

Perinatal Outcome in Multiple versus Singleton Pregnancies in Neonates Born in Fatemieh Hospital of Hamadan, Iran

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Abstract

Background: Multiple pregnancies are responsible for the increased risk of maternal and neonatal morbidity and mortality. This study aimed to compare the perinatal outcome between multiple and singleton pregnancies.

Materials and Methods: This is a retrospective cohort study. A sample of 50 multiple birth neonates-born in Fatemieh Hospital of Hamadan, Iran in 2015- was selected using simple random sampling. Meanwhile, they were compared with 50 single birth neonates in the same center on gender, gestational age, mean birth weight, Apgar score, the use of Assisted Reproductive Techniques (ART), delivery method, cause of neonatal admission, duration and short outcome of neonatal hospitalization. The data were collected from the medical files of neonates and their mothers. The data were analysed using SPSS version 16.0 software.

Results: In this study, 100 neonates (50 single births and 50 multiple births) were compared. The mean gestational age and mean birth weight of multiple births were lower than that of single births ($P<0.05$). The frequency of low birth weight was 4%, 95.5%, and 100% among the single births, twins, and triplets, respectively. A significant difference was also found between multiple and single births on 1-Minute and 5-Minute mean Apgar scores, neonatal hospitalization after birth, hyperbilirubinemia, respiratory distress syndrome (RDS), the need for mechanical ventilator, antibiotics intake and phototherapy ($P<0.05$). Frequency of gestational diabetes and preeclampsia were greater in multiple pregnancies than single ones; however, the difference was not significant ($P>0.05$). A significant difference was found on the frequency of in vitro fertilization (IVF) method, rate of cesarean section and preterm delivery ($P<0.05$).

Conclusion: In this study, multiple pregnancies were associated with maternal complications including preterm delivery and the increased cesarean section rate, and neonatal complications such as low birth weight, prematurity and increased rate of neonatal hospitalization that increases risk of perinatal morbidity and mortality.

Key Words: Multiple Pregnancies, Newborn, Perinatal outcome.

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1- INTRODUCTION

In the past two decades, the prevalence of multiple pregnancies has increased in industrial and developing countries (1). The dizygotic twin pregnancy rate varies around the world, significantly associated with various factors including race, maternal age, genetics, parity, and the use of Assisted Reproductive Techniques (ART) (2). Multiple pregnancies are considered as high-risk pregnancy due to a significant increase in maternal and neonatal mortality. Multiple pregnancies are associated with a 4-fold increase in fetal death and 6-fold increase in neonatal death. Gestational age and birth weight difference are believed to be the most important independent predictors for mortality and complications of multiple pregnancies (3).

According to the previous studies, maternal complications such as preeclampsia and preterm delivery increases in multiple pregnancies. Meanwhile, neonatal complications increase compared to single ones including neonatal mortality, preterm birth, low birth weight, respiratory distress, hypoglycemia, hypocalcemia and discordance between the weight of twins and twins to twins transfusion syndrome (TTTS) (4-5). Owing to the increase in women infertility, the use of modern medical methods to induce pregnancy, advance maternal age, and its effects on multiple pregnancies (6), this study aimed to compare the frequency of perinatal complications of multiple and singleton pregnancies in neonates born in Fatemeh Hospital of Hamadan, Iran.

2- MATERIALS AND METHODS

2-1. Study design and population

This is a retrospective cohort study. Multiple birth neonates (Case Group) born in the Teaching Hospital of Fatemeh of Hamadan, Iran, in 2015 were compared

with single birth neonates (Control Group) in the same center.

