mother Age |
| 0.167 | 37.86±0.54 | 39.88±0.9 | Birth Week |
| 0.000 | 3104.92±441.9 | 3502.45±463.7 | Birth Weight |
| 0.175 | 2 3.2% | 0 0.0% | Need for intubation |
| 0.609 | 5.87±1.396 | 5.76±0.637 | Admission Days |
| 0.027 | 8.8226±0.64 | 9.0179±0.133 | APGAR 1 |
| 0.222 | 9.8710±0.660 | 9.9821±0.133 | APGAR 5 |
| 0.051 | 4 6.6% | 0 0.0% | Need for Oxygen  |
| 0.046 | 6 11.3% | 11 27.5% | Congenital Anomaly |

Table 3

|  |  |  |  |
| --- | --- | --- | --- |
|  | Group 2 | Group 1 | P value |
| Mother age at birth | 5.7±29.6 | 5.9±30.69 | 0.358 |

|  |  |  |  |
| --- | --- | --- | --- |
| Birth Season | Group 2 | Group 1 | 0.63 |
| 1(winter) | 18 | 22 |
| 2(Spring) | 15 | 11 |
| 3(Summer) | 16 | 17 |
| 4(Autumn) | 14 | 2 |

|  |  |  |  |
| --- | --- | --- | --- |
| Newborn Sex | Group 2 | Group 1 | 0.398 |
| 1(Male) | 31 | 29 |
| 2(Female) | 25 | 32 |

|  |  |  |  |
| --- | --- | --- | --- |
| Spontaneous pregnancy/IVF | Group 2 | Group 1 | 0.835 |
| 1 (Spontaneous) | 54 | 58 |
| 2 (IVF) | 1 | 3 |

Table 4

|  |  |  |
| --- | --- | --- |
|  | Pierson | P |
| Respiratory Distress | 1.838 | 0.5 |
| Oxygen Need | 3.80 | 0.12 |

Table 5 Respiratory Function Test Results

|  |  |  |  |
| --- | --- | --- | --- |
| p | Group 2 | Group 1 |  |
| P= 0.02 | 1.62±0.53 | 1.22±0.24 | FEV1 |
| P=0.001 | 1.92±0.6 | 1.39±0.27 | FVC |
| P=0.035 | 2.04±0.57 | 1.68±0.5 | FEF |

Table 6

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | Group 2 | Group 1 | P0.067= |
| Passive Smoking | (Yes) 1  | 11 | 9 |
| (No) 2 | 6 | 16 |
| Pets at home | (Yes) 1  | 3(17.6%) | 2(7.7%) | P0.39= |
| (No) 2 | 14(82%) | 24 (92%) |
| Chronic Disease | (No) 1 | 41(74%) | 39(66%) | P0.325= |
| (Yes) 2  | 14(25.5%) | 20(33.9%) |
| Birth Season | Winter | 18(34%) | 22(42%) | P0.631= |
|  | Spring | 15(28%) | 11(21.2%) |
|  | Summer | 16(30.2%) | 17(32.7%) |
|  | Autumn | 4(7.5%) | 2(3.8%) |
| Place of residence  | Urban  | 32(58.2%) | 35(57.4%) | P0.93= |
|  | Not Urban | 23(41.8%) | 26(42.6%) |

1. Kamath, B.D., et al., *Neonatal outcomes after elective cesarean delivery.* Obstet Gynecol, 2009. **113**(6): p. 1231-8.

2. Levine, E.M., et al., *Mode of delivery and risk of respiratory diseases in newborns.* Obstet Gynecol, 2001. **97**(3): p. 439-42.

3. Hibbard, J.U., et al., *Respiratory morbidity in late preterm births.* Jama, 2010. **304**(4): p. 419-25.

4. *ACOG Practice Bulletin No. 97: Fetal lung maturity.* Obstet Gynecol, 2008. **112**(3): p. 717-26.

5. Boyle, A. and U.M. Reddy, *Epidemiology of cesarean delivery: the scope of the problem.* Semin Perinatol, 2012. **36**(5): p. 308-14.

6. Nakashima, J., et al., *Elective Cesarean section at 37 weeks is associated with the higher risk of neonatal complications.* Tohoku J Exp Med, 2014. **233**(4): p. 243-8.

7. Kubi bar, M.K., *The annual meeting of the Israeli society of maternal fetal medicine, the international meeting in fetal medicine.* November 2011.

.

8. Branch, D.W. and R.M. Silver, *Managing the primary cesarean delivery rate.* Clin Obstet Gynecol, 2012. **55**(4): p. 946-60.

9. D'Souza, R. and S. Arulkumaran, *To 'C' or not to 'C'? Caesarean delivery upon maternal request: a review of facts, figures and guidelines.* J Perinat Med, 2013. **41**(1): p. 5-15.

10. Stjernholm, Y.V., K. Petersson, and E. Eneroth, *Changed indications for cesarean sections.* Acta Obstet Gynecol Scand, 2010. **89**(1): p. 49-53.

11. Gregory, K.D., et al., *Changes in indications for cesarean delivery: United States, 1985 and 1994.* Am J Public Health, 1998. **88**(9): p. 1384-7.

12. Souza, J.P., et al., *Caesarean section without medical indications is associated with an increased risk of adverse short-term maternal outcomes: the 2004-2008 WHO Global Survey on Maternal and Perinatal Health.* BMC Med, 2010. **8**: p. 71.

13. Wood, N.S., et al., *Neurologic and developmental disability after extremely preterm birth. EPICure Study Group.* N Engl J Med, 2000. **343**(6): p. 378-84.

14. Sengupta, S., et al., *Adverse neonatal outcomes associated with early-term birth.* JAMA Pediatr, 2013. **167**(11): p. 1053-9.

15. Tita, A.T., et al., *Timing of elective repeat cesarean delivery at term and maternal perioperative outcomes.* Obstet Gynecol, 2011. **117**(2 Pt 1): p. 280-6.

16. Nir, V., E. Nadir, and M. Feldman, *Late better than early elective term Cesarean section.* Acta Paediatr, 2012. **101**(10): p. 1054-7.

17. *The Apgar score.* Pediatrics, 2006. **117**(4): p. 1444-7.

18. Ellis, M., et al., *An Apgar score of three or less at one minute is not diagnostic of birth asphyxia but is a useful screening test for neonatal encephalopathy.* Indian Pediatr, 1998. **35**(5): p. 415-21.

19. Modabbernia, A., et al., *Apgar score and risk of autism.* Eur J Epidemiol, 2019. **34**(2): p. 105-114.

20. Fainardi, V. and E. Lombardi, *Lung function tests to monitor respiratory disease in preschool children.* Acta Biomed, 2018. **89**(2): p. 148-156.

21. Schittny, J.C., *Development of the lung.* Cell Tissue Res, 2017. **367**(3): p. 427-444.

22. *ACOG Committee Opinion No. 386 November 2007: cesarean delivery on maternal request.* Obstet Gynecol, 2007. **110**(5): p. 1209-12.