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Research Article

Impact of some Risk Factors on Neonatal IUGR Incidence and Outcome in NICU at Al-Sadder Teaching Hospital, Misan, Iraq 2016

Eman K. Al-Sadi
College of Medicine, Misan University, IRAQ
*Author Email: emankhmmas@gmail.com

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Abstract

Intrauterine growth restriction IUGR is the second leading cause of perinatal morbidity and mortality in developing countries; it also increases adulthood risk of (hypertension, diabetes, coronary heart disease, and stroke) that reflects a major public health problem. We aim to identify the incidence and outcome of IUGR in our NICU and the relation with some risk factors. Across sectional study was conducted on 119 singleton newborn babies (Full term and Preterm) admitted to the NICU at Al-Sader teaching hospital, Amara city, Misan province in a period from the first of January to 31 December 2016 with low birth weight (<2.5 kg) whom may or may not have associated medical problems. LBW can be a consequence of IUGR, preterm birth, or both, but in developing countries most LBW births are due to IUGR (defined as below the tenth percentile of the Williams sex-specific weight-for-gestational age reference data).Neonates with lethal congenital anomalies, multiple pregnancies were excluded. Babies were examined and checked to fulfill the definition of (IUGR) through estimation of the following growth parameters (body weight, length, head circumference), and the Ponderal index. We studied various risk factors like maternal: age, parity, hypertension and delivery type as well as fetal gender and gestational age to find the most offending cause of IUGR in our NICU. Statistical significance considered when p value ≤ 0.05. We found that 43.7% of the admitted neonates had IUGR, those with low gestational age carried significant association with IUGR occurrence, p value=0.0001.

Keywords: IUGR, Risk factor, NICU, Misan, Iraq.

الخلاصة

تأثير بعض عوامل الاختطار على حدوث وتقييد النمو داخل الرحم الوليدي في وحدة العناية المركزة في مستشفى الصدر التعليمي ، ميسان ، العراق 2016. يعتبر تأخر النمو داخل الرحم من الأسباب الرئيسية الثانية لمراضة ووفيات الفترة المحيطة بالولادة في البلدان النامية ؛ كما أنه يزيد من خطر إصابة البالغين (فرط ضغط الدم والسكري وأمراض القلب التاجية والسكتة الدماغية) الذي يعكس مشكلة صحية عامة في المجتمع. تهدف الدراسة إلى تحديد حدوث تقييد النمو داخل الرحم الوليدي في وحدة الرعاية المركزة والعلاقة مع بعض عوامل الخطر. أجريت دراسة مقطعية على 119 طفلاً حديثي الولادة (كامل او خديج) تم قبولهم في وحدة العناية المركزة في مستشفى الصدر التعليمي، مدينة العمارة ، محافظة ميسان في الفترة من الأول من يناير إلى 31 ديسمبر 2016 مع انخفاض وزن المواليد (< 2.5 كغم) الذين قد يكون لديهم أو لا يكون لديهم مشاكل طبية مرتبطة، تم استبعاد حالات الحمل المتعددة و التشوهات الخلقية المميتة. تم فحص الأطفال لتحقيق تعريف تقييد النمو داخل الرحم الوليدي من خلال تقدير معايير النمو التالية (وزن الجسم ، الطول ، محيط الرأس)، ومؤشر (Ponderal). و درس عوامل الخطر المختلفة عند الأمهات: العمر ، تعدد الولادات ، ارتفاع ضغط الدم ونوع الولادة والجنس الجنيني وعمر الحمل للعثور على أكثر العوامل المسببة لتقييد النمو داخل الرحم الوليدي في وحدة العناية المركزة. وجدت الدراسة أن 43.7 ٪ من الرضع الراقدين لديهم تقييد النمو داخل الرحم الوليدي ، مع انخفاض عمر الحمل لديهم ارتباط كبير مع حدوث تقييد النمو داخل الرحم الوليدي مع وجود ارتباط إحصائي كبير.