2-2. Methods

In order to achieve the main sample size we utilized the following formula:

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \cdot [P_1(1-P_1) + P_2(1-P_2)]}{(P_1 - P_2)^2}$$

Where, $P_1 = 2.7\%$, $P_2 = 27\%$, $\alpha = 0.05$, $\beta = 20\%$, $n = 26^*$

The values for P_1 and P_2 were extracted from the study by Kiasari et al. (25), for perinatal death rate in single and multiple birth neonates. The sample size in each group was 26 according to the formula, but in this study, 100 neonates were selected (50 multiple birth neonates with 50 single birth neonates). First, multiple birth records were taken from the hospital information system (HIS). A number was assigned to each file. Then, a sample of 50 was selected using simple random sampling. Next, selected files were investigated in the Hospital Archive to extract the data and recorded in the checklist. The same number of single birth neonates was selected as control group so that their file numbers were in row with multiple birth neonates. Their information was also recorded in the checklist.

2-3. Measuring tools

Data included gestational age (based on ultrasound or the first day of the last menstrual period), type of pregnancy (single or multiple pregnancies), type of delivery (normal vaginal delivery or cesarean section), preeclampsia, gestational diabetes (diagnosed during pregnancy), the use of ART, neonatal gender, birth weight, Apgar score, duration, cause and consequences of the neonatal hospitalization

2-4. Ethical consideration

The study was approved by the Ethics Committee of the Hamadan University of Medical Sciences

2-5. Inclusion and exclusion criteria

Maternal inclusion criteria were single and multiple pregnancies. Infant exclusion criteria were outside delivery, less than 28 weeks gestation and incomplete records.

2-6. Data Analyses

In descriptive statistics, central indicators and distribution were used for quantitative variables and ratios and relative frequency for qualitative variables. Independent t-test and ANOVA were employed to compare the consequences of twins and multiple births. Chi-square test was used to compare the qualitative variables. The data were analyzed in SPSS version 16.0 software. Significance level and test power were considered 5% and 20%, respectively.

3- RESULTS

In this study, 100 neonates (50 single births and 50 multiple births) were compared. No significant difference was found on gender between two groups ($P>0.05$). Gestational age was minimum 35 and maximum 43 weeks among the single pregnancy; minimum 30 and maximum 38 weeks among twins; and minimum 33 and maximum 34 weeks among the triplets.

Also, 93.2% of twins and 100% of triplets experienced preterm birth. The mean gestational age of single births was greater than that of twins, triplets, and the statistical difference was significant ($P<0.05$). However, no significant difference was found between twin and triplets on mean gestational age ($P>0.05$). The frequency of low birth weight (LBW) (birth weight less than 2500gr) was 4%, 95.5%, and 100% among the single births, twins, and triplets, respectively. Mean

birth weight of single births was significantly greater than that of twins and triplets ($P<0.05$); however, no significant difference was found between twins and triplets in this regard ($P=0.37$). 1-Minute and 5-Minute mean Apgar scores were significantly greater among the single birth neonates than those of twins and triplets ($P<0.001$); however, no significant difference was found between twins and triplets at 1-Minute ($P=0.57$) and 5-Minute ($P=0.56$) Apgar scores. Single birth neonates had a significant difference with multiple births on the need for hospitalization ($df=2$, $P<0.001$). Hyperbilirubinemia ($P=0.001$), and respiratory distress syndrome (RDS) ($P=0.005$) were significantly greater among twins and triplets than single births.

A significant difference was found between single and multiple births on mean length of hospitalization ($P<0.001$); however, the difference was not significant between twins and triplets ($P=0.08$). A significant difference was also found between single and multiple births on the frequency of the need for mechanical ventilator, antibiotics intake, and phototherapy ($P<0.05$) (**Table.1**).

Significant association was observed between fertilization method and multiple births ($P=0.032$ and $\chi^2=6.85$). Multiple pregnancy likelihood was greater by in vitro fertilization (IVF) than intrauterine insemination (IUI). IUI was also greater than normal pregnancy.

