A Study Protocol to Follow a Birth Cohort: Fars Birth Cohort

Najmeh Maharlouei [1], Sina Atefi [1] and Kamran Lankarani [1, *]

[1]Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran

[*]*Corresponding author*: Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran. Email: lankaran@sums.ac.ir

Abstract

Considering that the birth cohort study is the most appropriate model for studying and evaluating the relationship between exposures during the initial evolution and its long-term effects on the development of diseases, this prospective cohort study is designed for this purpose. Through a stratified random sampling, 6921 women, who were in the 20th to 30th week of gestation and lived in Fars province for at least six months prior to the interview, participated in this prospective cohort study. The study started in 2011 and the 4th follow up was finished in 2017. During the enrolment phase and four follow up after birth, the following information was collected in detail: socioeconomic status, knowledge and attitude of mother, husband toward normal vaginal delivery (NVD) and cesarean section (SC), early and late complications of delivery in mothers and babies, breastfeeding, any medical history in mothers and children, physical activity in children, and common psychiatric problems in mothers. So far, several articles have been published on the first results of the study. Mothers and children under the study will have three more follow ups until the children are 12 years old.

Keywords: Cohort, Birth, Fars, Iran

1. Why Was the Cohort Set Up?

The impact of genetic factors, socioeconomic status, and exposure to environmental factors during pregnancy on fetal health have been shown by many studies, as well as the long-term effects of these factors on the health of individuals in different life spans, including cardiovascular disease, cancer, respiratory diseases, cognitive and psychological disorders (1).

During the 1990 - 2000 years, the role of nutrition, exposure to environmental factors, and contaminations during and around birth (fetal and postnatal months) were considered as potential determinants of individual health in other life-stages (2).

Several studies have shown the impact of early breastfeeding and the development of eating habits in children at school age. In the same way, the consumption of fruits and vegetables was higher in children who have been exclusively breast-fed for a long time. The study by Bielemann et al. indicated that the time to start exclusive breastfeeding and duration of breastfeeding has a negative relationship with the age of the onset of ancillary food consumption by consuming processed foods (3).

Mental health in childhood is one of the most important public health issues that continues to affect adolescence and post puberty as well as affects social health and performance (4). Several psychological studies using the DOHaD model have investigated the cognitive cause of mental disorders and their relationship with the person's attitudes in the elementary period of life (5). The prenatal period is the most sensitive period of brain development. Prematurity, congenital anomalies, and other factors that directly lead to brain damage are known as the source of neuropsychological and developmental disorders. Several epidemiological studies have pointed to the potential role of some intrauterine infections in the development of neurodevelopment disorders, such as autism c. In addition, the socio-demographic characteristics of the mother, including the age and level of education, are related to the evolution of the child, thus, a lower education level or higher age of the mother is associated with an increased risk of mental retardation. Koutra et al. also found that the level of mother's education was relevant to children's ability to speak (6). The results of studies conducted in high-income countries indicate an increased risk of behavioral problems and the occurrence of mental disorders in preterm infants. However, Santos et al. in his study in Brazil, found that behavioral problems in the middle of childhood and up to early adolescence were more effective than socioeconomic factors and other birth-related conditions compared to the gestational age at birth (7).

The results of a population-based study in Brazil

showed that the low age of the mother, lower socioeconomic status, and the low level of mother's education are associated with an increased risk of accidents in children under the age of four. The relationship between maternal mental disorders and accidents in children under the age of 16 years has also been reported by a British study in 1978. Recent studies have reported a direct relationship between the duration of maternal depression and the incidence of accidents in children (8).

Etiologic studies on birth cohorts have a long history in Europe (9), however, this type of studies is infrequent in the Middle East (5). The results of these studies are very helpful in increasing the understanding of the role of exposures on childhood and adolescence health. Therefore, considering that the birth cohort study is the most appropriate model for studying and evaluating the relationship between exposures during the initial evolution and its long-term effects on the development of diseases, this prospective cohort study is designed for this purpose.

2. Who is in the Cohort?

The study was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1397.464) and began in 2011. The population under study was pregnant women living in the Fars province in southern Iran. Since 2010, about 68000 live births were registered in the Fars province, we decided to randomly select 10% of the pregnant mothers. Considering any non-response or lack of cooperation, we added 700 more individuals to the sample and finally decided to have a sample of 7500 pregnant women. Women in the 20th to 30th week of gestation and lived in the Fars province for at least six months before the interview were eligible for this study. Considering the residency area of pregnant women in rural or urban areas, as well as the place of receiving maternity care in the public or private sectors, sampling was done randomly and proportional to the percentage of pregnant women in these four classes. Therefore, by using stratified random sampling, 7500 eligible women were selected for this study from different parts of the Fars province. However, 579 women did not participate and the first phase of the study started with 6921 individuals.

