

## Maternal Risk Factors of Neonatal Mortality in Iran: A Case-Control Study

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### Abstract

**Background:** Neonatal death is defined as death at any point in time during the first four weeks of life. It is one of the most important criteria used to evaluate the effectiveness of interventions in public areas. We aimed to investigate pre-pregnancy risk factors associated with neonatal death.

**Materials and Methods:** This population-based case-control study was conducted in eight provinces and two cities of Iran in 2,788 mothers referred to health care centers during 2015 to 2018. Participants were divided into two cases (1162), and control (1626) groups. Expert staff to interview the participants for case and control groups used a structural interview checklist based on the same protocol. We evaluate the association factor between neonatal mortality, the dependent variable, and the maternal demographic and health status characteristics. Data collection was a multi-stage cluster sampling method. Expert staff interviewed parents to collect data based on the same protocol for case and control groups.

**Results:** This study was conducted on 2,788 participants, 90% of cases (n=1162), and 94% of controls (n=1626) were under 35 years of age. The chance of neonatal death was higher in Kurdish mothers [OR: 2.02; 95% CI (1.1 – 4.16)], mothers with low level illiteracy [OR: 1.82; 95% CI (1.01 – 3.27)], mothers with previous stillbirth [OR: 8.84; 95% CI (5.88 – 13.29)], using contraceptives [OR: 1.66; 95% CI (1.33- 2.06)], and passive smokers [OR: 1.49; 95% CI (1.20 – 1.86)].

**Conclusion:** Based on the results, maternal educational level, maternal body mass index, ethnicity, using contraceptives, pregnancy intervals, and history of stillbirth, abortion, and passive smoking were associated with neonatal mortality.

**Key Words:** Iran, Mother, Neonatal Mortality, Pregnancy, Risk Factors.

\*Please cite this article as: Valadbeigi T, Dara N, Tabatabaee HR, Tajalli S, Etemad K, Hosseini A, et al. Maternal Risk Factors of Neonatal Mortality in Iran: A Case-Control Study. Int J Pediatr 2020; 8(2): 10865-874. DOI: [10.22038/ijp.2019.44502.3683](https://doi.org/10.22038/ijp.2019.44502.3683)

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Received date: Aug.25, 2019; Accepted date: Jan.12, 2020

## 1- INTRODUCTION

Neonatal death is defined as deaths among live births during the first 28 completed days after birth (1), which can be divided into two subgroups: early and late neonatal deaths. Early neonatal deaths are defined as deaths between birth time and seven days after birth; late neonatal deaths are defined as deaths after seven days to 28 completed days after birth (2). Neonatal death is one of the most critical indexes used to evaluate the effectiveness of public health interventions such as children's and maternal health care services (3). Neonatal death accounts for 4 million out of an annual 130 million live births (4, 5), with a considerable proportion in low and middle-income countries (6). Accordingly, the neonatal death rate is reported to be 36 per 100,000 in developing countries compared to 7 per 10,000 in developed countries (7). These rates include 50% of child (before five years of age) mortality rates and 57% of infant mortality rates (8-13).

According to the third-millennium development goals (MDGs), children's mortality rate reaches a decreasing trend globally. However, this trend is not observed for the neonatal mortality rate, with its minimum decreasing trend in Sub Saharan Africa (14, 15). Neonatal death is an important index to evaluate child health status. However, in the rural area of Iran, it has improved slightly (16). Neonatal death can be partially attributed to socioeconomic status, cultural factors, and the mother's health during pregnancy (17, 18). Other well established contributory factors are congenital defects, mother's level of education, and her health status during pregnancy and after delivery (8). Previous studies also indicated that poor pregnancy outcomes (stillbirth, abortion, etc.), and increased risk of neonatal mortality are associated with mother's age, prior history of abortion, tobacco use, and cesarean section (17, 19-21). Researches

also suggest that there is a J-shape association between increased risks of neonatal death and pregnancy intervals (22). It is necessary to determine modifiable risk factors of neonatal death to develop interventional programs to promote neonatal health and improve their survival. However, some risk factors of neonatal mortality in Iran have been recognized, but there is not sufficient national evidence to illustrate maternal risk factors and neonatal death. Therefore, we aimed to investigate the association between pre-pregnancy risk factors and neonatal death.

