



Risk Factors Associated with Neonatal Mortality and Their Status: A Matched Case-Control Study in Kurdistan

Siros Hemmatpour¹, Ghobad Moradi^{2,3}, Mehdi Zokaie², Zhaleh Karimi⁴, Yousef Moradi², Elham Noori^{3*}

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Abstract

Background: Neonatal mortality is a significant public health issue that can often be prevented. The present study was designed and conducted to determine the causes of neonatal mortality and the status of their mothers in Kurdistan Province in 2019.

Methods: In this matched case-control study, the case group comprised 171 deceased neonates, while the control group consisted of 171 healthy neonates, along with their mothers' status in Kurdistan Province in 2019. For each case in each city, one control from the same city within the same week of the case's birth was randomly selected. Data were collected using a checklist containing information on the neonates and their mothers. The analysis was performed using STATA 17 software, which involved descriptive tests and analytical tests. These included frequency calculation, chi-square test, conditional logistic regression, and a stepwise backward elimination method for multivariate analysis with ($P = 0.1$). A significance level of $P < 0.05$ was considered.

Results: The results, after matching the odds ratio with a CI 95% using the backward method, showed a significant association between prematurity (OR:15.99, 95%CI:4.38-58.31), complications during pregnancy (OR:8.64, 95% CI:2.80-26.66), weight gain during pregnancy (OR:3.04, 95% CI:1.06-8.70).

Conclusion: The findings of our study suggest a positive association between neonatal mortality and specific maternal and neonatal factors, namely neonatal prematurity, complications during pregnancy, and inappropriate weight gain during pregnancy. Therefore, there is a compelling need to implement effective measures to control these identified risk factors, with the goal of reducing neonatal mortality.

Keywords: Risk factors, Neonatal Mortality, Matched Case-Control

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Introduction

Neonatal mortality is a significant global public health issue, referring to the death of neonates in the first 28 days of life. In the first month of life, which is mostly preventable, neonatal mortality accounted for 47% of all deaths in children under five years of age in 2020. In 2020, approximately 2.4 million neonates lost their lives in the first month of life. Neonatal mortality rates have decreased worldwide, from 40 deaths per 1000 live births in 1990 to 18 deaths per 1000 live births in 2020 (1-3). Most neonatal

deaths (75%) occur in the first week of life, with around one million neonates losing their lives within the first 24 hours in 2019. The chance of survival from birth varies greatly depending on the place of birth (4).

Several factors have been identified as influential in neonatal mortality, including prematurity, low birth weight, asphyxia, infections, congenital abnormalities, and complications during pregnancy and childbirth. In addition, social determinants of health, such as poverty, inadequate access

Corresponding author: Elham Noori, elham.noori70@yahoo.com

¹ Department of Pediatrics, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran

² Social Determinants of Health Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran

³ Department of Epidemiology and Biostatistics, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran

⁴ Department of Vice Chancellor for Health Affairs, Family and School Health Group, Kurdistan University of Medical Sciences, Sanandaj, Iran

↑What is “already known” in this topic:

Neonatal mortality refers to the death of a newborn within the first 28 days of life. Scientific evidence shows some risk factors related to neonatal mortality. This study was designed and conducted to determine the causes of neonatal mortality and the status of their mothers.

→What this article adds:

This study provided confirmation of the evidence and demonstrated that prematurity is a significant risk factor for neonates, while inappropriate weight gains and pregnancy complications are important maternal risk factors that contribute to increased neonatal mortality.

to healthcare, and inadequate nutrition, are also associated with neonatal mortality. Most neonatal deaths occur in low- and middle-income countries (5-7). The most common causes of neonatal mortality in Iran are prematurity (44.14%), neonatal respiratory distress syndrome (RDS) (31.93%), congenital abnormalities (16.09%), and sepsis (12.66%) (8). In developing countries, the underlying causes of neonatal mortality are closely linked to poor access to and limited utilization of maternal and childbirth healthcare services. Additionally, to address these causes of mortality, mothers and newborns require safe and accessible care. Timely access to simple interventions such as treating maternal infections during pregnancy, ensuring clean and safe deliveries, caring for the umbilical cord, and immediate exclusive breastfeeding can prevent many preventable neonatal deaths (9).