Introduction

Intrauterine growth restriction (IUGR) babies delivered in the developing countries reaching nearly 30 million live births per year [1]. IUGR means that the newborn baby is unable to reach it is genetically predetermined growth potential. Often suspected during fetal life by serial ultrasound study of (fetal size, symmetry), and after getting birth by assessing the newborn growth parameters (weight. Length, head circumference) all should be less than the 10 percentile for their predictors for gestational ages in symmetrical IUGR or sparing head size smallness in a symmetrical type, and the estimation of the ponderal index values [1]. In fact, small for gestational age Infants (SGA), are those newborns delivered with body weights of < the 10th percentile for their gestational age, hence they can grow appropriately thereafter and often mature neurologically, while IUGR newborns, their body weights are < the 10th percentile for their gestational age, but predisposed to many complications, including perinatal asphyxia, Meconium aspiration and hypoglycemia [1]. The usual method of detection a newborn as being below 2500 g (LBW), does not distinguish between smallness due to prematurity (less than 37 weeks of gestation) and smallness due to (IUGR) as several factors, affect the fetal growth and birth weight rather than the gestational age only, these factors either physiological or pathological. Physiological factors include maternal (parity, height, weight, ethnicity) and fetal gender [2]. While pathological factors are include (maternal diabetes, hypertensive diseases, antepartum hemorrhage, placental insufficiency, cigarette smoking, alcohol consumption, and social deprivation). Actually, maternal constitutional or pathological factors and the outcome of pregnancies, in addition to appropriate birthweight documentation used to optimize the coefficients required for constitutional variation adjustment [3]. IUGR babies are sub classified according to their growth setting to those with symmetrical or asymmetrical IUGR The causes of symmetric IUGR are mainly genetic, teratogenic, chromosomal, intrauterine infections and severe hypertensive etiologies, these causes a reduction in total number of fetal cells, usually occurs during early cell divisions (early months of gestation), while asymmetric IUGR is often of a later onset, mainly associated with maternal vascular disease (pre-eclampsia, chronic hypertension) or with insufficient maternal nutrition and dietary support causes fetal hypoplasia (decrease fetal cell size) [4]. Neonatal morbidity and mortality increased in IUGR babies that reflect a major public health problem [5]. In addition; the adverse intrauterine environment may increase their adulthood risk of hypertension, diabetes, coronary heart disease, and stroke [6]. That is why it is now recommended that gestation dates should preferentially be determined by ultrasound study [7]. Moreover, by scanning as Scan dates are known to be more accurate than LMP dates in predicting the actual date of delivery [8].

Ponderal index used to identify infants with IUGR when it is below the 10th percentile; which can affect the long-term outcome as in the following formula [9]:

$$PI = \frac{\text{birth weight} \times 100}{(\text{Length})^3}$$

IUGR is the second leading cause of perinatal morbidity and mortality with a 10-fold greater risk of fetal death if compared to normal fetuses.

AGA: referring to an infant whose gestational age

and weight are synchronous according to Stand ardized age and growth curves. Moreover, the less is the percentile of body weight from expected at a given gestational age, the higher is the morbidity and mortality rate [10].

IUGR in early neonatal life causes short-term complications as it increases the risk of hypothermia, hypoglycemia, hypocalcemia and hyperbilirubinemia, furthermore, increases the rate of prematurity, perinatal asphyxia, delivery room interventions and it obligate the newborn to respiratory, digestive, neurological or renal complications. On the other hand, other changes manifested later in childhood or adulthood considered rather long-term complications [11] [12].

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Patients and Methodology

A cross sectional study was conducted in the neonatal intensive care unit (NICU) at Al-Sader teaching hospital in the period from the 1st of January to 31st of December 2016. All singleton newborn babies admitted to the NICU with LBW (cutoff birth weight <2.5 kg) were collected (119 case) regardless gestational age. We checked neonatal birth parameters [Body weight (B.W), birth length (B.L), and head circumferences (H.C)] in correlation to their gestational ages to assess the presence of IUGR. They should be less than 10 percent of predicted potential weight, length, and H.C for their gestational age. We used gender specific growth charts to rule out any miss interpretations of values. In addition, we used a special formula to calculate Ponderal index values PI as a predictor for IUGR diagnosis in a neonate; those with pi < 2.25 for term and < 2 for preterm were regarded as growth restricted. We studied some maternal characteristics, including age, parity, delivery type and maternal hypertension. In addition, two fetal characteristics (gender, gestational age), to assess any correlation with the occurrence of IUGR, and finally, we studied the impact of IUGR on neonatal morbidity and mortality. Data was analyzed using SPSS version 20.0 and presented as tables of number and percentage. Statistical significance considered when p. value ≤ 0.05. Permission was obtained from families of the neonates enrolled in the study, also from Misan directorate health services and Al-Sadder Teaching Hospital researches committee to carry out this study.