## 2- MATERIALS AND METHODS

### 2-1. Study Design

The total population in this case-control study was 2,788 mothers referred to health care centers that were divided into case and control groups. The case group was defined as mothers whose neonates have died during the first 28 days of life, which was 1,162 participants (41.67 %). Controls were mothers with live birth as a result of the last pregnancy that was 1,626 participants (58.33 %). Regarding the results of previous studies, considering mother's age above 35 as the risk factor, using the formula for estimating two proportions,  $z_{0.95}=2$ ,  $z_{(1-\beta)}=0.8$ , and considering design effect = 2, the sample size was estimated to be 700 for case and control groups (17). We aimed to investigate the effect of 14 variables. Therefore, per each variable, we included 20 additional participants in each study group. The final sample size reached 650 individuals in each study group. Therefore, per each variable, we included 20 additional participants in each study group. The final sample size reached to 650 individuals in each study group.

### 2-2. Study Area

In the period 2015-2018, data were collected from public health care centers in

provinces of Fars, Hormozgan, Kermanshah, Hamedan, Kohgiluyeh and Boyer-Ahmad, Yazd, Southern Khorasan, Golestan, as well as from Mashhad and Zahedan cities.

### 2-3. Variables

We aimed to examine the association between neonatal mortality and mother's age and job, ethnicity, place of residence, educational level, family marriage, Bone Mass Index (BMI), the interval between pregnancies, miscarriage history, cesarean history, regular menstruation, contraceptive usage, chronic disease, passive smoking and smoking during pregnancy. In this study, we aimed to evaluate the association between neonatal mortality and the mother's demographic and health status characteristics. Demographic information included age (being before or above 35 years of age), place of residence (urban vs. rural area), occupation (housewife, employee, farmer, rancher, carpet weaver, other), level of education (illiterate, elementary, guidance school, high school, academic), ethnicity (Fars, Turk, Lor, Kurd, Arab, Baloch, Turkman, other), marriage (whether the couples were relatives or not). Data regarding maternal characteristics included pregnancy interval (first pregnancy/less than or longer than three years/less than one year), history of abortion and stillbirth (present/absent), use of contraceptives (yes/no), tobacco use during pregnancy (yes/no).

### 2-4. Data Collection Method

We used a multi-stage cluster sampling method. Study subjects were recruited through a multi-stage cluster sampling method. In the first stage regarding geographical divisions of Iran, ten clusters (provinces) were randomly selected: provinces of Fars, Hormozgan, Kermanshah, Hamedan, Kohgiluyeh and Boyer-Ahmad, Yazd, Southern Khorasan, Golestan, and the cities of Mashhad and

Zahedan. Then, in each of the ten clusters (provinces), four clusters (cities) were randomly selected from the north, south, east, west, and central areas. In each city, two health care centers (one urban and one rural health care center) were randomly selected. In each health care center, well-trained interviewers according to a protocol filled in ten checklists. Expert staff based on the same protocol for case and control groups using a structural interview checklist interviewed mothers. The data collection process was conducted simultaneously on the same day for cases and controls. Data of the control group were collected from a random sample of mothers referring to the health care center. If < 10 cases were available in each health care center, the remaining checklists were filled in the nearest center, and if there were > 10 cases, the checklists were filled in for a random sample of mothers.

### 2-5. Data analysis

Data were first entered into Excel and were cleaned. Then, SPSS software version 22.0 was used to perform analyses. We used descriptive statistical methods to calculate frequencies and proportions. Univariate analyses were performed using the Chi-square test. To adjust the model for potential confounders, we used multivariable regression analyses. All analyses were presented at the significance level  $p < 0.05$ .