A study showed that maternal diseases such as preeclampsia, hospitalization during pregnancy, and poor antenatal care can lead to neonatal mortality (10). Many of these neonatal deaths can be prevented with improved healthcare services in healthcare centers, maternity wards, and hospitals, and do not necessarily require expensive equipment and advanced technology (11). The presence of skilled personnel during delivery and postnatal examinations is essential for the health of both the mother and neonate. Postnatal care is an important opportunity to check for warning signs such as inadequate nutrition, rapid breathing (a respiratory rate of over 60 breaths per minute), lethargy, fever, and low body temperature. Meanwhile, mothers can receive counseling on how to identify and respond to these symptoms (1).

Recognizing the significance of identifying factors influencing neonatal mortality and the need to minimize intervention and prevention measures, this matched case-control study was conducted. The objective was to determine the risk factors associated with neonatal mortality and the status of mothers in Kurdistan Province in 2019.

Methods

Study design

The present study is a matched case-control study based on the variables of birthplace city and time of birth (within the same week of the case's birth) in Kurdistan Province, which aimed to investigate the risk factors for neonatal mortality in the year 2019. To select cases and controls, we initially obtained a comprehensive list of births and deliveries in the year 2019 from the registry system of the Health Deputy of Kurdistan University of Medical Sciences. This registry includes a list of all pregnant women and their subsequent births and outcomes. A case was defined as a neonate who died within 28 days after birth. The total number of deceased neonatal cases in that year was 171, all of whom were selected as cases and included in the study. The controls were also selected from the same registry system and matched based on the variables of birthplace city and time of birth. For selecting controls, a list of all surviving neonates was first extracted, and then, for each case in each city, one control from the same city with the same birth week as the case was randomly chosen.

Data for this study were collected using a checklist. This

checklist was prepared by reviewing the literature to extract all risk factors for neonatal mortality. The checklist included demographic variables, neonatal risk factors, and maternal risk factors for neonatal death. Some of the information on mothers and neonates were obtained from registries and records of pregnancies and births in the healthcare system, including the integrated health record systems, locally known as the "SIB", the Iranian Maternal and Neonatal Network (IMAN) system and medical records. If necessary, visits to households were made to gather information. Trained healthcare personnel in each city were utilized to record the information in the checklists.

Variables include outcome, exposures, potential confounders

In this study, the outcome was neonatal mortality. Cases were selected among neonates who died within 28 days in the year 2019 in Kurdistan Province. The control group in this study consisted of healthy or surviving neonates under 28 days old in the year 2019 in Kurdistan Province. The risk factors under investigation were divided into two categories: neonatal risk factors and maternal risk factors.

The following variables were considered as neonatal risk factors and were defined accordingly:

Prematurity: Defined as being born before 37 weeks of gestation. **Respiratory distress Syndrome:** Diagnosed by a physician and characterized by respiratory symptoms such as a respiratory rate above 60, grunting, nasal flaring, and retractions, as recorded in the registry or neonatal medical file. **Gross anomaly:** Referring to structural, anatomical, or functional abnormalities present at birth or diagnosed by a physician before or at the time of birth or during the neonatal period and recorded in the registry or neonate's medical file. **Low birth weight:** Defined as a birth weight less than 2500 grams. **Neonatal gender:** Categorized as girl or boy.

The maternal risk factors included the following variables, along with their respective definitions:

Place of residence: Referring to the mother's primary residence at the time of delivery and during pregnancy. **Maternal age:** Refers to the mother's age in years at the time of the child's birth. **Maternal education:** Refers to the highest educational attainment of the mother at the time of the child's birth. **Maternal occupation:** Referring to the mother's main occupation. **Delivery method:** Categorized as natural or cesarean section. **History of infertility:** Refers to a history of difficulty conceiving or maintaining a pregnancy for more than 12 months of unprotected sexual intercourse. **Maternal weight gains during pregnancy:** Categorized as desirable or undesirable based on the amount of weight gained by the mother during pregnancy. **History of abortion:** Referring to the termination of pregnancy before the 20th week of gestation. **History of stillbirth:** Referring to the birth of a non-viable fetus after the 20th week of gestation. **Timely making of pregnancy file:** Defined as receiving prenatal care either before or after the 12th week of pregnancy. **Unwanted pregnancy:** Referring to a pregnancy that was not intended or planned. **Prenatal care:** Refers to the care provided to pregnant women before and during childbirth. **Underlying maternal diseases:** Predispose pregnant women to