Multiple birth pregnant mothers experienced caesarean section by 100%. The difference was significant between the delivery of single birth mothers and multiple birth mothers ($P<0.001$). Although preeclampsia and gestational diabetes were greater among the multiple birth mothers than single birth ones, the difference was not significant (**Table.2**)

Table-1: Perinatal characteristic and outcome of multiple vs single pregnancy

Characteristic	Single, Number (%)	Multiple, Number (%)		P-value
		Twin	Triple	
Gender				
Male	20(40)			0.66
Female	30(60)			
Gestational age <37 week	10(20)	40(90.1)	6(100)	0.001
Mean gestational age (SD)	38.7±1.5	34.5±1.8	33.5±0.5	0.005
Mean birthweight (SD)	3173±398	2228±252	2033±168	<0.001
Mean 1 min Apgar (SD)	7.9±1	6.9±1	6±0.5	<0.001
Mean 5 min Apgar (SD)	8.8±0.9	7.7±0.8	7±0.8	<0.001
NICU admission	11(22)	25(56.8)	5(83.3)	<0.001
RDS	4(8)	10(22.7)	4(64.7)	0.005
Need to Mechanical ventilation	1(2)	1(2.5)	1(16.7)	<0.001
Sepsis	3(6)	6(13.6)	0(0)	0.13
Hyperbilirubinemia	6(12)	18(40.9)	1(16.7)	0.005
Hypoglycemia	2(4)	3(6.8)	1(16.7)	0.44
Hypocalcemia	1(2)	1(2.3)	1(16.7)	0.13
Phototherapy	4(8)	15(34)	1(16.7)	0.005
Antibiotic therapy	10(20)	25(56.8)	5(83.3)	<0.001
Mean length of stay (SD)	1.4 ± 2.8	5.2 ± 5	9 ± 4.4	<0.001
Neonatal death	3(6)	6(13.6)	1(16.7)	0.036

SD: Standard deviation.

Table-2: Maternal characteristic of multiple vs single pregnancy

Characteristic	Single, Number (%)	Multiple, Number (%)		P-value
		Twin	Triple	
Preeclampsia	5(10)	9(20)	0(0)	0.07
Gestational diabetes	3(6)	7(15.9)	0(0)	0.15
Mode of delivery				
NVD	36(72)	0(0)	0(0)	0.001
Cesarean	14(28)	44(100)	6(100)	
Assisted reproductive technology (ART)				
IVF	4(8)	5(22.7)	1(50)	0.032
IUI	1(2)	2(9.1)	1(50)	
Preterm delivery	10(20)	20(90.1)	2(100)	0.001

NVD: Normal vaginal delivery; ART: Assisted Reproductive Techniques; IVF: In Vitro Fertilization; IUI: Intra Uterine Insemination.

4- DISCUSSION

Dizygotic pregnancy varies in different ethnic groups, ranging from 1.3 births per thousand births in Japan, 8 per thousand in

Europe and the USA to 50 per thousand in Nigeria (2, 7, 8). The incidence of dizygotic multiple pregnancies is

associated with advance maternal age, parity, and family history of multiple births (7, 9, 10). On the contrary, monozygotic multiple pregnancies, which are almost 4 per thousand births, are not associated with maternal age and race; however, they might be influenced by genetics (11, 12). Today, multiple pregnancies have increased due to increased infertility rate in women and use of modern medical methods to induce pregnancy and advanced maternal age (6). Twin pregnancy is considered as high-risk one due to a significant increase in maternal and neonatal morbidity and mortality (3).

Preterm delivery is an important consequence of multiple pregnancies, ranging from 5% to 50% around the world (13). In our study, this rate is far greater. The study by Kazemir et al. showed that preterm delivery of previous sibling is also responsible for the increased rate of prematurity in multiple pregnancies (14). Other studies such as Sua et al.'s study (13) proved the greater rate of cesarean delivery in multiple pregnancies, 85.8% opposed to 100% in our study. Due to higher rates of cesarean delivery in multiple pregnancies, new recommendations have been made on the delivery method by the American College of Obstetricians and Gynecologists (8).

Numerous studies and the bulletin by the American College of Obstetricians and Gynecologists have proven the relationship between gestational diabetes and multiple pregnancies (13, 15); however, some others, including ours, did not prove the relationship (7). According to the report by the American Society for Reproductive Medicine (16), modern practices of infertility treatment are believed to be an important risk factor of multiple pregnancies. Multiple pregnancies are responsible for increased risk of death, gestational diabetes, preterm delivery, and low birth weight. In our study, induction

pregnancies, gestational diabetes and preterm delivery were greater among multiple pregnant mothers than single ones. Low birth weight was also common.

