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Disparities of Clinical Features and Associated Maternal Factors among Symmetrical and a Symmetrical Intra-Uterine Growth Restriction (IUGR) in NICU at Al-Yarmouk Teaching Hospital in Baghdad, Iraq

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Abstract

Background: Worldwide Intra-Uterine Growth Restriction carries out high rate of fetal and neonatal morbidity and mortality. Perinatal mortality rates are 4-8 times higher for growth-retarded infants. Intra-Uterine Growth Restriction (IUGR) is subdivided into symmetrical and asymmetrical subtypes. We aimed to focus on the actual incidence of each subtype of IUGR and disparities.

Materials and Methods: Across-sectional descriptive study applied on 52 singleton newborns admitted to the NICU at Al-Yarmouk Teaching Hospital, Baghdad, Iraq, from January to December2015.We assessed them for some demographic characteristics, anthropometric measures, investigation and a thorough physical examination with an estimation of the Ponderal Index (PI) values; these data were analyzed using SPSS software version 18.0.

Results: We found equal gender distribution for each sex. The 63.46% of IUGR babies were of asymmetrical type, while 36.53% were symmetrical. Incidence rate was higher among multiparous mothers than primiparous as 51.9%. The asymmetrical subtype mostly delivered by Normal Vaginal Delivery (63.6%), while the symmetrical subtype mostly delivered by Cesarean section (68.4%). Respiratory distress syndrome was the commonest early complication, the higher percentage was among symmetrical than asymmetrical subtypes 57.9%, 27.3%, respectively. Among all deaths, 33.35% had asymmetrical subtype. The mean birth weight for a symmetrical subtype was 1.410 gr, while for the symmetrical subtype it was 1.760 grams.

Conclusion: The asymmetrical IUGR newborns were more than symmetrical type. More than two thirds of symmetrical IUGR were delivered with Cesarean section, while more than two thirds of asymmetrical IUGR were delivered normally and more than half of symmetrical IUGR were with RDS. Sex had no effect on IUGR distribution.

Key Words: Intra uterine growth restriction, Iraq, Neonate, Ponderal Index.

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1- INTRODUCTION

Worldwide 3-10% of pregnancies are affected by Intrauterine Growth Restriction (IUGR); 20% of stillborn infants have IUGR. Perinatal mortality rates are 4-8 times higher for growth-retarded infants, and morbidity is present in 50% of surviving infants (1). Low-birth-weight (LBW) infants (born at a weight < than 2.500 gr) either born preterm or term with low weight regarding their gestational age (GA). IUGR, defined fetal growth as less than normal in light of the growth potential of that specific infant, Risk factors for LBW related to both prematurity (less than 37 weeks of gestation) and IUGR (2). IUGR occurs in three phases; the first phase lasts from conception to 16 weeks of gestation, characterized by a rapid increase in cell number (Hyperplasia). In the second phase, hyperplasia continues and is accompanied by a rapid increase in cell size (Hypertrophy); this phase lasts until 32 weeks of gestation. While in third phase, the fetus grows only by an increase in cellular size, here, the fetus develops most of its fat and muscle weight (3).

IUGR caused whenever normal fetal growth processes interrupted throughout the pregnancy, it can be categorized as being either symmetric or asymmetric depending on the insult timing during pregnancy (4). When IUGR originated during early fetal life it results in symmetrical growth restriction in which the weight, length, and head circumference simultaneously are affected, hence, their causes include genetic disorders (constitutional or chromosomal abnormalities), harmful drug exposures, TORCH infections like Cytomegalovirus (CMV) cytomegalovirus infection or toxoplasmosis, Herpes, hepatitis, some inborn errors of metabolism and dwarf syndromes (2).While late onset growth restriction, result in asymmetrical growth delay which is usually related to impaired utero-placental function (preeclampsia, chronic hypertension, class D and F diabetes), or nutrient deficiency usually in the 3rd trimester where two-thirds of fetal growth occurs (2). A fetus with asymmetric IUGR has a normal head circumference, but a small abdominal circumference dimensions (due to decreased liver size), scrawny limbs (because of decreased muscle mass) and thinned skin (because of decreased fat). If the insult causing asymmetric growth restriction is sustained long enough or is severe enough, the fetus may lose the ability to compensate and will become symmetrically growth-restricted (5). Both subtypes are prone to perinatal complications, including fetal morbidity and mortality, iatrogenic prematurity, fetal compromise in labor that necessitates induction of labor or cesarean delivery (6). They need regular antenatal visits and monitoring especially when sono-graphic evidence of placental disease is sought with arrangement for early delivery by (induction or caesarean section [C.S]) as required.