various underlying diseases, including cardiovascular diseases such as hypertension, heart failure, congenital heart diseases, and a history of heart attack. It also includes renal diseases such as dialysis and kidney failure, gastrointestinal diseases such as inflammatory bowel disease, respiratory diseases including asthma, infectious diseases leading to taking medication during pregnancy, diabetes, and other significant diseases that can impact the course of pregnancy and were recorded in the medical files. The mental health status was assessed through mental health screening during the pre-pregnancy period and throughout the pregnancy. For this purpose, a 6-item questionnaire was completed in the initial assessment, including questions about the individual's experience of anxiety, hopelessness, restlessness, depression, difficulty performing tasks, and feelings of worthlessness in the past 30 days. If the score was 10 or higher or if there were 3 "I don't know" responses, additional questions about suicidal ideation were asked, including two questions about feeling tired of life and thinking about death and suicide. The healthy or unhealthy mental health status was determined based on this method. The variable "supplement receiving" was assessed by measuring the consumption or non-consumption of supplements recommended during pregnancy, including folic acid/iodine, iron, multivitamin-mineral, and vitamin D. This variable was evaluated and measured as either complete receipt, non-receipt, or incomplete receipt, and recorded in the SIB system. The variable "performance of laboratory tests during pregnancy" in this study refers to routine tests that the mother undergoes during her pregnancy at two intervals, between weeks 6-10 and weeks 23-30. The tests include CBC (Complete Blood Count), BG (Blood Glucose), RH (blood type), FBS (Fasting Blood Sugar), U/A (Urine Analysis), BUN (Blood Urea Nitrogen), Crea (Creatinine), HBsAg (Hepatitis B surface Antigen), VDRL (Venereal Disease Research Laboratory), the first session indirect Coombs test (in Rh-negative mothers after determining the positive status of the partner), TSH (Thyroid-Stimulating Hormone) if necessary, and HIV. The second round of tests includes CBC, U/A, the second session of indirect Coombs test (in Rh-negative mother with Rh-positive partner), FBS, and OGTT (Oral Glucose Tolerance Test) for non-diabetic individuals between weeks 24 and 28 of pregnancy. If any of the mother's test results are not normal, the result is recorded as undesirable. Sonography during pregnancy was

performed with the aim of evaluating the fetal status, placental location, and fetal anomalies between weeks 16-18 of pregnancy. Additionally, it is applied during weeks 31 to 34 of gestation. Another fetal screening variable during pregnancy included screening in the first trimester between weeks 11-13 and, if necessary, in the second trimester between weeks 15-17 to assess fetal health. The variable for screening oral and dental problems involved the mother's oral and dental examinations during the first, second, and third visits. The dentist examined and diagnosed the presence of plaque, cavities, gum inflammation, dental infections, and swelling. The variables for the cause of maternal delivery included term delivery, natural pain of delivery, bleeding, Prelabor rupture of membranes, and danger to the mother's health. In this study, two potential confounding variables, the birthplace and birth time of the neonatal, were considered and controlled for as potential confounders. The variable of low birth weight was not included in the model due to collinearity with the variable of prematurity. These variables were recorded in the registry system and other relevant systems. In cases where a variable was not available, it was completed by referring to the pregnancy and delivery records or through interviews with the mother.

Statistical analysis

The collected data underwent analysis utilizing STATA 17 software. Descriptive tests, including frequency calculation and analytical tests, such as chi-square, conditional logistic regression, and a stepwise backward elimination method for multivariate analysis (with $P = 0.1$), were employed. The analyses were conducted with a 95% confidence level, and statistical significance was set at $P < 0.05$.

Results

Basic information on the distribution of the participants

In this case-control study, a total of 342 subjects were examined, consisting of 171 deceased neonates as the case group and 171 healthy neonates as the control group. The demographic variables of the neonatal (case and control), including the gender of the neonatal and prenatal events, are shown in Table 1. The maternal factors, including demographic variables, maternal status during pregnancy, and related variables during childbirth, were investigated in both the case and control groups and are shown in Table 2.

