The Evaluation of Examining Pregnancy Outcomes in Pregnant Women with Intrauterine Growth Restriction Stages Two and Three: A Cross Sectional Retrospective Study

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Abstract

Background: Intrauterine growth restriction (IUGR) is one of the major problems in developing countries such as Iran. **Objective:** The aim of this study was to determine the pregnancy outcomes in pregnant women with intrauterine growth restriction. **Materials and methods:** This study was a retrospective and cross-sectional epidemiological study that was performed from the beginning of December 2019 to the end of September 2021 on all pregnant women referred to Ahvaz Hospital with the diagnosis of IUGR in stages two and three. Patient information such as gestational age, number of pregnancies,underlying diseases and additional information such as age of delivery, cause of termination and method of Apgar and neonatal hospitalization were retrospectively extracted from their files and finally the data using soft SPSS software was analyzed. **Results:** In this study, 54 women with a mean age of 27.7 years were studied. In this study, 18.5% of infants died,which was more likely to die in 3th grade of IUGR. The age of termination of pregnancy in the majority of women was more than 32 weeks (50%). Regarding IUGR grade, 49 patients (90.7%) had grade 2 intrauterine growth restriction and 5 patients (9.3%) had grade 3 intrauterine growth restriction. **Conclusion:** The results showed that neonatal weight, 1 and 5 minute Apgar scores, length of hospital stay in NICU and neonatal mortality had a significant relationship with their gestational age so that at older gestational ages there were fewer complications and consequences.

Keywords: fetal growth restriction, pregnancy, mothers, childbirth

Introduction:

Intrauterine Growth Restriction (IUGR) is one of the most common complications of pregnancy, which can be defined as the inability of the fetus to reach the genetically programmed size, in which the newborn is smaller than normal and fails to grow normally in the mother's womb (1). IUGR is associated with increased mortality of infants, children, and adults, increased risk of cardiovascular diseases, obesity, and type 2 diabetes (2).

IUGR occurs between 3 and 7% of the total population of infants (1). In IUGR, a full-term (term) infant's weight at birth is less than the 10th percentile, although the 3rd and 5th percentiles are a limit of IUGR that is used in deliveries (3). Babies whose birth weight is below the 5th percentile, especially if it is below the 9th percentile, are much more likely to have severe problems. The risk of short-term and long-term complications for premature infants is higher as well (4).

Many factors cause IUGR, such as maternal factors including extending fertility life (i.e., a woman not getting pregnant for a long time), fertility treatment,

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nutrition, obesity and overweight, drug use, smoking, caffeine, alcohol, lifestyle, maternal age or diseases such as chronic hypertension, preeclampsia (especially when preeclampsia is severe and diagnosed in the second trimester, or to have both chronic hypertension and preeclampsia) (5).

Fetal and placental factors include chromosomal abnormalities similar to Down syndrome or structural birth defects similar to anencephaly, placenta previa, premature rupture of the membranes (amniotic sac), blood clotting disorders, kidney or abdominal wall defects, low amniotic fluid levels, twins or multiple births, placental mosaicism, fetal arterial thrombosis, placental tumors, and small placental size, which a problem with the placenta is the most important cause (6).

At least 60% of the 4 million infant deaths associated with low birth weight that occur worldwide every year are caused by IUGR, premature birth, and genetic and chromosomal disorders (7). Low birth weight can indicate a combination of IUGR and prematurity. There are few human studies on the low birth weight that have separately examined IUGR and prematurity

(8). Further, the long-term consequences of IUGR include the early onset of diabetes, cardiovascular diseases, obesity, and metabolic syndromes.

The prevention of IUGR includes primary and secondary prevention. Primary prevention, as the main prevention, is to prevent disease in people at risk and against risk factors. Secondary prevention is the prevention of complications after the initial symptoms of the disease development, to prevent irreparable harm from this disease (9). The key to this prevention is to identify people at risk (10).