## 3- RESULTS

This study was conducted on 2,788 participants, including 1,162 mothers with neonatal death in the case group and 1,626 mothers with live birth as a result of the last pregnancy in the control group. Ninety percent of cases ( $n=1045$ ), and 94% of controls ( $n=1528$ ) were under 35 years of age, 32.5% of parents in the control group and 26.4% of parents in the case group were relatives. Tobacco use during pregnancy was denoted in 4.8% of cases, and 5.2% of controls, history of abortion

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and stillbirth were reported 14.8% and 17.6% in the case group and 9% and 2.9% in control group respectively (**Table.1**). Compared with Fars ethnicity, the chance of neonatal death was higher in Kurdish mothers [OR: 2.02; 95% CI (1.1 – 4.16)], and the association between ethnicity and neonatal death was protective for Turkish [OR: 0.64; 95% CI (0.48 – 0.86)], Baloch [OR: 0.35; 95% CI (0.21 – 0.58)], and Turkman mothers [OR: 0.35; 95% CI (0.18 – 0.67)]. Compared to mothers with academic education, higher chance of neonatal death was determined in illiterate mothers [OR: 1.82; 95% CI (1.01 – 3.27)],

those with elementary education [OR: 1.91; 95% CI (1.25 – 2.92)] and guidance school graduates [OR: 2.07; 95% CI (1.38 – 3.12)]. Analyses also revealed an increased chance of neonatal death in mothers with a history of stillbirth [OR: 8.84; 95% CI (5.88 – 13.29)], and passive smokers [OR: 1.49; 95% CI (1.20 – 1.86)]. Using contraceptives was associated with a higher chance of neonatal death [OR: 1.66; 95% CI (1.33- 2.06)] (**Table.2**). However, no significant association between mother's age, regular menstruation, cesarean section, and tobacco use during pregnancy and stillbirth was found.

**Table-1:** Maternal Demographic Findings across the groups in eight provinces and two cities of Iran during 2015-2018.

Variables	Case, (41.7) n:1162	Control, (58.3) n:1626	Total
Mother age(years)			
<35	(90.0)1035	(94.0)1514	(92.3)2549
>35	(10.0)115	(6.0)97	(7.7)212
Job			
Housewife	(93.3)1074	(89.2)1433	(91.25) 2507
Employee	(3.9)45	(8.4)135	(2.15)140
Agricultural/ Livestock/ Carpet	(2.1)24	(1.2)19	(1.15)43
Other	(0.7)8	(1.2)19	(0.45)27
Ethnic			
Fars	(65.7)741	(63.8)1019	(64.6)1760
Lor	(6.8)77	(6.8)108	(6.8)185
Turk	(15.1)170	(15.7)250	(15.4)420
Kurd	(3.5)39	(1.0)16	(2.0)55
Arab	(1.2)14	(1.0)16	(1.1)30
Baloch	(3.5)40	(6.3)101	(5.2)141
Turkaman	(2.0)23	(3.9)62	(3.1)85
Other	(2.0)23	(1.6)25	(1.8)48
Place of Residence			
Urban	(41.0)462	(48.0)761	1223(45.1)
Rural	(59.0)666	(52.0)825	1491(54.9)
Education level(mother)			
Illiterate	(5.4)62	(4.2)68	130(4.7)
Primary	(24.2)280	(19.4)315	595(21.4)
Guidance	(26.7)309	(21.4)347	656(23.6)
High school	(35.7)413	(39.9)648	1061(38.1)
Collegiate	(8.1)94	(15.1)246	340(12.2)
Family Marriage			
Yes	(32.5)369	(26.4)419	(28.9)788
No	(67.5)768	(73.6)1170	(71.1)1938
BMI			
Normal	(48.2)508	(54.8)821	1329(52.1)
≤ 19	(22.7)239	(16.2)242	481(18.9)
25-30	(19.4)204	(21.6)323	527(20.7)
30-35	(8.5)89	(5.6)84	173(6.8)
≥35	(1.2)13	(1.8)27	40(1.6)
Interval Between Pregnancies			
≤3	(25.1)286	(33.5)534	(11.4)319
≤ 1	(8.2)93	(3.5)56	(88.6)2469