Table 1. Characteristics of cases and controls. Univariate logistic regression (Neonatal factors)

Variable		Case (171) N (%)	Control (171) N (%)	P-value chi 2	CMOR ^b (95%CI)	P-value
Sex ^a	Girl	68 (40)	82 (47.95)	0.139	1 ^c	0.097
	Boy	102 (60)	89 (52.05)			
Gross anomaly	No	157 (91.81)	166 (97.08)	0.034	1	0.039
	Yes	14 (8.19)	5 (2.92)			
Low birth weight	No	37 (21.64)	144 (84.21)	<0.001	1	<0.001
	Yes	134 (78.36)	27 (15.79)			
Prematurity	No	53 (30.99)	143 (83.63)	<0.001	1	<0.001
	Yes	118 (69.01)	28 (16.37)			
RDS ^d	No	131 (76.61)	150 (87.72)	0.007	1	<0.001
	Yes	40 (23.39)	21 (12.28)			

^aSum of the subgroup is less than the total number due to missing data, ^bCMOR: Crude matched odds ratio, ^cReference category, ^dRDS: Respiratory Distress Syndrome.

Table 2. Characteristics of cases and controls. Univariate logistic regression (Maternal factors)

Variable		Case (171) N (%)	Control (171) N (%)	P-value chi 2	CMOR ^b (95%CI)	P-value
Place of residence ^a	Urban	106 (62.35)	114 (66.67)	0.405	1 ^c	0.393
	Rural	64 (37.65)	57 (33.33)			
Age of mother	<20	9 (5.26)	7 (4.09)	0.175	1.15 (0.42-3.13)	0.775
	20-34	125 (73.10)	112 (65.50)			
	>35	37 (21.64)	52 (30.41)			
Delivery type	Natural	77 (45.03)	107 (62.57)	0.001	1	0.002
	Cesarean	94 (54.97)	64 (37.43)			
Level of mother education	Illiteracy	15 (8.77)	8 (4.68)	0.107	2.58 (0.98-6.80)	0.054
	<Diploma	97 (56.73)	88 (51.46)			
	=>Diploma	59 (34.50)	75 (43.86)			
Job of mother	Employed	6 (3.51)	8 (4.68)	0.585	1	0.594
	Housewife	165 (96.49)	163 (95.32)			
Infertility history ^a	No	149 (89.76)	166 (97.08)	0.007	1	0.016
	Yes	17 (10.24)	5 (2.92)			
Weight gain during pregnancy ^a	Favorable	71 (42.77)	114 (66.67)	<0.001	1	<0.001
	Unfavorable	95 (57.23)	57 (33.33)			
Abortion history ^a	No	96 (69.57)	88 (76.52)	0.216	1	0.306
	Yes	42 (30.43)	27 (23.48)			
Stillbirth history ^a	No	138 (93.88)	121 (95.28)	0.612	1	0.177
	Yes	9 (6.12)	6 (4.72)			
Make a pregnancy file	<12(wk)	132 (77.19)	136 (79.53)	0.599	1	0.587
	=>12	39 (22.81)	35 (20.47)			
Unwanted pregnancy ^a	No	142 (84.02)	148 (86.55)	0.511	1	0.538
	Yes	27 (15.98)	23 (13.45)			
Pre-natal care	No	94 (54.97)	96 (56.14)	0.828	0.94 (0.60-1.48)	0.819
	Yes	77 (45.03)	75 (43.86)			
Complications during pregnancy ^a	No	69 (41.07)	140 (81.87)	<0.001	1	<0.001
	Yes	99 (58.93)	31 (18.13)			
Underlying disease	No	95 (55.56)	121 (70.76)	0.004	1	0.005
	Yes	76 (44.44)	50 (29.24)			
Mental health screening ^a	No	29 (19.59)	17 (10.00)	0.015	2.16 (1.093-4.29)	0.027
	Yes	119 (80.41)	153 (90)			
Supplement receiving	Complete	156 (91.23)	142 (83.04)	0.024	1 ^c	0.027
	Incomplete or don't receive	15 (8.77)	29 (16.96)			
Laboratory results ^a	Normal	119 (71.26)	141 (82.46)	0.015	1	0.020
	Abnormal	48 (28.74)	30 (17.54)			
Sonography results ^a	Normal	138 (84.15)	164 (95.91)	<0.001	1	0.001
	Abnormal	26 (15.85)	7 (4.09)			
Fetal Screening results ^a	Normal	112 (90.32)	163 (95.32)	0.092	1	0.350
	Abnormal	12 (9.68)	8 (4.68)			
Dental problem screening ^a	No	50 (34.72)	42 (26.58)	0.125	1.76 (1.03-3.00)	0.038
	Yes	94 (65.28)	116 (73.42)			
Cause of delivery	Natural pain of delivery	72 (42.11)	81 (47.37)	<0.001	1	-
	bleeding	19 (11.11)	3 (1.75)			
	Prelabor rupture of membranes	24 (14.04)	17 (9.94)			
	Danger of Mother's health	36 (21.05)	12 (7.02)			
	Term delivery	20 (11.70)	58 (33.92)			

