

**Original article:**

**Risk Factors Associated With Intrauterine Growth Restriction (IUGR) in Neonates: A Matched Case –Control Study in Tertiary Care Hospital.**

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**Abstract**

Background: Intrauterine growth restriction (IUGR) is considered the most common cause of low birth weight or small for gestational age (SGA) birth considered the main cause of intrauterine fetal death and the second leading cause of death in neonates.

Objective: To identify and to quantify Maternal risk factors for IUGR of Indian population and sociodemographic factors associated.

Methodology: A case control study was done involving 130 cases (IUGR singleton babies) and 130 controls ( normal birth weight singleton babies) in a tertiary care hospital of Aurangabad. The study population was administered a pre-designed, pre-tested, semi-structured interview schedule. Data was analyzed using SPSS version 20, regression analysis was done to find out key factors affecting birth weight under socio-economic factors, maternal factors and quantifying risk factors by preparing Models.

Results: Key Socio economic variables affecting IUGR were place of residence, religion and socioeconomic class. Maternal variables affecting IUGR were registration of pregnancy, number of antenatal visits, birth interval in between pregnancy, H/O IUGR in previous pregnancy, bad obstetric history, anemia, TORCH infection, high risk pregnancy, workload & rest.

Conclusion: Study emphasizes the need for improving the quality and utilization of antenatal care, nutritional education to improve the weight gain during pregnancy, spacing, avoidance of tobacco.

Key words: Intrauterine Growth Restriction or Retardation (IUGR), Gestational age, Preterm delivery.

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**Introduction:**

Intrauterine growth restriction (IUGR), also known as “intrauterine growth retardation” or “fetal growth restriction”, is a term applied to a condition of poor growth of the fetus in utero. The condition results in an “infant small for date” or “dysmature infant”. Intrauterine growth restriction (IUGR) is considered the most common cause of low birth weight or small for gestational age (SGA) birth. When the maternal

environment during pregnancy is perturbed, from events such as hypoxia, stress, toxins, inflammation, and placental hypo perfusion, impaired fetal development will result. The main underlying mechanism of IUGR is chronic placental insufficiency that interrupts oxygen and nutrients supply to the fetus resulting in an abnormal fetal growth. (1) Fetuses at risk for IUGR are susceptible

to potential intrauterine environment that leads to fetal hypoxia and fetal acidosis [2].

IUGR is considered the main cause of intrauterine fetal death and the second leading cause of death in neonates; it seems that female babies are more prone to develop IUGR [3].

IUGR increases the risk of neurodevelopment impairment during childhood [4]. The fetal brain is particularly vulnerable in IUGR and there is an increased risk of long-term neurological disorders including cerebral palsy, epilepsy, learning and behavioral difficulties as well as psychiatric conditions [5]. In late-onset IUGR, functional and morphological brain disturbances develop earlier before compensatory blood flow redistribution towards the fetal brain, as detected by Doppler measurements between the fetal brain (in the middle cerebral artery) and the placenta (in the umbilical artery) [6]. Low birth weight, caused by either preterm birth or IUGR, is associated with increased rates of short and long-term renal and cardiovascular diseases. IUGR fetuses experience cardiovascular remodeling that persists into infancy and is related to hypertension and cardiovascular diseases in adulthood [7].

#### **Definition**

Small gestational age (SGA) refers to a weight below the 10th percentile for gestational age as per the population growth charts [5].

#### **Classification of IUGR:**

There are predominately three types of IUGR: asymmetrical IUGR (malnourished babies), symmetrical IUGR (hypoplastic small for date), and mixed IUGR. This is based on various clinical and anthropometric features. A third variety, which is usually seen in developing countries, has been named as mixed IUGR. Infants with this type have lesser

number of cells and small cell size. These neonates have clinical features of both symmetrical and asymmetrical IUGR at birth. This type of IUGR results when early IUGR is affected further by placental causes in late pregnancy[9].

Any insult occurring in the fetal growth period can result in fetal growth abnormalities. The earlier the insult is, more likely it will affect the cellular hyperplasia stage of the fetal growth, thereby resulting in symmetrical reduction of the organ size and a symmetrical IUGR fetus. In contrast, if the insult happens later in the gestation (after cell hyperplasia stage), the cell size will be affected, therefore resulting in asymmetrical IUGR [10]. The significance of the symmetrical and asymmetrical IUGR classification is unclear. The asymmetrical IUGR fetuses are noted to be at higher risk for major anomalies, low birth weight, perinatal mortality, hypertensive disorders of pregnancy, preterm delivery, cesarean section, and overall poor outcomes, compared to symmetrical IUGR [11].