2- MATERIALS AND METHODS

2-1. Study design and setting

A cross-sectional descriptive study with analytic element applied on 52 singleton newborns admitted to the neonatal intensive care unit (NICU) at Al-Yarmouk Teaching Hospital, Baghdad, Iraq. They studied from 1st January -31st December 2015 for their low birth weight (body weights [B.W] <10 percentile for their norms of same gestational ages) with IUGR as the Ponderal Index (PI) (B.Wx100 /body length^3) value were <10%.

2-2. Data Collection

Information regarding maternal history including; age, parity, hypertensive disease, and type of delivery were collected. These inborn babies were

assessed for sex, gestational age, birth weight, head circumference and the Crown heel length, the results were plotted on a customized neonatal growth chart for sex and the birth weight regarding their gestational age were calculated. Moreover, PI values had been used to categorize the subtypes to symmetrical and asymmetrical IUGR, when PI<2.2 it indicates asymmetrical IUGR and when its>2.2 indicates symmetrical type, (cutoff point PI=2.2) for term newborn and (cutoff point =2) for preterm. Moreover, complete physical examination for any disease or abnormality had been done by same pediatrician to overcome any bias, all patients were investigated for complete blood count(CBC), blood test for (sugar, Calcium ion [Ca^{+2}], bilirubin) levels were estimated. In addition, some required Chest X-ray (CXR), abdominal ultrasound (US) study and sepsis screen.

2-3. Statistical Analysis

Data were entered and analyzed using the statistical package for social sciences (SPSS) version 18.0, results were summarized and presented in tables with figures. Chi- square test was used to assess the association between variables; p- value of ≤ 0.05 was considered significant.

3- RESULTS

3-1. Regarding IUGR subtype distribution:

The percentages of asymmetrical / symmetrical cases in our study were 63.46% and 36.53%, respectively in a ratio of 1.7:1 (**Table.1**); with equal gender distribution of 50%. Nevertheless, gender distribution differs among subtypes as follows: in symmetrical subtype; female had a higher percentage than male, 52.6% and 47.4%, respectively; while male in asymmetrical had a higher percentage than female, 51.5% and 48.5%, respectively, (**Table.1**),with no significant.

3-2. Regarding maternal characteristics of IUGR cases, our study results were as follows:

IUGR incidence was higher among multiparous mothers than primiparous, 51.9% and 48.1%, respectively. Furthermore, regarding IUGR subtype distribution; multiparous mothers had a higher percentage of neonates with asymmetrical IUGR than primparous, 57.6% and 42.4%,respectively; while primparous had a higher percentage of neonates with symmetrical type than a symmetrical type, 57.9% and 42.1%, respectively, with no significant statistical value(**Table.2**). Most of the IUGR admitted newborns delivered by National Vulnerability Database (NVD) (51.9%), and the remaining (48.1%) delivered by caesarean section. Nevertheless, delivery type among subtypes of IUGR new born was different. Most of a symmetrical babies delivered by NVD, while the remaining delivered by caesarean section, 63.6% and 36.4%, respectively. Oppositely, in symmetrical subtype, CS delivery was higher than NVD, 68.4% and 36.4%, respectively. This was of significant statistical value (p=0.026) (**Table.2**). Hypertensive mothers had higher incidence of having IUGR babies than non-hypertensive mothers, 51.9% and 48.1%, respectively. Moreover, hypertensive mothers regardless etiology, had a higher percentage of having neonates with symmetrical subtype IUGR (52.6%), while normotensive mothers had higher percentage of having neonates with asymmetrical subtype (54.5%), with no significant statistical value (p=0.618) (**Table.2**).

3-3. Our study results regarding morbidities and outcome:

Respiratory distress syndrome (RDS) was the commonest early complication among overall IUGR admitted patients (38.5%), the higher percentage was among the symmetrical subtype (57.9%); while in a

symmetrical subtypes it was 27.3%.On the other hand, other morbidities; were the less common early complications constitute only 19.2% including (hypoglycemia, hypocalcemia, hypothermia, necrotizing enterocolitis, bleeding, sepsis, apnea, jaundice, etc.) were higher among symmetrical than asymmetrical subtypes 21.1% and 18.2%,respectively. Fortunately, neonates with no morbidity, 42.3%with asymmetrical subtype, while only 21.1% with symmetrical subtype (p=0.045) (**Table.3**).

Results showed that 69.2% of admitted newborns with IUGR discharged well from the NICU mostly of the symmetrical type (73.7%), while asymmetrical subtype equals 66.7%. On the other hand, among all deaths 33.35% had asymmetrical IUGR, while only 26.3% had symmetrical subtype, although of no significant statistical value (p=0.598) (**Table.3**).