IUGR is a multifaceted problem associated with a significant increase in morbidity and perinatal mortality and it not only increases the mortality of the fetus but also affects the stages of infancy and adulthood. On the other hand, several studies have been conducted on the impact of this disorder on newborns, while no comprehensive study has been done on pregnancy outcomes. Therefore, the present study aims to determine pregnancy outcomes in pregnant women with IUGR referred to Imam Khomeini Hospital in Ahvaz from 2019-2021.

Materials and methods:

This epidemiologic cross-sectional study was conducted on all pregnant women referred to Ahvaz Hospital from the beginning of December 2019 to the end of September 2021 after obtaining the necessary permits from the Research Council and Research Ethics Committee of Ahvaz University of Medical Sciences. In this research, due to the very low rate of 3 to 7% of IUGR in stages 2 and 3, using G Power software, the sample size of 53 patients was estimated for a confidence level of 95%, the test power of 90%, and the effect size of 0.2.

All the patients who were referred by the attending or visiting the gynecology clinic and diagnosed for hospitalization (based on ultrasound by the respected prenatal and radiology attending) and fetal growth restriction in stages two and three were included in the retrospectively study. Given the retrospective nature of the study, the exclusion criterion was only the incompleteness of the patients' files and their lack of response.

Patient information including pregnancy age, number of pregnancies, systematic diseases, and additional information including age of delivery, cause of termination and its method, Apgar 1 and 5 minutes, length of infant stay in NICU, the color of amniotic fluid, and mortality rate Newborns were recorded retrospectively using patient records in a researcher-made questionnaire.

Ethical Considerations:

This study was approved by the Ethics Committee of Jundishapur University of Medical Sciences Ahvaz, Iran and registered with the protocol number "IR.AJUMS.HGOLESTAN.REC.1401.011". In this study, except for maintaining the secrets of the patient in accordance with the Helsinki Treaty, it is assured to patients that their information will be confidential and will be used only for the purposes of the research. In addition, no additional costs were imposed on patients.

Statistical Analysis:

The collected data were analyzed using SPSS version 22. The frequency and percentage of qualitative data, and mean and standard deviation of the quantitative data were presented. The Chi-square test was used to compare nominal variables, the Kolmogorov-Smirnov test was used to determine the normality of distribution of quantitative data, and the independent t-test and ANOVA test was used to compare quantitative variables. *P* values of less than 0.05 were considered significant for all analyses.

Results:

During this study, the files of 62 patients with IUGR were extracted. The information of 8 patients was incomplete and they did not respond to the phone call. These cases were excluded from the study and finally, 54 patients were examined. In this study, the majority of mothers were illiterate or had cycle school education (70.4%), or were housewives (87%).

The average age of the patients was 27.7 with a standard deviation of 6.04 years, a range of 15 to 39 years, and a body mass index (BMI) of 28.8 ± 4.94. Forty-four percent (44%) of the mothers had a history of hypertension, 22.2% suffered from diabetes, and 22.2% got hypothyroidism. Seventy-nine point six percent (79.6%) of mothers had no history of abortion, while 3.7% had 1 abortion, 3.7% had 2 abortions, and 13% had 3 abortions.

The average pregnancy age of patients with IUGR was 31.9 ± 2.33 weeks with a range of 24 to 35 weeks. The average weight of newborns was 1215.9 ± 347.6 grams. Furthermore, the Apgar scores 1 and 5 in infants were 5.57 and 7, respectively (Table 1).

The results showed that the baby's weight, Apgar scores 1 and 5, as well as the duration of hospitalization in the NICU, have a significant relationship with the age of pregnancy termination (Table 2).

In IUGR 2, 12.2% of infants died, while in IUGR 3, 80% of infants died (Table 3). In grade 3 IUGR, 4 infants died, and the minimum weight of infants who survived in IUGR was 1600 grams and in grade 2 IUGR, it was 750 grams. In IUGR 3, the average weight of infants was 1239.9 grams, and in 3rd-degree IUGR, it was 980 grams.