Results and Discussion

Out of the total studied sample of 119 newborns admitted to the NICU, 62 (52%) were male and 57 (48%) were female with approximately near male: female ratio of 1.08:1. Moreover, 100 neonates were preterm and 19 were term with a 4-fold risen titer of preterm over terms as shown in Table1.

In our study, the IUGR rate was 43.7%. This is less than AGA rate, which was 56.3%. Neonates with (AGA) male sex was higher than female 35 (29.4%), 32 (26.9%) respectively, as well as in (IUGR) group: male 27 male (22.7%), female 25 (21%). (p. value=0.9) as shown in Table 2.

Regarding gestational age, we divided the gestational week's duration to three groups: 28-32weeks, 33-36weeks, and 37-42 weeks. Neonates with (AGA) group had higher rates of admission in 28-32 weeks followed by 33-36 weeks and lastly by 37-42 weeks with the following rates (35.3%, 17.6, and 3.36%) respectively, while neonates with IUGR; the higher admission rate was in 33-36 weeks. Group followed by 28-32wks group and finally, in 37-42 weeks group with the following rates (21%, 11.75%, 10, 92%) respectively. P value= 0.0001. This is highly significant as shown in Table 2.

Regarding maternal characteristics;

For delivery type: in (AGA) group, 42 delivered vaginally (35.3%) which is higher than CS delivery 24 (20.16%) in addition, in IUGR group, still vaginal delivery higher than CS delivery 37 (31.1%, 16 (13.44%) respectively (p.value=0.5).as Shown in Table 3. Multigravidas had higher (AGA) newborns than primigravidus 44 (36.97%), 23 (19.33%) respectively, and the same for IUGR newborns: 28 (23.53%), 24 (20.17%), (p. value=0.1) Shown in Table 3.

Considering maternal age: we divided the maternal ages to 4 groups, <20yrs, 20-29yrs, 30-39yrs, >40yrs. For both (AGA, IUGR) groups, the neonatal admission was higher for maternal age from 20-29 yrs [37] (31%), [26 (21.85%)] followed by 30-39yrs [22] (18.5%),13(10.92%)] (2.57%), 4(3.36%)], (p. value=0.2), shown in Table 4.

Then by < 20yrs [5 (4.2%), 9(7.6%)] and lastly,≥40 years [3].

Maternal hypertension in (AGA) neonate was positive in 23\119 (19.26%) and negative in 43\119 (36.14%) while for IUGR group: it was

positive in 18\119 (15.2%) and negative in 35\119 (29.4%), (p. value= 0.9) shown in Table 4. Regarding respiratory diseases; including (commonly: RDS, less commonly: Apnea, TTN, Meconium aspiration, birth asphyxia) the respiratory diseased \ not diseased neonate ratio was 2.3:1 Moreover; the ratio was higher among IUGR neonates 2.7:1 than AGA group 2:1. Reflected by following results: (AGA) was positive in 45 (37.8%) and negative in 22(18.5%) while IUGR was positive in 38 (31.93%) and negative in 14 (11.76%) (p. value=0.4), shown in Table 5.

The positive non respiratory disease cases were 40\67 for AGA (59.7%) while in IUGR group was 41/52 (80.7%) and the ratio of non-respiratory diseased / not diseased neonates in IUGR group was 3.7:1 which is higher than AGA group 1.4:1 (p. value = 0.0001), which is highly significant, shown in Table 5.

Concerning neonatal mortality:

In AGA group, neonates who died were 33 (27.73%) and those discharged 34 (28.6%) while in IUGR group: the dead neonates were 29 (24.4%) and the discharged were 23 (19.3%), which alarmed a higher death rate among IUGR \ AGA group, (p.value =0.8) shown in Table 5.

Table 1: NICU admission distribution according to neonatal gender and maturity.

		NICU distribution according to neonatal charecrestic		
variables		**Admission**	**%**	**ratios**
Gender	Male	62	52	Male: Female
	female	57	48	1.08 : 1
maturity	Full term	19	15.96%	Preterm: term
	preterm	100	84.04%	5.2:1

Table 2: Neonatal gender and gestational distribution for NICU admission.