IUGR fetuses have approximately a fivefold to tenfold increased risk of dying in utero, with up to 23 % to 65 % of stillbirths. Approximately half of preterm stillbirths and one fourth of term stillbirths are growth restricted. [12, 13]. The corrected perinatal mortality in the entire SGA population is 17.8 per 1,000 live births .The perinatal rate is 21.3 per 1,000 live births in unscreened/undetected SGA versus 8.4 in screened/detected SGA .

IUGR infants are noted to have increased risk of adverse short- and long-term outcomes compared with SGA children [15]. IUGR increases the risk for intrapartum asphyxia, preterm delivery, and risks associated with preterm delivery, including but not limited to respiratory distress syndrome, intraventricular hemorrhage, and necrotizing

enterocolitis [15, 16]. These infants also are found to have an increase incidence of low Apgar scores, umbilical cord pH less than 7.0, need for intubation, seizures, sepsis, and neonatal death [15,17]. Other neonatal morbidities include polycythemia, hyperbilirubinemia, hypoglycemia, and hypothermia.

**AIM & Objectives:**

**AIM:** To identify and to quantify Maternal risk factors for IUGR of a Indian population in a tertiary level Hospital.

**Objective:**

1. To study maternal and fetal risk factors associated with intrauterine growth restriction (IUGR) in neonates.
2. To assess sociodemographic factors associated with intrauterine growth restriction (IUGR) in neonates.
3. To compare risk factors in case and control group
4. To develop a model to predict for possible risk factors of IUGR.

**Material & Methods:**

**Study design:** Hospital based observational analytical case –control study

**Study area:** MGM Medical college Aurangabad [MS], India.

**Cases:**

**Inclusion Criteria:**

- Neonate below 10<sup>th</sup> percentile for gestational age
- Singleton live births
- exact duration of amenorrhea was known (to calculate the gestational age at the time of delivery)
- mother willing to participate in the study.

**Exclusion Criteria:**

1. Multiple pregnancies
2. Babies with congenital anomalies

**Controls:**

**Inclusion criteria:**

- A matched control, having normal birth weight i. e. more than 2500 g, was selected for every case.
- Neonate within 1 month.
- Sex were matched for selection of the control in each and every pair.
- If two or more suitable matched controls were available for a case, only one was selected randomly.
- Those who are willing to participate in study

**Exclusion criteria:**

- Controls having congenital anomalies.
- Controls birth weight above 4 kg.

**Study Period:** 1september 2017 to September 2018

**Sample size:** A total of 260 neonates were studied. 130 cases and 130 controls

**Operational definition:**

**Cases:** - IUGR refers to a weight below the 10th percentile for gestational age as per the population growth charts.

**Results:**

Present case control study on Intrauterine growth retardation(IUGR) are having 130 cases and controls matched for age and sex having 85 male and 45 female neonates.

**Table No.1: Demographic Profiles of parents in Cases and Controls**

		Cases	Control	Chi-square value & (P-value)	Odds Ratio [95% CI of OR]
Place of Residence	Rural	96(73.8%)	55(42.3%)	26.55 (0.0001)	3.56 [2.281- 6.499]
	Urban	34(26.2%)	75(57.7%)		---
Type of Family	Nuclear	49(37.7%)	51(39.2%)	0.109 (0.947)	--
	Joint Family	51(39.2%)	51(39.2%)		0.960 [0.553- 1.66]
	Three Generation	30(23.1%)	28(21.5%)		0.89 [0.46-1.79]
Religion	Hindu	82(63.1%)	84(64.6%)	0.258 (0.968)	
	Muslim	38(29.2%)	38(29.2%)		
	Christian	4(3.1%)	3(2.3%)		
	Other	6(4.6%)	5(3.8%)		
Socioeconomic class	Class I	4(3.1%)	37(28.5%)	104.02 (0.0001)	---
	Class II	8(6.2%)	43(33.1%)		1.72 [0.47-6.47]
	Class III	21(16.2.1%)	30(23.1%)		6.47 [2.0-20.91]
	Class IV	65(50.0%)	10(7.7%)		60.125 [17.61-205.2]
	Class V	32(24.6%)	10(7.7%)		29.6 [8.46-103.55]