Discussion and Conclusion

Intrauterine growth restriction (IUGR) is one of the major problems in developing countries like Iran. IUGR is one of the main causes of perinatal mortality and complications, which is caused by abnormal placental formation and placental blood flow and includes 21 to 28% of cases in Asia (11). IUGR is a common complication involving 8% of pregnancies in developed countries and about 30% in developing countries (12,13).

Severe fetal growth restriction can lead to a range of devastating outcomes including an infant or fetal death, neurological disability, and lifelong health risks for the suffered child (14). Approximately 30% of IUGR fetuses are at risk of increased perinatal morbidity and mortality, while 70% of IUGR fetuses are normal (such as short stature) (15). Perinatal mortality is higher when the birth weight is below 3%, in addition, these children due to reduced intrauterine growth are at increased risk of middle-aged diseases, including diabetes, stroke, and death from coronary artery diseases, (16).

The results of this study showed that in terms of pregnancy outcomes in pregnant women with IUGR, the average age of pregnancy termination was 31.9 weeks, and there was a significant relationship between the weight of the babies, their Apgar score 1 and 5 minutes, the length of stay in the NICU and the mortality of the infants with their age of termination of pregnancy, with fewer complications and consequences at higher pregnancy stages.

Further, in this study, 18.5% of infants died, with more percentage in IUGR grade 3. The age of termination of pregnancy in the majority of women was more than 32 weeks (50%), and the death rate of infants at the pregnancy stage over 32 weeks was zero, and in cases between 30 to 32 weeks and less than 30 weeks, it was 23.5% and 60%, respectively. In IUGR grade 3, 80% of babies died and the minimum weight of babies who survived in IUGR was 1600 grams and in grade 2 intrauterine growth restriction, it was 750 grams. Furthermore, the mode of delivery was cesarean in 96.3% of cases, and among the causes that led to cesarean delivery were pre-eclampsia, IUFD, and premature rupture of membranes. Concerning IUGR grade, 49 people (90.7%) had grade 2 and 5 people (9.3%) had grade 3 intrauterine growth restriction.

According to studies, some factors are effective on infant mortality in early and late-onset fetal growth restriction. In the latter case, the increase in the resistance of uterine artery vessels is significantly higher than that of the umbilical cord vessels, as observed in Doppler (17). The umbilical artery can be considered a predictive factor of side effects in fetal growth restriction. Premature onset of fetal growth restriction is usually detected by abnormal Doppler of the umbilical cord and uterine vessels and often with preeclampsia, as in the present study, 18.5% of women had preeclampsia. However, the late onset of fetal growth restriction has a strong correlation with prenatal death.

Desh et al. found that pregnancy outcomes such as infant death, amniotic fluid color, and frequency of cesarean in isolated oligohydramnios were not significantly different compared to oligohydramnios with IUGR. Only the probability of NICU admission in infants with IUGR was more than twice that of isolated oligohydramnios, although this was not statistically significant. In that study, the pregnancy outcomes in women with IUGR included 90% clear amniotic fluid, 10% mortality, and 83.3% cesarean, which was consistent with the present study. Dehesh et al. showed that in patients with IUGR, in 20% of the cases, Apgar scores of newborns at 1 and 5 minutes after birth were abnormal (18).

William et al. reported that IUGR increases with the rate of preterm delivery. In addition, the time of pregnancy termination had a significant relationship with the mortality rate of newborns, their weight, and the duration of hospitalization in the NICU (19). The results of the present study regarding the low Apgar score of the newborns were consistent with those of Pallotto et al. who evaluated the fetal complications of IUGR. In both studies, the Apgar score of the newborns was lower in the cases where the pregnancy was terminated in the early weeks (20).