^asum of subgroups are less than the total number due to missing data, ^bCMOR: Crude matched odds ratio, ^c Reference category

Univariate and multivariate analysis

The chi-square test showed statistically significant differences between the case and control groups in gross anomaly ($P = 0.034$), prematurity ($P \leq 0.001$), Low birth weight ($P \leq 0.001$), RDS ($P \leq 0.001$), type of delivery ($P = 0.001$), history of infertility ($P = 0.007$), weight gain during pregnancy ($P \leq 0.001$), underlying disease ($P = 0.004$), pregnancy complication ($P \leq 0.001$), mental health screening ($P = 0.015$), receiving supplements ($P = 0.024$), sonographic results during pregnancy ($P \leq 0.001$), laboratory results during pregnancy ($P = 0.015$), and the cause of delivery (P

≤ 0.001) (Tables 1 and 2). Additionally, there were no significant differences between the case and control groups in terms of sex, place of residence, mother's age, mother's education level, mother's occupation, history of stillbirth, history of abortion, time of pregnancy record formation, unwanted pregnancy, pre-pregnancy care, dental health screening, and screening results (Tables 1 and 2).

Univariate conditional logistic regression results are shown in Tables 1 and 2. The stepwise backward elimination was also used for multivariable analysis with $P = 0.1$. After removing some variables and presenting the final

Table 3. Multivariate logistic regression analysis

Variable	AMOR ^a (95%CI)	P-value
Prematurity ^b	No	1
	Yes	15.99 (4.38-58.31)
Laboratory results	Normal	1
	Abnormal	5.02 (1.09-22.96)
Underlying disease	No	1
	Yes	0.34 (0.11-1.02)
Weight gain during pregnancy	favorable	1
	Unfavorable	3.04 (1.06-8.70)
Sonography results	Normal	1
	Abnormal	6.25 (0.81-48.03)
Complications during pregnancy	No	1
	Yes	8.64 (2.80-26.66)

^a An adjusted matched odds ratio, ^b these variables selected by the backward elimination procedure in the multivariate logistic regression analysis with a significance level set as 0.1

model, the results showed that some factors, including prematurity (OR:15.99, 95%CI:4.38-58.31), complications during pregnancy (OR:8.64, 95% CI:2.80-26.66), inappropriate weight gain during pregnancy (OR:3.04, 95% CI:1.06-8.70), and laboratory results during pregnancy (OR:5.02, 95% CI:1.09-22.96) were significantly associated with neonatal mortality (Table 3).

Discussion

Based on the findings of this study, neonatal mortality was found to be associated with various neonatal and maternal factors, such as prematurity, complications during pregnancy, inappropriate weight gain during pregnancy, and laboratory results during pregnancy.

The study revealed that prematurity may significantly elevate the risk of neonatal mortality, which is consistent with previous research (12-16). Prematurity stands as the predominant cause of neonatal mortality and the second most prevalent contributor to mortality among children under five years of age. Complications stemming from preterm birth are responsible for 35% of neonatal fatalities occurring within the initial week following delivery. Infants born preterm, prior to 37 weeks of gestation, face an elevated susceptibility to health complications stemming from the incomplete maturation of vital organ systems, notably the pulmonary, neurological, and immunological systems. Premature neonates exhibit heightened vulnerabilities to respiratory distress, infectious morbidity, and other grave pathologies, which substantially elevate the risk of neonatal mortality (17). The increased risk of neonatal mortality among premature neonates highlights the importance of efforts to reduce the rate of premature births. Premature births can result from a variety of factors, including maternal age, stress, and certain medical conditions (18-20). Therefore, interventions focusing on reducing these risk factors may help lower the rate of preterm delivery and reduce the associated risk of neonatal mortality. In addition to medical interventions, social and economic factors also play a role in the risk of preterm delivery and neonatal mortality (21). Avoiding unnecessary interventions such as early induction of labor or elective cesarean delivery can help reduce the risk of preterm delivery (22). Improving access to prenatal care, promoting maternal health, and addressing social determinants of health are crucial in addressing the complex factors contributing to prematurity and neonatal mortality.