Variables		**Outcome**						**p. value**
		AGA		**IUGR**		**total**		
		N	%	N	%	N	%	
Gender	**male**	35	29.4	27	22.7	62	52	0.9
	female	32	26.9	25	21	57	47.9	
Gestational age (weeks)	**28-32**	42	35.3	14	11.75	56	47	0.0001
	33-36	21	17.64	25	21	46	38.65	
	37-42	4	3.36	13	10.92	17	14.3	

Table3: distribution of delivery type, parity with neonatal outcome.

Maternal Variables		**Outcome**						**P. value**
		AGA		IUGR		Total		
		N	%	N	%	N	%	
Delivery type	vaginal	43	35.3	37	31.1	79	66.4	**0.5**
	C\S	24	20.16	16	13.44	40	33.6	
Parity	multiparous	44	36.97	28	23.53	72	58.82	**0.1**
	Primigravidas	23	19.33	24	20.17	47	39.5	

Table 4: Distribution of maternal age, maternal hypertension with neonatal outcome.

Maternal Variables		**Outcome**						**P. value**
		AGA		**IUGR**		**Total**		
		N	**%**	**N**	**%**	**N**	**%**	
Maternal age	less than 20 yrs.	5	4.2	9	7.6	14	11.76	0.2
	20-29yrs.	37	31	26	21.85	63	52.94	
	30-39yrs.	22	18.5	13	10.92	35	29.42	
	≥40yrs.	3	2.57	4	3.36	7	5.88	
M. hypertension	**Yes**	23	19.32	18	15.12	42	35.44	0.9
	no	44	36.97	34	28.59	77	65.56	

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Table 5: Distribution of morbidity and mortality among the NICU growth outcome.

Variables			Outcome						p. value
			AGA		IUGR		total		
			N	%	N	%	N	%	
Morbidity	Mortality	Yes	33	27.73	29	24.4	62	52	0.8
		No	34	28.6	23	19.3	57	48	
	RDS	Yes	45	37.8	38	31.93	83	70	0.4
		No	22	18.5	14	11.76	36	30	
	Hypoglycemia hypocalcemia, Hypothermia Jaundice ,NEC	Yes	40	33.6	41	34.5	81	68	0.0001
		No	27	22.7	11	9.25	38	32	

Discussion

Intrauterine Growth Restriction (IUGR) is considered as one of important and serious cause of perinatal morbidity and mortality with a highly risk of fetal death if compared to normal fetuses [10], in our study, the IUGR rate was high (43.7%). The higher incidence of AGA over IUGR in neonates is probably related to the higher rate of premature delivery in relation to term delivery as most of these low birth weight babies when adjusted for gestational age attributed to be preterm, which agreed piper's study and another study as preterm admission been higher than term [12]. Worldwide, the preterm birth currently accounts for 9.6% of births; moreover, the higher incidence of prematurity was in developing countries [13]. Male admission to NICU for both IUGR and AGA was higher than female which indicates male sex fragility and vulnerability to different hazards that necessitates NICU admission our result agreed with a study from Bangladesh [14].Furthermore, the male predominance for IUGR agreed by a study in Ohio (USA) 2004 [15] while disagreed with Melamed study, which Indicates a female predominance [16]As premature babies (<37 weeks of gestation) usually had birth weight < 2.5 kg, therefor, neonates of low birth weight after adjustment for gestational age, most of them actually are premature but with appropriate weight AGA this explain the higher incidence of AGA in 28-32weeks (35.3%). While for IUGR group, the higher incidence category period was between 33-36weeks (21%) explained by the fact that, birth weight in this gestational period (mid and late 3rd trimester) of <2.5 Kg. mostly are pathological for different maternal and fetal causes probably indicates a symmetrical type of IUGR which is more common than the symmetrical type that occurs in early gestation, this finding agreed with pipers study and another study [12] [14]while disagreed by Zeitlins study showed that the highest proportion of pathological smallness (IUGR) are found between 28 and 33 weeks of gestation when approximately one-third of all preterm infants are classified as small for gestational age [17].