Health centers are distributed all across the province and pregnant women referred to these centers to receive prenatal care. Eligible women were selected and invited to participate in the study at these centers. Those who signed the study consent form were interviewed by a trained study team. The first visit and interview was performed at the health center.

3. How Often Have They Been Followed Up?

The first phase of the study started in August 2011 and finished in June 2012. Since then we had four follow-ups. To evaluate the status of the neonate and mother and also the early complications of delivery, the first follow up was conducted eight weeks after birth. At this follow up, the mother and her newborn baby were visited at the health center and by interview and checking their health records the necessary data was collected. This follow up was finished in February 2013.

Since one objective of the study was the evaluation of breastfeeding and its effect on infants' growth and development, the second follow up was at the age of six months. All mothers participated in a phone interview. After interview and review of their records at the health center, data regarding the breastfeeding and infant's diet was obtained. The 2nd follow-up was finished on June 2013.

The third follow-up was at the age of two years, which ended in December of 2014. The forth follow-up started in January 2017, when children were five years old, and finished in December of 2017.

After the forth follow up, the mother and children under the study will be followed up every two years. Therefore, until the age of 12 all mothers and children will be followed up every two years and will have three more follow ups.

4. What Has Been Measured?

At the first visit, the following information was received through interviews and examinations from those who participated in the study: demographic information, maternal knowledge, main sources of knowledge, attitude of the mother, husband, parents, close friends, and gynecologist, regarding the route of delivery, convenience factors, and barriers to choosing normal vaginal delivery (NVD), and mother's preference for the route of delivery. The preliminary results of this visit are shown in Tables 1 and 2.

At the first follow up, the mother and her newborn baby were visited at the health center and by interview and checking their health records the following data was obtained: mother's socioeconomic status, birth place, mode of delivery and its details, baby's health status just after delivery and during the first eight weeks of life including history of any injury, infection, jaundice and congenital anomaly, history of any maternal complication of NVD or cesarean section (C-section), and the type of feeding, such as breastfeeding or formula.

For the second follow-up, which was at the age of six months, after the phone interview and review of the

Table 1. Distribution of Demographic Information of Pregnant Women[a]

Variable	
Mothers' age	27.02 ± 5.07
Marriage age	21.35 ± 4.15
Number of living children	0.84 ± 0.9
Number of abortions	0.24 ± 0.58
Mothers' job	
House wives	6215 (89.8)
Employed	642 (9.3)
Mothers' education degree	
Less than diploma	2818 (40.7)
Diploma	2521 (36.4)
University degree	1582 (22.9)
Husbands' education degree	
Less than diploma	3122 (45.1)
Diploma	2326 (33.6)
University degree	1473 (21.3)
Type of clinic for receiving services	
Governmental	4522 (65.3)
Private	2399 (34.7)
Mothers' insurance status	
Not insured	540 (7.8)
Insured	6345 (91.7)
Supplementary insured	1848 (26.7)
History of infertility in mothers	
Yes	462 (6.7)
No	6459 (93.3)

[a] Values are expressed as mean ± SD or No. (%).

Table 2. Scores Associated with Knowledge, Attitude, Barriers, and Conveniences Based on The Preference of Mothers for the Route of Delivery

	Mean ± SD	Median (Min - Max)
Knowledge about outcomes of NVD versus C-section	4.4 ± 3.1	4 (0 - 12)
Pregnant women attitude toward C-section	33.6 ± 5.7	34 (12 - 60)
Husbands' attitude toward C-section	7.7 ± 2.8	8 (3 - 15)
Family's attitude toward C-section	7.3 ± 2.7	7 (3 - 15)
Peers' attitude toward C-section	7.4 ± 2.6	7 (3 - 15)
Gynecologist's attitude toward C-section	7.3 ± 2.6	7 (3 - 15)
Barriers	10 ± 3.1	10 (4 - 20)
Conveniences	15.6 ± 3.7	16 (4 - 20)

Abbreviations: C-section, cesarean section; NVD, normal vaginal delivery.

records at health center data regarding the time of start of breastfeeding and its duration, duration of exclusive breastfeeding and all intakes of infants during the first six months of life was recorded.

The third follow up was at the age of two years, at this point data regarding the child anthropometric features, history of breastfeeding and other auxiliary foods in detail, history of any infection, allergic reaction, and hospitalization of the child during the first two years of life were recorded.

At the 4th follow up, all mothers and their children were invited to attend related health centers and three questionnaires were completed for them. The mothers' questionnaires comprised of perceived SES, demographic information, reproductive history, medical history during the past six years, history of smoking, alcohol consumption, and any usage of narcotics. To access the common psychiatric problems, General Health Questionnaire (GHQ) is also completed for all mothers. Moreover, using a standard questionnaire, the physical activity of mother is also evaluated at this visit. At the 4th follow up, children also evaluated for anthropometric measures, physical activity, and any medical history since the past four years. Development of all children is also accessed at this follow up using standard questionnaires' and measurements.