[ P<0.05 Significant , P ≥ 0.05 Not Significant, CI : Confidence Interval ]

Table no 1 depicts the demographic profile of cases and controls, there has been 73.8% of IUGR cases from rural area and 42.3% in control group which was highly significant. The rural neonate has got 3.56 times more risk of IUGR than urban. As per B.G. Prasad modified classification for socioeconomic

class higher number of IUGR cases were found in lower socioeconomic class which was statically highly significant. Lower socioeconomic class has got 60 times more risk of IUGR than Upper socioeconomic class. Type of family and religion differences in cases and control was not significant.

**Table No.2: Birth weight and Gestational age at delivery**

Particular		Cases	Control	Chi-square value & P-value
Birth weight of baby	Normal	0(0.0%)	130(100.2%)	260.0 [ < 0.0001]
	Low birth weight	118(90.8%)	0(0.0%)	
	Very Low birth weight	12(9.2%)	0(0.0%)	
Gestational age delivery	Preterm	114(87.7%)	36(27.7%)	96.305 [ < 0.0001]
	Term	15(11.5%)	92(70.8%)	
	Post term	1(0.7%)	2(1.5%)	

[ P < 0.05 Significant, P ≥ 0.05 Not Significant ]

Table no 2 gives the birth weight and gestational age at delivery in cases and controls, There has been 118(90.8%) of cases in low birth category and 12(9.2%) in very low birth weight category.

114(87.7%) of cases were preterm delivery that is born before 37 weeks of gestation and 15(11.5%) of term IUGR cases were found.

**Table No.3 Information on Mother**

Particular		Cases	Control	Chi-square value & P value	Odds ratio [95% CI of OR]
Gravida	Primigravida	66(50.8%)	75(57.7%)	13.907 (0.001)	--
	Multigravida	42(32.3%)	51(39.2%)		0.93 [0.55-1.58]
	Grand Multipara	22(16.9%)	4(3.1%)		6.25 [2.04-19.07]
Pregnancy Registered	Yes	85(65.4%)	116(89.2%)	21.069 (0.0001)	4.38 [2.26-8.50]
	No	45(34.6%)	14(10.8%)		-----
Number of antenatal Visits	<4	54(41.6%)	12(19.3%)	61.597 (0.0001)	11.25 [4.29-29.49]
	5-8	66(50.8%)	93(71.5%)		1.77 [0.79-3.94]
	>9	10(7.7%)	25(19.3%)		---
Present pregnancy	Preterm	113(86.9%)	33(25.4%)	99.976 (0.0001)	19.53 [10.25-37.23]
	Term	17(13.1%)	97(74.6%)		---
	Yes	42(32.3%)	21(16.2%)	9.239	2.47

H/O preterm				(0.002)	[1.36-4.48]
	No	88(67.7%)	109(83.8%)		---
H/O IUGR	Yes	24(18.5%)	2(1.5%)	20.684	14.49
	No	106(81.5%)	128(98.5%)	(0.0001)	[3.34-62.72] -----
Birth Interval*	<2 years	66(50.8%)	75(57.7%)	38.366	13.16
	>2 years	54(41.5%)	16(12.3%)	(0.0001)	[5.39-32.08] -----
H/O Bad Obstetrics History	Yes	44(33.8%)	10(7.7%)	27.019	6.139
	No	86(66.2%)	120(92.3%)	(0.0001)	[2.92-12.87] -----
TORCH in present pregnancy	Yes	27(20.8%)	8(6.2%)	11.919	3.99
	No	103(79.2%)	122(93.8%)	(0.0001)	[1.74-9.18] ----
H/O Anemia in present pregnancy	Yes	110(84.6%)	81(62.3%)	16.592	3.32[1.83-6.02]
	No	20(15.4%)	49(37.7%)	(0.0001)	-----
H/O High risk in present pregnancy	No	72(55.4%)	104(80.0%)		----
	Pregnancy induced hypertension	25(19.2%)	13(10.0%)		2.77
	Gestational diabetes	10(7.7%)	3(2.3%)	22.110	4.81
	Ecalmpsia	1(0.8%)	0(0.0%)	(0.001)	[1.33-5.79] --
	Antepartam hemoharrage	8(6.2%)	4(3.1%)		2.88
	Oligohydromnio us	9(6.9%)	1(0.8%)		[0.83-9.95] 13
	Other	5(3.8%)	5(3.8%)		[1.61-104.86] 1.44
H/O Uterine pathologies	Yes	16(12.3%)	7(5.4%)	3.864	2.46
	No	114(87.7%)	123(94.6%)	(0.03)	[0.97-6.2] -----