In addition, we found that both AGA and IUGR neonates delivered vaginally at a higher rate than CS delivery, actually attributed to the fact that the majority of LBW (<2.5Kg) neonatal admission in our NICU (80%) were preterm $\pm$ IUGR, resulting from premature contraction and may have premature rapture membrane due to different fetal or maternal causes followed by spontaneous vaginal delivery usually at hospital for the sake of the mother and the prematurely delivered neonate whom may need NICU admission. This agreed with zeitlins study, which showed a significant correlation for (IUGR) among preterm births after spontaneous labour or premature rupture of membranes [17]. And another study in Norway showed that of Out of 370 growth

restricted neonates, (77%) had a vaginal delivery, while (5%) and (19%) were delivered by elective and emergency CS, respectively [18]. Our result disagreed a Sweden study [19] that showed nearly similar rates of IUGR for both vaginal and CS deliveries .Furthermore, disagreed another study in Brazil which, showed preterm cesarean delivery were higher in IUGR group than spontaneous preterm labor [20]. In addition, Vaginal delivery was further higher among AGA with LBW neonates than IUGR neonates because of suggestive obstetric thought that early neonatal death and morbidity is usually lower with vaginal delivery among the LBW/AGA group which disagreed a study that found no difference in neonatal outcomes between fetuses of (birth weight of less than 10^{th} percentile) born by spontaneous vaginal delivery or elective cesarean delivery [21]. This kind of distribution applied simultaneously to CS delivery in which the higher rate of C\S among AGA (31.5%) over IUGR (30%) group may be explained by application of C\S for maternal or fetal indications other than fetal smallness, this finding disagreed with a study in California showed a higher CS rate among small newborns (IUGR) compared to those considered AGA [22].

Maternal hypertension in (AGA) group was positive in (19.32%) of total admissions and negative in (36.97%) while for IUGR group maternal hypertension was positive only in (15.12%) and negative in (28.59%). It was not significant statistically this indicates that maternal hypertension alone either gestational or chronic type already had a negative impact on IUGR, but of low significant values unless superimposed by eclampsia or pre-eclampsia. This result agreed with a study in South America in which women with chronic hypertension do not have the highest prevalence of IUGR, suggesting disparate pathways by which IUGR develops [23].

Limitations of this study need to be mentioned, as type of hypertension, whether gestational or chronic, with or without pre-eclampsia or eclampsia were not checked. Nevertheless, gestational hypertension has better outcomes than chronic hypertension regarding IUGR rate and sequences which may be the case in this study, so we need a more detailed study dealing with hypertension types severity $\pm$ eclampsia or preeclampsia to find out the exact correlation with neonatal IUGR.

Regarding morbidity; RDS in AGA neonates was high (80.6%), the highest percentage of AGA was between 28 - 32 weeks of gestation, which indicates high prematurity indices including RDS as a common cause of morbidity in premature babies simultaneously in IUGR group, RDS was high (73%) mostly in late preterm group i.e. 33-36 weeks, which carries higher, incidence for IUGR as mentioned before. Finally, RDS lower incidence found in IUGR babies compared to AGA newborns conferred possibly by intra-uterine stress leading to accelerated lung maturation) in agreement with Sharma et al. [24] which observed a lower incidence of RDS in neonates with IUGR comparing to those with AGA while disagreed with Tyson et al. [25] and Piper *et al.* [13] suggests that IUGR infants had significantly increased risk in some analyses of RDS.

Regarding hypoglycemia, hypocalcemia, hypothermia, jaundice, NEC: the incidence was higher (80%) among IUGR neonates than among AGA group especially for hypoglycemia this result was in agreement with many studies [26] [27], and disagreed with others [28] [30]. Many factors predispose IUGR neonates to hypoglycemia, including failure to maintain normal glycogenolysis, gluconeogenesis, ketogenesis, reduced adipose tissue stores and hyperinsulinism. Simultaneously, AGA neonates in our study actually most of them were preterm whom liable to various hypoglycemic symptoms. In fact, the severity of symptoms diversely proportioned to the gestational age at delivery, these results agreed with various studies [28] [29] [30]. Regarding mortality**,** this study show that death rate was higher in IUGR group than AGA group .This result agreed by two studies, pipers study and another studies [12] [31] [32] [33].

Conclusions

The present study concluded that IUGR rate was high in our NICU; especially between 33-36 wks. of gestation, It carried a significant risk of neonatal complications especially for RDS and hypoglycemia with high mortality rate.

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