1-3 Nulipara	(27.7)315 (39.1)445	(27.1)432 (35.9)572	
Miscarriage History			
Yes	(14.8)172	(14.8)172	252(9.0)
No	(85.2)990	(85.2)990	2536(91.0)
Stillbirth History			
Yes	(17.6)205	(17.6)205	(11.9)331
No	(82.4)957	(82.4)957	(88.1)2457
Cesarean History			
Yes	(11.9)138	(11.9)138	(87.3)2354
No	(88.1)1024	(88.1)1024	(12.7)343
Regular Menstruation			
Yes	(86.4)970	(86.4)970	(45.3)1249
No	(13.6)153	(13.6)153	(54.7)1506
Contraceptive Usage			
Yes	(38.3)438	(38.3)438	(6.2)169
No	(61.7)707	(61.7)707	(93.8)2561
Chronic Disease			
Yes	(8.5)97	(8.5)97	(28.7)777
No	(91.5)1039	(91.5)1039	(71.3)1934
Passive Smoking			
Yes	(32.2)364	(32.2)364	(5.0)138
No	(67.8)766	(67.8)766	(95.0)2622
Smoking During Pregnancy			
Yes	(4.8)55	(4.8)55	
No	(95.2)1097	(95.2)1097	

BMI: weight (kg)/height (m)<sup>2</sup>.

**Table-2:** Univariate and Multivariable logistic regression model of risk factors of neonatal mortality in eight provinces and two cities of Iran during 2015-2018.

Parameter	Crude			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Mother age(years)	-	-	-			
<35	1.73	1.30-2.29	0.001			
>35						
Job						
Employee	-	-	-	--	-	-
Housewife	2.24	1.59-3.18	0.001	1.77	1.07-2.91	0.02
Agricultural	3.78	1.90-7.55	0.001	1.65	0.66-4.14	0.2
Livestock	1.26	0.51-3.08	0.6	0.92	0.29-2.93	0.8
Carpet						
Other						
Education level(mother)						
Illiterate	2.38	1.57-3.62	0.001	1.82	1.01-3.27	0.04
Primary	2.32	1.74-3.10	0.001	1.91	1.25-2.92	0.003
Guidance	2.33	1.75- 3.09	0.001	2.07	1.38-3.12	0.001
High school	1.66	1.27-2.18	0.001	1.30	0.89-1.89	0.1
Collegiate	-	-	-	-	-	-
Family Marriage						
Yes	1.34	1.13-1.58	0.001	1.56	1.26-1.92	0.001
No	-	-	-	-	-	-
Miscarriage history						
Yes	1.74	1.38-2.21	0.001	2.32	1.66-1.19	0.003
No	-	-	-	-	-	-
Place of residence						
Urban	-	-	-	-	-	-
Rural	1.33	1.14-1.55	0.001	1.22	0.98-1.51	0.06