\* Pramigravida are not included. [ P<0.05 Significant , P ≥ 0.05 Not Significant, CI : Confidence Interval ]

According to Table no 3 , grand multipara(16.9%) were found in case group which was stastically significant showing as parity progresses chances of having IUGR increases. Registered pregnancy were having lower chance of IUGR than nonregistered pregnancy which was also stastically significant. 41.6% Of cases were having less than 4 visits to health center showing regular follow up with doctor can reduce chances of IUGR. H/O previous preterm and previous IUGR in mother found to be stastically highly significant. Birth interval between two pregnancies for more than 2 year is protective than

less than 2 year was stastically proven. Bad obstetric history, H/O anemia and presence of TORCH in present pregnancy was stastically highly significant showing causal association for IUGR. Having high risk pregnancy like PIH, gestational DM, Ecalmpsia, Antepartam hemoharrage , Oligohydromniuous, sever anemia, H/O of uterine pathologies were associated with IUGR which was stastically highly significant. All above mentioned risk factors are having higher odds ratio, showing higher chances of having IUGR with presence of these risk factors.

**Table No. 4 H/O Physical activity, addiction and treatment received during pregnancy**

Particular		Cases	Control	Chi-square & P value	Odds ratio
Work done during pregnancy	Light	70(53.8%)	97(74.6%)	14.041 (0.001)	----
	Moderate	29(22.3%)	21(16.2%)		1.97 [1.00-3.62]
	Heavy	31(23.8%)	12(9.2%)		3.57 [1.71-7.45]
Adequate Rest	Yes	54(41.5%)	77(59.2%)	8.139 (0.003)	2.04 [1.24-3.35]
	No	76(58.5%)	53(40.8%)		----
H/O Smoking	Yes	26(20.0%)	8(6.2%)	16.592 (0.001)	3.81 [1.65-8.78]
	No	104(80.0%)	122(93.8%)		--
H/O Alcohol	Yes	19(14.6%)	3(2.3%)	12.712 (0.0001)	7.24 [2.08-25.14]
	No	111(85.4%)	127(97.7%)		---
*H/O received Iron folic acid tablet	Yes	78(60.0%)	104(80.0%)	12.381 (0.0001)	2.66 [1.53-4.64]
	No	52(40.0%)	26(20.0%)		----

\*H/O Iron and folic acid received for 100 days at least.

[ P<0.05 Significant , P ≥ 0.05 Not Significant, CI : Confidence Interval ]

In Table no 4 heavy work done during pregnancy not having enough rest by mother was more associated with IUGR and also having habits of smoking and alcohol was stastically highly significant with IUGR. H/O having received Iron and folic acid tablets was

having protective effect on IUGR. H/O addictions during pregnancy are having higher odds of getting IUGR on the contrary adequate rest during pregnancy and receiving iron & folic acid tablets during pregnancy has protective effect.

**Table No. 5 Linear regression models for IUGR**

Particular		$\beta$ value	Std. error	P value
Model I	Constant	1.195	0.091	<0.0001
	Residence	0.151	0.045	0.001
	Socio economic Class	-0.150	0.018	<0.0001
	Gestational age	0.402	0.045	<0.0001
	Gravida	-0.037	0.032	0.258
Model II	Constant	0.751	0.090	<0.0001
	Preg. Registered	0.266	0.066	<0.0001
	No. ANC visits	0.090	0.013	<0.0001
Model III	Constant	1.678	0.36	<0.0001
	H/O previous IUGR	-0.394	0.094	<0.0001
	H/O BOH	-0.347	0.070	<0.0001
	TORCH in present pregnancy	-0.239	0.082	0.004
	High risk pregnancy	-0.040	0.017	0.021
Model IV	Constant	-0.557	0.412	0.177
	Birth interval	0.017	0.024	0.472
	Weight gain in pregnancy	0.225	0.010	<0.0001
	Maternal height	0.002	0.003	0.562
Model V	Constant	1.478	0.059	<0.0001
	H/O smoking	-0.235	0.086	0.007
	H/O Alcohol	-0.333	0.104	0.002
	Workload	-0.129	0.038	0.001
	H/O Iron and Folic acid received	0.212	0.063	0.001