Studies in different countries have reported that low birth weight (LBW) and Small for Gestational Age (SGA) are the most important consequences of multiple pregnancies (9, 10, 13), which are consistent with our study. Such low birth weight and prematurity are believed to be the most important causes of fetal death and risk factors of adulthood diseases such as diabetes and high blood pressure (11-13). The need for the neonatal hospitalization of multiple births in neonatal intensive care unit (NICU) was 56.8% compared to 22%. It was consistent with the results of other studies, but greater (9, 13), mainly associated with greater rate of prematurity in our study.

The study by Mosaiebi et al. (17), showed that prematurity and hyperbilirubinemia were the main reasons of multiple births hospitalization; however, the study by Faraji et al. (18), reported that low birth weight was the main factor. In our study, hyperbilirubinemia and RDS, mostly caused by prematurity, were the most common causes of hospitalization of infants. In the study by Faraji et al. (18), most twins were preterm and they were born by cesarean section. Almost 8.8% of their mothers had the history of preeclampsia and 2.3% had the history of gestational diabetes. In our study, more than 90% of the multiple births were premature and the frequency of gestational diabetes and preeclampsia was greater among the twin and triplets mothers than single birth mothers; however, the relationship was not significant.

The study by Kavehmanesh et al. (19) showed that mean weight of multiple births was less than single births. The most frequent complications of multiple births were prematurity, respiratory distress, low

birth weight and increased neonatal death rate. Their finds were consistent with ours. The study by Qazi et al. (5), showed that multiple pregnancy complications included Low Birth Weight, low 5-Minute Apgar score, increased need for hospitalization, RDS, and increased neonatal death. Their results were consistent with ours. The study by Mesa et al. (20) on economic costs of multiple pregnancies in Spain showed that length of hospital stay and cesarean section costs were far greater among multiple pregnancies than single ones. They claimed that multiple pregnancies were both effective in economic costs and maternal and neonatal mortality rate. In our study, mean length of stay of twins was greater than single births and that of triplets was greater than that of twins. The study by Chaabane et al. (21) on the role of ART in multiple pregnancy showed that twins and triplets were more in IVF method. In our study, the frequency of using IVF was greater than IUI among mothers with multiple pregnancies. The study by Ombelet et al. (22) , Qin et al. (23), and Bouzar et al. (24), also showed that ART was associated with increased multiple pregnancies.

The study by Kiasari et al. (25), showed that the most common causes of the neonatal death were unexplained death, LBW and respiratory distress syndrome, while multiple pregnancies were the main cause of maternal death. In our study, respiratory distress syndrome and neonatal death were greater among the multiple than single births. But neonatal death was not investigated. In the study by Chaudhary S et al. (26), 10.87% of twins and Nasserri et al. (27), 13.5% of twins and 26.8% of triples died; and in our study, 13.6% of twins and 16.7% of triplets died.

5- CONCLUSION

At current study, multiple pregnancies were associated with maternal complications including preterm delivery

and the increased cesarean section rate, and neonatal complications such as low birth weight, prematurity and increased rate of neonatal hospitalization. By improving prenatal care for multiple pregnancies and preventing premature birth can reduce the rate of these complications.

6- ABBREVIATIONS

- **LBW:** Low birth weight;
- **SGA:** Small for Gestational Age;
- **ART:** Assisted Reproductive Techniques;
- **IVF:** In Vitro Fertilization;
- **IUI:** Intra Uterine Insemination;
- **RDS:** Respiratory Distress Syndrome;
- **TTTS:** Twins to Twins Transfusion Syndrome;
- **NICU:** Neonatal Intensive Care Unit.

7- CONFLICT OF INTEREST

The authors had not any financial or personal relationships with other people or organizations during the study. So there was no conflict of interests in this article.

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