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Ethnic						
Fars	-	-	-	-	-	-
Lor	0.98	0.72-1.33	0.9	1.01	0.67-1.52	0.9
Turk	0.93	0.75-1.16	0.54	0.64	0.48-0.86	0.003
Kurd	3.35	1.85-6.04	0.001	2.02	1.01-4.16	0.049
Arab	1.20	0.58-2.48	0.6	1.08	0.40-2.87	0.8
Baloch	0.54	0.37-0.79	0.002	0.35	0.21-0.58	0.001
Turkaman	0.51	0.31-0.83	0.007	0.35	0.18-0.67	0.002
Other	1.26	0.71-2.24	0.4	1.15	0.57-2.28	0.6
Mother's education level	2.38	1.57-3.62	0.001	1.82	1.01-3.27	0.04
Illiterate	2.32	1.74- 3.10	0.001	1.91	1.25-2.92	0.003
Primary	2.33	1.75-3.09	0.001	2.07	1.38-3.12	0.001
Guidance	1.66	1.27-2.18	0.001	1.30	0.89-1.89	0.16
High school	-	-	-	-	-	-
Collegiate						
Gap pregnancy	-	-	-	-	-	-
>3	3.10	2.16-4.45	0.001	2.18	1.35-3.51	0.001
<1	1.36	1.11-1.67	0.001	1.01	0.7-1.32	0.89
1-3	1.45	1.20-1.75	0.003	1.35	1.03-1.78	0.02
Prim parity						
Regular menstruation	-	-	-			
Yes	1.14	0.91-1.44	0.23			
No						
BMI						
Normal	-	-	-	-	-	-
≤ 19	1.59	1.29-1.96	0.001	1.52	1.18-1.97	0.001
25-30	1.02	0.83-1.25	0.84	1.001	0.77-1.29	0.9
30-35	1.71	1.24-2.35	0.001	1.68	1.14-2.47	0.008
≥35	0.77	0.39-1.52	0.46	0.97	0.43-2.17	0.9
Disease						
Yes	1.97	1.44-2.70	0.001	2.35	1.55-3.55	0.001
No	-	-	-	-	-	-
Stillbirth history						
Yes	7.19	5.18-9.98	0.001	8.84	5.88-	0.001
No	-	-	-	-	-	-
Cesarean history						
Yes	1	0.79-1.26	0.99			
No	-	-	-			
Contraceptive Usage						
Yes	-	-	-	-	-	-
No	1.63	1.40-1.91	0.001	1.61	1.29-2.01	0.001
Passive Smoking						
Yes	1.34	1.13-1.58	0.001	1.49	1.20-1.86	0.001
No	-	-	-	-	-	-
Smoking during pregnancy						
Yes	0.92	0.64-1.30	0.64			
No	-	-	-			

OR: odds ratio, CI: confidence interval.

#### 4- DISCUSSION

In this study, we aimed to investigate pre-pregnancy risk factors associated with neonatal death. There is no

significant association between neonatal death and ethnicity, place of residence, mother's level of education, histories of stillbirth and abortion, maternal diseases

during pregnancy, second-hand smoking, BMI <19, and 30 <BMI<35, pregnancy interval and contraceptives. More than 50% of children's mortality rate includes neonatal mortality and it is more prevalent in low and middle-income countries (1, 4, 5). In this study, findings indicated that the chance of neonatal death is 8.84 fold higher in mothers with a history of stillbirth. Our result was in agreement with Ibrahim et al.'s study (23). This can be attributed in part to this fact that the mother with a dead neonate tends to compensate for the loss of her child and so has a shorter pregnancy interval (24). However, Kaboré et al.'s study reported the opposite results in this regard (25). The findings showed mothers with a history of abortion had a 2.32 fold higher chance of neonatal death, and rural mothers were more likely to experience neonatal death as Field and Adewuyi's studies reported compatible results in this regard (26, 27).