Our findings indicated that unfavorable weight gain during pregnancy may increase the risk of neonatal death. This finding is supported by previous research that has identified maternal weight gain during pregnancy as an important predictor of neonatal outcomes (23, 24). Inappropriate weight gain during pregnancy can lead to adverse outcomes for both the mother and the neonate. Interventions focusing on improving maternal nutrition and weight gain, such as nutritional counseling and education, have been shown to be effective in improving neonatal outcomes. Research suggests the need for pre-conception counseling about diet and physical activity, as well as continued monitoring and counseling throughout pregnancy. Pregnant women should aim to achieve their ideal weight gain to ensure the best possible outcomes for their infants (25). It is important for pregnant women to follow the recommended guidelines for weight gain during pregnancy to ensure the best possible outcomes for themselves and their babies.

Our findings have shown that complications during pregnancy in pregnant mothers may increase the risk of neonatal mortality, which is supported by previous research (26-28). A complication during pregnancy refers to any health issue such as Gestational diabetes, Pre-eclampsia, Placenta Previa, or Fetal growth restriction.

Having a healthy lifestyle and receiving proper healthcare before and during pregnancy can help reduce the risk of complications (29). Diabetic disorders, such as gestational diabetes mellitus (GDM) have been associated with an increased risk of congenital anomalies and macrosomia, which can lead to birth trauma. Approximately 30% of all pregnancies complicated by diabetes mellitus result in the death of the fetus or the newborn infant (5). The neonatal mortality rate is still over five times that of infants of non-diabetic mothers (30). We designed the study as a community-based approach to reduce selection biases. All cases were enrolled during a specific time period using a census method. Controls were randomly selected from among the surviving neonates of the same year, which reduces selection bias. To control for information bias, we provided training to data collectors. If any data were missing in the registry system, we referred to the individual's medical records. To control for potential confounding, we adjusted for residency and birth time through logistic regression modeling in the adjusted analysis.

Limitations

One of the limitations of this study was the lack of access to some data required in the electronic registration system. Although we tried to complete the data by referring to the families of the study participants, in some cases, these data were not available. Also, as with any case-control study that is subject to confounding, we tried to eliminate this confounding in the design by matching and in the analysis by adjusting. However there may be other potential confounding variables that we have not identified.

Conclusion

According to our findings, neonatal mortality may be associated with certain maternal and neonatal risk factors, including prematurity, inappropriate weight gain during pregnancy, complications during pregnancy, and abnormal laboratory results during pregnancy. Therefore, it is necessary to control these risk factors in order to reduce neonatal mortality.

List of abbreviation

IMAN: Iranian Maternal and Neonatal Network
SIB: Integrated health system
GDM: gestational diabetes mellitus
CMOR: Crude matched odds ratio
AMOR: Adjusted matched odds ratio
RDS: Respiratory distress syndrome
CBC: Complete Blood Count
BG: Blood Glucose
FBS: Fasting Blood Sugar
U/A: Urine Analysis
BUN: Blood Urea Nitrogen
Crea: Creatinine
HBsAg: Hepatitis B surface Antigen
VDRL: Venereal Disease Research Laboratory
TSH: Thyroid-Stimulating Hormone
OGTT: Oral Glucose Tolerance Test

Authors' Contributions

Conceptualization: Hemmatpour S, Moradi Gh, Noori E, Moradi Y, Data collection: Karimi Zh, Zokaei M, Methodology: Hemmatpour S, Moradi Gh, Noori E, Moradi Y, Writing – original draft: Hemmatpour S, Moradi Gh, Noori E, review & editing: all authors (Hemmatpour S, Moradi Gh, Noori E, Moradi Y, Karimi Zh, Zokaei M).

Ethical Considerations

The ethics committee of the Kurdistan University of Medical Sciences approved this study (IR.MUK.REC1401.400).

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Conflict of Interests

The authors declare that they have no competing interests.

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