3-4. IUGR subtypes distribution attributed by gestational age, neonatal weight and maternal age:

Results showed that 65.34% of patients delivered prematurely, with gestational age <37 weeks; while the remaining 34.61% delivered with > 37 weeks gestational age, the asymmetrical subtype was the commonest among both gestational groups (<37, >37weeks) as 67.6% and 55.6%, respectively. The mean gestational age for a symmetrical IUGR baby was 35.24 weeks with (SD) standard deviation of 2.75; while the mean GA for the symmetrical subgroup babies was 36.2weeks with 2.65 SD. All of no significant statistical value (p=0.222) (**Table.4**).

3-5. Regarding IUGR subtype distribution in relation to neonatal birth weight:

The mean birth weight for a symmetrical subtype was 1,410 gr, while for the symmetrical subtype it was 1,760 gr, this result had a highly significant statistical value (p=0.004) (**Table.4**). The mean maternal age for the asymmetrical subtype was 25.78 years with 7.67 SD from the mean, while for the symmetrical subtype the mean maternal age was 25.68 years with 6.8 SD from the mean. Both of no significant statistical value (p= 0.961) (**Table.4**).

Table-1: IUGR subtype and gender distribution among admitted newborns

Variables		Asymmetrical	Symmetrical	Total	P-value
		Number (%)	Number (%)	Number (%)	
Gender	Female	16(48.5)	10(52.5)	26(50)	0.773
	Male	17(51.5)	9(47.4)	26(50)	
Total		33(63.46)	19(36.53)	52(100)	

Table-2: Maternal characteristics of IUGR cases

Variables		Asymmetrical	Symmetrical	Total	P-value
		Number (%)	Number (%)	Number (%)	
Parity	Multiparous	19(57.6)	8(42.1)	27(51.9)	0.282
	Primigravidas	14(42.4)	11(57.9)	25(48.1)	
Type of delivery	CS	12(36.4)	13(68.4)	25(48.1)	0.026
	NVD	21(63.6)	6(31.6)	27(51.9)	
Maternal Ht	Yes	15(45.5)	10(52.6)	25(48.1)27(51.9)	0.618
	No	18(54.5)	9(47.4)		

NVD: normal vaginal delivery; CS: cesarean section; Ht: hematocrit.

Table-3: Morbidities and outcome among IUGR admitted neonates.

Variables		Asymmetrical	Symmetrical	Total	P-value
		Number (%)	Number (%)	Number (%)	
Morbidity	RDS	9(27.3)	11(57.9)	20(38.5)	0.045
	Others*	6(18.2)	4(21.1)	10(19.2)	
	Normal	18(54.5)	4(21.1)	22(42.3)	
Outcome	Died	11(33.3)	5(26.3)	16(30.8)	0.598
	Discharged	22(66.7)	14(73.7)	36(69.2)	

*Others: hypoglycemia, hypothermia, hypocalcemia, necrotizing enterocolitis (NEC) sepsis, jaundice, apnea; RDS: Respiratory distress syndrome.

Table-4: Distribution of IUGR cases by gestational age, neonatal weight and maternal

Variables	Asymmetrical	Symmetrical	t-test	P-value
	Mean (SD)	Mean (SD)		
Gestational age	35.24(2.75)	36.2(2.65)	1.237	0.222
Neonatal weight	1.41(0.41)	1.76(0.38)	3	0.004
Maternal age	25.78(7.67)	25.68(6.8)	-0.049	0.961

SD: standard deviation.

4- DISCUSSION

In our study, the ratio of asymmetrical to symmetrical IUGR cases was approximated two-third and one-third, respectively, agreed to a study in USA (the asymmetric pattern is most commonly occurring in 70 % of growth-restricted infants, while symmetric type occurs in 30% of IUGR infants) (7) as well as agreed Campbell and Thomas study (8); while disagreeing with a study find half of all IUGR infants are asymmetrically restricted and half are symmetrically restricted (9). Other study showed that symmetrical IUGR was more than asymmetrical (10), maybe related to the fact that the prevalence of the different types of IUGR babies varies greatly among different population firstly and secondly to their different primary causes (11). Male and female newborns were equally affected by IUGR in our study, nearly (50%) for each with a slight female predominance among symmetrical type (52.6%), while male predominates among asymmetrical type 51.5%.These results agreed by Murki and Sharma's study (12); while disagreed with a study in Nigeria which showed no sex predilection for neither IUGR subtypes(13). Our finding of higher incidence of fetal IUGR among multiparous mothers disagreed Shoham-Vardi et al.,, and Kliegman et al. studies (14, 20), in which IUGR were higher among primiparas mothers. Furthermore, asymmetrical fetal IUGR predominates among multiparous mothers which may be attributed mainly to their higher incidence of chronic medical diseases like (diabetes mellitus, hypertension, cardiovascular diseases, renal problems and others) causing negative impacts on fetal growth due to placental insufficiency; while primiparas had higher rates of symmetrical IUGR babies agreed by a study in USA (21), that is may be related to the higher possibility of unknown yet inborn error of metabolism or genetic or chromosomal diseases as it is the 1stpregnancy. In addition, their small size uterus, which resists restrain during pregnancy, as well as the high rate adolescent marriage in our society as a risk factor for preterm delivery and IUGR. Overall cases of IUGR babies in our study delivered by normal vaginal delivery more than cesarean section, which agreed with Shavit et al. study (16); while