5. What Has Been Found? Key Findings and Publications

Using the data, at the time of enrolment, which was between the 20th to 30th weeks of pregnancy, we evaluated the preference of the pregnant women to have a NVD or C-section. Of the 6921 participants, 2197 (31.7%) preferred a C-section and 4308 (62.2%) favored NVD, while 416 (6%) had no idea regarding the preferred route of delivery. The score of knowledge regarding NVD and C-section in 904 (13.1%) participants was zero, and 1261 women (18.2%) achieved an acceptable level of knowledge. Using binary logistic regression, positive history of previous abortion and/or infertility, higher education level of mother and husband, mother's unacceptable level of knowledge regarding complications of C-section, and a positive attitude toward C-section from the mother and husband were determinant factors in choosing C-section as a preferred route of delivery. Then, we concluded that the awareness and knowledge of mothers and all families regarding complications of the C-section should be raised. Establishment of clinics for painless NVD and assuring mothers of benefits and lower complications of NVD can reduce the tendency for C-sections (10).

Another study on risk factors for C-section showed that the rate of C-section was remarkably lower in mothers whose maternity care was done in governmental centers comparing to the private clinics. It was also revealed that local healthcare, supplementary insurance, maternal age, age of marriage, place of birth, family income, as well as parental education and occupation played a fundamental role in choosing the mode of delivery (11).

Then, we conducted another study to identify non-medical factors affecting antenatal preferences for delivery route and actual delivery mode of women. In this study, of the 748 women who had expressed a desire to deliver their babies by C-section in 20 - 30 weeks of gestation, 87% gave birth to their baby through elective C-section. We found that the desire for delivery through elective C-section was associated with normative beliefs, control beliefs, expectations regarding maternity care, medical influences, evaluation of outcome, age, spouse educational level, and number of live births (12).

We also compared the selected outcomes in neonates born by low-risk planned C-section versus planned NVD. We examined early and late neonatal complications among 1071 neonates born through low-risk planned C-section and 1367 neonates born through planned NVD during 2012 - 2014. Gestational age of neonates born through C-section was significantly lower than their counterparts in the NVD group. Accordingly, babies' birth weights were 3166 ($\pm$ 442.4) grams in the C-section group and 3213 ($\pm$ 454.8) grams in the NVD group. Normal skin color at birth was more prevalent in the C-section group compared to the NVD group (85% vs. 81.3%, P = 0.04). No significant differences were detected between the two groups regarding birth trauma, birth height and head circumference, and developing infection, icterus, and convulsion during neonatal period. In addition, height and weight at two years of age did not significantly differ in both groups. The results of this study show that neonates born by C-section and NVD had the same early and late outcomes. The results of this study have been accepted for publication in Eastern Mediterranean Health Journal and will be published soon.

By another study, we evaluated the affecting factors of exclusive breastfeeding (EBF). The mean duration of EBF was 4.63 $\pm$ 1.99 months. We found that mothers with a university degree had

significantly (P < 0.001) lower EBF period. On the other hand, an employed mother, especially those with full-time jobs less practiced EBF (P < 0.001). By eliminating the confounders, we found that factors contributing to extended duration of EBF were acceptable weight gain of the baby during EBF, singleton comparing to twin or triplet pregnancies, adequacy of quantity of breastmilk

based on the mother's perception, maternal infection during puerperium, not using a pacifier for calming the baby, neonate's tranquility, birth place in governmental hospitals, and mother's unemployment (13).

Moreover, we found that the rate of C-section was significantly higher in expecting mothers who had less regular and standard exercise. This point could be useful for those who are involved in maternity care to inform pregnant mothers regarding the importance of maintaining themselves physically active during pregnancy (14).

6. What Are the Main Strengths and Weaknesses?

The main strengths of the study include the fact that, for a large proportion of mothers, data were prospectively collected since fetal life instead of retrospectively as in most birth cohorts. In addition, up to our knowledge, there is no registered birth cohort in Iran, which has collected data since fetal life.

7. Can I Get Hold Of The Data? Where Can I Find Out More?

This project is being conducted by the Health Policy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran. Collaborations for the analysis of the data are welcome. To request the access to data or to discuss any collaboration please contact fars.birth.cohort@gmail.com.

Footnotes

References

1. Al-Rifai RH, Ali N, Barigye ET, Al Haddad AHI, Loney T, Al-Maskari F, et al. Maternal and birth cohort studies in the Gulf Cooperation Council countries: Protocol for a systematic review and narrative evaluation. *BMJ Open.* 2018;**8**(1). e019843. doi: 10.1136/bmjopen-2017-019843. [PubMed: 29374677]. [PubMed Central: PMC5829589].
2. Heude B, Forhan A, Slama R, Douhaud L, Bedel S, Saurel-Cubizolles MJ, et al. Cohort Profile: The EDEN mother-child cohort on the prenatal and early postnatal determinants of child health and development. *Int J Epidemiol.* 2016;**45**(2):353–63. doi: 10.1093/ije/dyv151. [PubMed: 26283636].