It seems that differences in socioeconomic status and quality of health care, long-distance, traditional belief and insufficient knowledge, and poor skill of rural health providers are determinants of higher neonatal deaths in rural areas (28). On the other hand, urban mothers have better access to prenatal health care (18). In agreement with other studies (8, 29, 30), our findings revealed that illiterate mothers had a higher chance of neonatal death compared to those with academic education. It seems that a mother's level of education is associated with her knowledge and skill regarding children's health. The higher level of education improves the mother's health behaviors regarding her children's health (8). This study also revealed that ethnicity is a significant contributory factor for neonatal death. This finding was consistent with another study in Nigeria (18). The rationale behind this observed association can be differences in the biogeographic characteristics of mothers as well as

socioeconomic factors. Other studies in this regard indicate that cultural, behavioral, nutritional, and environmental factors can contribute to pregnancy outcomes (18, 31-34). There are controversial results regarding the association between neonatal death and mother's weight before pregnancy. In the present study, it was demonstrated that neonatal death was more likely for obese (30<BMI<35), and low weight (BMI<19) mothers. This finding was in agreement with Ghaedmohammadi's study (17), however, it was inconsistent with Akinyemi's study (18). It seems that nutritional habits and status in childbearing age women are a contributory factor for neonatal death (18). Our findings showed that passive smoking was associated with a 1.49-fold chance of neonatal death. The diverse effects of passive smoking are due to higher toxins of second-hand smoke. However, another study disagreed with these findings (22). Our study findings showed that mothers' diseases during pregnancy increase the chance of neonatal death. Several studies showed similar results in this regard (23, 25).

Eclampsia and preeclampsia, through decreasing blood flow to the fetus and hindering its growth contributes to hypoxia and stillbirth (24). Field et al. demonstrated that obesity increases the chance of neonatal death. Although preeclampsia cannot be completely prevented, screening programs and medical interventions such as using calcium supplements during pregnancy can potentially reduce the chance of neonatal death (27). Our study revealed an increased chance of neonatal death in the first pregnancy and for women with pregnancy intervals shorter than one year compared to those mothers with pregnancy intervals longer than three years. Williams et al. also demonstrated an increased chance of neonatal death for women with pregnancy intervals shorter than 36 months

(35). Furthermore, stillbirth and neonatal death are a contradiction for lactation; and ovulation period is shorter and may lead to shorter pregnancy intervals. There is controversy regarding the association between neonatal death and the use of contraceptives.

#### 4-1. Limitations of the study

The large sample size of the present study selected from several provinces includes different ethnic groups and increases the generalizability of results to the general population. In addition, well-trained interviewers according to a predetermined protocol collected data. However, the results of the present study should be interpreted with caution due to potentially uncontrolled confounding effects, recall bias related to history of the stillbirth, and reporting bias due to the self-report nature of data collection method. Another limitation is the lack of collaboration of Khorasan Razavi, Sistan, and Baluchestan provinces. Therefore, we were unable to collect data from Mashhad and Zahedan, respectively.

#### 5- CONCLUSION

In our study, we examined the association between neonatal death and some of the risk factors. We observed significant results in maternal level of education, maternal BMI, ethnicity, using contraceptives, and pregnancy intervals, history of stillbirth and abortion and passive smoking. These findings were in agreement with some of the previous studies and inconsistent with some others. One prominent disagreement in our study was an insignificant association for smoking, which can be in part attributed to the few number of smoking reports. Providing appropriate perinatal health care services as well as raising the awareness of pregnant women, especially for high-risk groups, can reduce the proportion of preventable preterm births.

**6- CONFLICT OF INTEREST:** None.

#### 7- AUTHORS' CONTRIBUTIONS

Hajipour (data acquisition, drafting the manuscripts in Persian and revising the manuscripts in English), Tabatabaee and Etemad (designing project and supervision), Valadbeigi (data acquisition and revising the manuscripts in English), Zolfizadeh (data acquisition, quality control of data in Hormozgan province), (designing project in statistical analysis section, data analysis and preparation of results), Ghorbani & Piri (data acquisition, focal point of data gathering in southern Khorasan province), Dara, Tajalli and Hosseini and Kazemian (editing and revising the manuscripts in English), Zolfizadeh (data acquisition, focal point of data gathering in Hormozgan province), Sayyari and Fallahi (designing project, checking quality of final data), Hajipour (data analysis, prepare of tables).

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