[ P<0.05 Significant , P  $\geq$  0.05 Not Significant]

Model - I : Multipal regression was carried out to investigate whether residence, socioeconomic class, gestational age and gravida would significantly predict the IUGR outcome of babies. The result of regression indicated that Model I explained 53% of

variance and that model was a significant predictor of IUGR outcome. F= 71.95 & P < 0.0001 while residence SE class and G. age was contributed significantly to the model on the contrary gravida was insignificant.



Model II- The result of regression indicated that Model II explained 23% of variance and that model was a significant predictor of IUGR outcome.  $F=38.52$  &  $P < 0.0001$  while pregnancy registered and number ANC visits was contributed significantly to the model.

Model III- The result of regression indicated that Model III explained 21% of variance and that model was a significant predictor of IUGR outcome.  $F=17.84$  &  $P < 0.0001$  while H/O IUGR, bad obstetric history, TORCH and high risk pregnancy was contributed significantly to the model.

Model IV - The result of regression indicated that Model IV explained 65% of variance and that model was a significant predictor of IUGR outcome.  $F=162.49$  &  $P < 0.0001$  while only weight gain during pregnancy was contributed significantly to the model on the contrary birth interval and maternal height was insignificant.

Model V - The result of regression indicated that Model I explained 16% of variance and that model was a significant predictor of IUGR outcome.  $F=12.28$  &  $P < 0.0001$  while H/O receiving IFA tablets, H/O addictions and workload was contributed significantly to the model.

### **Discussion**

The present case control study was done to find out maternal risk factors associated with Intrauterine growth retardation.

Proportion of Preterm IUGR was found to be 87.7% and term IUGR was 11.5% in the cases. In present study proportion of IUGR was higher in people residing in rural area and with lower socioeconomic status as per findings by Deepa Ragnath (18)(1). Present study has found significant association of parity and registration of pregnancy

with IUGR inconsistent with findings by Mumabare (19) Malvankar (20) and Fikree(21).

Risk of delivering IUGR babies with h/o addictions like smoking and alcohol was 3.8 times and 7.2 times respectively consistent with findings by Mumbare et al(19). A significant difference was found between cases and control for weight gain during pregnancy and number of antenatal visits similar findings were found with Deepa Ragnath(18) and in a study done at Mumbai.(22) Anemia and high risk pregnancy were found to be significantly related to IUGR as found in other studies done for low birth weight.(18)(19) (1)(8)

Birth interval between pregnancies, bad obstetric history and workload was found significant association to IUGR similar to Deepa Ragnath(18) and dissimilar to findings by Yadav et al.(12)

As per regression analysis models, it has shown that intrauterine growth retardation(IUGR) was significantly associated with place of residence, socioeconomic status, registration of pregnancy, number of antenatal visits, birth interval in between pregnancy, H/O IUGR in previous pregnancy, bad obstetric history, anemia, TORCH infection, high risk pregnancy, workload & rest.

### **Conclusion**

From this present case control study it can be concluded that the outcome of IUGR babies can be predicted by considering the risk factors like place of residence, socioeconomic status, registration of pregnancy, number of antenatal visits, birth interval in between pregnancy, H/O IUGR in previous pregnancy, bad obstetric history, anemia, TORCH infection, high risk pregnancy, workload & rest.

Using present study different multiple regression models the IUGR outcome can be predicted. Thus findings of this study emphasizes the need for

improving the quality and utilization of antenatal care, nutritional education to improve the weight gain during pregnancy, spacing, avoidance of tobacco, and

prevention and proper management of risk factors like anemia and hypertension.

**Acknowledgment:** Dr R. Bhora, Dean, MGM Medical College, Aurangabad for allowing us to carry out the study and providing the required manpower. Dr Rajesh Dase for helping in data feeding and analysis.

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