3. Bielemann RM, Santos LP, Costa CDS, Matijasevich A, Santos IS. Early feeding practices and consumption of ultraprocessed foods at 6 y of age: Findings from the 2004 Pelotas (Brazil) Birth Cohort Study. *Nutrition*. 2018;**47**:27–32. doi: 10.1016/j.nut.2017.09.012. [PubMed: 29429531]. [PubMed Central: PMC5825382].

4. Leung CY, Leung GM, Schooling CM. Mode of delivery and child and adolescent psychological well-being: Evidence from Hong Kong's "Children of 1997" birth cohort. *Sci Rep*. 2017;**7**(1):15673. doi: 10.1038/s41598-017-15810-x. [PubMed: 29142203]. [PubMed Central: PMC5688155].

5. Sadoun E, Leventakou V, Casas M, Ahmed HF, Kogevinas M, Fthenou E. A birth cohort study in the Middle East: The Qatari birth cohort study (QBiC) phase I. *BMC Public Health*. 2017;**17**(1):836. doi: 10.1186/s12889-017-4848-9. [PubMed: 29061134]. [PubMed Central: PMC5654141].

6. Koutra K, Chatzi L, Roumeliotaki T, Vassilaki M, Giannakopoulou E, Batsos C, et al. Socio-demographic determinants of infant neurodevelopment at 18 months of age: Mother-Child Cohort (Rhea Study) in Crete, Greece. *Infant Behav Dev*. 2012;**35**(1):48–59. doi: 10.1016/j.infbeh.2011.09.005. [PubMed: 22018719].

7. Santos IS, Barros FC, Munhoz T, Matijasevich A. Gestational age at birth and behavioral problems from four to 11 years of age: Birth cohort study. *BMC Pediatr*. 2017;**17**(1):184. doi: 10.1186/s12887-017-0936-3. [PubMed: 28835237]. [PubMed Central: PMC5569485].

8. Siqueira Barcelos R, da Silva Dos Santos I, Matijasevich A, Anselmi L, Barros FC. Maternal depression is associated with injuries in children aged 2-4 years: The Pelotas 2004 Birth Cohort. *Inj Prev*. 2018. doi: 10.1136/injuryprev-2017-042641. [PubMed: 29483241].

9. Chatzi L, Leventakou V, Vafeiadi M, Koutra K, Roumeliotaki T, Chalkiadaki G, et al. Cohort profile: The mother-child cohort in Crete, Greece (Rhea Study). *Int J Epidemiol*. 2017;**46**(5):1392–1393k. doi: 10.1093/ije/dyx084. [PubMed: 29040580].

10. Maharlouei N, Rezaianzadeh A, Hesami E, Moradi F, Mazloomi E, Joulaei H, et al. The preference of Iranian women to have normal vaginal or cesarean deliveries. *J Res Med Sci*. 2013;**18**(11):943–50. [PubMed: 24523780]. [PubMed Central: PMC3906784].

11. Rajabi A, Maharlouei N, Rezaianzadeh A, Rajaeefard A, Gholami A. Risk factors for C-section delivery and population attributable risk for C-section risk factors in Southwest of Iran: A prospective cohort study. *Med J Islam Repub Iran*. 2015;**29**:294. [PubMed: 26913257]. [PubMed Central: PMC4764292].

12. Rajabi A, Maharlouei N, Rezaianzadeh A, Rajaeefard A, Keshavarzi S, Lankarani KB, et al. Non-medical factors affecting antenatal preferences for delivery route and actual delivery mode of women in southwestern Iran. *J Matern Fetal Neonatal Med*. 2016;**29**(22):3622–8. doi: 10.3109/14767058.2016.1140137. [PubMed: 26753876].

13. Maharlouei N, Pourhaghighi AS, Raeisi Shahraki H, Zohoori D, Lankarani KM. Factors affecting exclusive breastfeeding, using adaptive LASSO regression. *Int J Community Based Nurs Midwifery*. 2018;**6**(3):260–71. [PubMed: 30035142]. [PubMed Central: PMC6048001].

14. Rajabi A, Maharlouei N, Rezaianzadeh A, Lankarani KB, Esmaeilzadeh F, Gholami A, et al. Physical activities (exercises or choreses) during pregnancy and mode of delivery in nulliparous women: A prospective cohort study. *Taiwan J Obstet Gynecol*. 2018;**57**(1):18–22. doi: 10.1016/j.tjog.2017.12.003. [PubMed: 29458897].