Antonio et al. indicated that due to the length of stay in the NICU, infant mortality has a significant relationship with the type of delivery and the time of termination of pregnancy. In mothers who underwent induction of labor (IOL) by mechanical method, neonatal complications were less than induction of labor with dinoprostone (21). Shinar et al. examined the outcomes of IUGR grade 3 pregnancies and showed that the rate of infant mortality is directly related to the time of termination of pregnancy so that at 16 weeks, the risk of mortality was 8.1%, and at 32.6 weeks, it was less than 1. % (22). Ziai et al., in a longitudinal study conducted on 574 pregnant women in Baqiyatullah and Maryam hospitals, reported a significant relationship between the amount of maternal weight gain during pregnancy and IUGR, so that in women with weight gain less than normal, more IUGR was observed and mothers with a high BMI were less likely to suffer from IUGR (23).

Past studies have found that perinatal morbidity increases in IUGR fetuses, which is caused by increased respiratory distress, grade 3 and 4 intraventricular hemorrhage, sepsis, seizures, necrotizing enterocolitis, and retinopathy of prematurity. Infants born are at risk of growth restriction, cerebral palsy, small size, and cognitive disorders (24). Prospective studies have shown that these fetuses are at increased risk of hypertension, coronary artery disease, stroke, type 2 diabetes, and obesity in the future, as well. Other non-medical problems associated with IUGR include increased low social status, suicide, and economic stress in life (25).

This study evaluated all patients with IUGR and outcomes resulting from pregnancy, which is considered a positive aspect of it. However, it was impossible to follow up with the patients for 6 months and evaluate newborns for a long time so future research needs to include this. Moreover, due to the limited number of studies in this field, it is recommended to conduct more extensive studies. Therefore, considering the importance of IUGR in different stages of pregnancy, it is recommended that, in addition to the existing training, the issues related to the creation of IUGR during pregnancy should be included in these training programs. Because IUGR can be prevented in the early stages, that is, before irreversible changes occur. Thus, early and appropriate diagnostic methods are necessary for successful treatment.

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Conflict of Interest:

The authors declare that there is no conflict of interest in the publication of this paper.

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Table 1. Variables Studied in Pregnant Women With IUGR

Variables		Mean±SD/Frequency(Percent)
Age (Years)		7202 ± 4006
Body Mass Index(Kg/m^2)		7202 ± 604
Newborn weight(gr)		575104 ± 66204
Duration of hospitalization(day)		7701 ± 6507
The age of termination of pregnancy(week)		6504 ± 7066
The age of termination of pregnancy	Less than 30 weeks	50)%5201(
	30 to 32 weeks	52)%6501(
	More than 32 weeks	72)%10(
Apgar Score	first minute	1012 ± 7064
	The fifth minute	2 ± 706
Type of delivery	Cesarean	2(4%)
	Natural childbirth	52(96%)
Amniotic Fluid	Clear	4(7.5%)
	Contains meconium	50(92.5%)
Infant Mortality	Live	44(81.5%)
	Dead	10(18.5%)

Table 2. Determining the factors related to the age of termination of pregnancy in mothers with IUGR

Gestational age / Variables		Less than 30 weeks	30 to 32 weeks	More than 32 weeks	P-value
Duration of NICU stay(Mean±SD)		5206 ± 7604	66046 ± 41071	50052 ± 5502	0007*
first minute of Apgar Score(Mean±SD)		607 ± 704	106 ± 706	401 ± 501	00005*
fiifth minute of Apgar Score(Mean±SD)		6 ± 601	205 ± 502	2 ± 004	00005*
Newborn weight(Mean±SD)		261 ± 54404	5042046 ± 71502	561006 ± 74602	00005*
infant mortality (Frequency)	Live	4	13	72	0.001**
	Dead	6	4	0	

*ANOVA test

** Chi-square test

Table 3. Birth weight and infant mortality rate according to the Grade of IUGR

Garde of IUGR / Variables		Grade 2	Grade 3	P-value
Newborn weight(Mean±SD)		576404 ± 66506	420 ± 61604	0055*
Infant Mortality (Frequency)	Live	5	66	00005**
	Dead	6	4	

*T-test

**** Chi-square test