disagreeing with an Indian study in which 80% cases underwent cesarean section and 20% cases had a normal vaginal delivery (17). Furthermore, among IUGR subtypes, we found a cesarean section delivery applied more for symmetrical type than asymmetrical type 68.4% and 36.4%, respectively, which attributed mainly to early fetal compromise in symmetrical type that necessitates early intervention to avoid future neurons developmental and cognitive defects. Our study disagreed with Dashe study in USA (18) in which CS applied more for asymmetrical type.

Hypertension was present in less than half cases in both subtypes with a slight predilection for symmetrical type, which may be related to severe sustained early maternal hypertension that retards fetal growth globally not solely the weight. Also, agreed by Kliegman et al., study (20) and a study in Pakistan (25); while disagreed with Dashe study (18), as pregnancy induced hypertension found more in asymmetrical type.

The high morbidity found in symmetrical type, especially (RDS) which predominates the Asymmetrical type probably related to the higher incidence of prematurity and associated surfactant deficiency that causing poor lung maturation in this group as it occurs in early pregnancy (1^{st} trimester mainly), that agreed with a Nigerian study (13). While more than half asymmetric type neonates had no morbidity, which may be attributed to the late gestational occurrence (2^{nd} and 3^{rd} trimesters) with less growth delay and less harmful effects and squally, this disagreed by two studies in which morbidities were found higher among the asymmetrical group because of loss fatness (19, 20). Overall outcome, approximately two-third of neonates improved and discharged well, while the remaining one-third (33.3%) died, which disagreed with Muniyar et al, study (21) as (only 5% died) this indicates poor awareness for early case detection and management through regular antenatal care visits and follow up. On the other hand, the better prognosis for symmetrical type may be attributed to the higher rate of CS delivery at the appropriate time during follow-up period, while the higher mortality incidence was among the asymmetrical type, which may be attributed to the higher incidence of normal vaginal delivery with delayed or unplanned interventions that causes prolonged and irreversible fetal injury which negatively impacts perinatal and postnatal life. Mean gestational age for the asymmetrical IUGR was less than the symmetric IUGR by 1week $\pm$ 2.62. Although both are more in premature babies (< 37 weeks of gestation), hence, morbidity is inversely related to gestational age. It is now believed that most IUGR is a continuum from asymmetry (early stages) to symmetry (late stages) agreed by a study in Pennsylvania (22); but this result had no significant statistical value.

Regarding birth weight, the mean birth weights of the asymmetric group were less than the symmetric group 1.410, 1.760 gr, respectively, may be related to the fact that energy in asymmetrical IUGR babies utilized maintaining growth of vital organs, such as the brain and heart, at the expense of the liver, muscle and fat which causes reduction of body mass and weight (fetal brain is normally about three times the weight of the liver, but in asymmetrical-type IUGR, the value may increase to two or three times that value because of liver smallness); while in symmetrical type all organs are small except the liver, which increases in size this may explain our results, our findings agreed with a study in USA (23); while disagreed with a study in Chicago (24). There was no difference regarding maternal age for both IUGR subtypes, as it is nearly the same; although, the mean maternal age for symmetrical subtypes

which slightly lower than for asymmetrical subtype, but still of no significant statistical value.

4-1. Recommendations

IUGR reducing programs should be carried out in all Primary Health Centers PHC (primary health care) and maternity subtypes, individual planning applied by a specialist obstetrician to improve their predictive values for subsequent morbidity, mortality and future growth and development.

5- CONCLUSION

The asymmetrical IUGR newborns were more than symmetrical type. More than two thirds of symmetrical IUGR were delivered with Cesarean section, while more than two thirds of asymmetrical IUGR were delivered normally and more than half of symmetrical IUGR were with RDS. Sex had equal proportions with no effect on IUGR distribution. Multiparities and maternal hypertensions have no rules in IUGR events. Maternal age, gestational age, neonatal birth weight are not affected on and/or not affected by IUGR.

6- CONFLICT OF INTEREST: None.

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