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CORD AND MATERNAL BLOOD LEVEL OF IGF-II IN NORMAL PREGNANCY, PREGNANCY INDUCED HYPER TENSION AND GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Cord and maternal blood levels of insulin- like growth factor (IGF) -II were studied in women with either pregnancy induced hypertension (PIH) (n=15), gestational diabetes mellitus (GDM, n=14) and women with normal uncomplicated pregnancies (n=15). IGF-II levels were measured by enzyme linked immunosorbent assay. Maternal and cord blood levels of IGF-II were compared between three groups (Kruscal wallis analysis of variance) and correlated (Spearman rank correlation) with neonatal anthropometric measurements (Birth weight, length and head circumference). Birth size did not significantly differ between the three groups studied. There was no significant difference in cord or maternal blood IGF-II levels between the three groups. In normal pregnancies cord blood IGF-II positively correlated with birth weight (r = 0.5676, P= 0.0273). In conclusion, maternal or cord blood IGF-II levels did not significantly differ between the groups. Correlation observed between cord blood IGF-II with birth weight in normal pregnancy. A larger number of subjects need to be studied to further clarify the association between cord blood IGF-II and infant anthropometric variables.

KEY WORDS: *Insulin-like growth factor (IGF)-II, neonatal anthropometry, fetal growth*

INTRODUCTION

Insulin like growth factor -II is a mitogenic polypeptide with a structure similar to proinsulin. It stimulates cell proliferation and differentiation effects on fetal growth. It is the major secretary growth factor in embryonic tissues and placenta. IGF-II is known to play a key role in fetal growth and development (Daughday and Rotwein, 1989).

Circulating level of IGF-II increases during second and third trimesters of pregnancy and it has been shown to be associated with size at birth (Jones and Clemmons, 1995; Lauszus *et al*, 2001).

In an elegant study in a mouse knockout model, the litter lacking IGF-II gene was shown to be only 60% in size compared to their wild-type littermates at birth but a normal postnatal growth rate was observed (DeChiara *et al*, 1990).

Pregnancy Induced Hypertension (PIH) and Gestational Diabetes Mellitus (GDM) are known to cause fetal growth retardation and macrosomia respectively. (Lala and Chakraborthy,2003). These deviant fetal growths are associated with higher rates of mortality and morbidity (Cambel and Lees, 2000). In view of lack of any data on the circulating IG-II in pregnancies complicated by PIH or GDM for Sri Lankan women the present investigation was carried out.

MATERIALS AND METHODS

Subjects

This was a cross sectional study carried out on normal healthy pregnant mothers (n=15) and pregnancy with diabetes mellitus (n=15). Study was approved by the Institutional Review Board and written informed consent was obtained from the mothers and fathers. The subjects enrolled were women in para 1 or 2, aged 21-35 years who had naturally conceived and who delivered a singleton baby with no apparent congenital malformation or hereditary / genetic disorder. GDM were diagnosed by attending medical staff using following criteria GDM was defined as either a raised fasting blood glucose level of >7.8 m mol/L or a blood glucose level of > 11.1 mmol/L 1 - 2 hours following a 75 g oral glucose load.

On admission to the study, socio-demographical and clinical data were recorded.

Samples

Maternal blood was collected either at the onset or after the delivery. Cord blood was collected at the delivery.

Measurements

Newborn anthropometry including birth weight (Seca baby weighing scale), crown-heel length (infantometer), and head circumference (standard measuring tape) were measured within 24 hours after delivery. Ponderal index was calculated as weight (Kg)/height (m^3)

IGF-II Assay

Maternal and cord blood IGF-II levels were measured by ELISA using commercially available kits (IGF-II active non-extraction ELISA - Catalog No: DSL-10-2600, Diagnostic System Laboratories, Inc. Webster, USA). All the kit reagents stored at 4°C were brought to room temperature before use. Standards, samples and controls were assayed in duplicates. All the assays were performed according to the manufacturer's recommendations.

Statistical Methods

All statistical analysis was performed by using a statistical package GraphPad prism 2.01 (GraphPad Prism, San Diego, CA). non parametric analysis of variance (Kruskal Wallis test) was used to compare maternal and cord blood levels of IGF-I, IGF-II and IGFBP-1 between the three groups. Spearman Rank correlations test was used to examine the relationship between IGF-II IGF-I, IGF-II and IGFBP-1 levels with infant anthropometric indices within each group.. The level of significance was considered as p-value< 0.05.

RESULTS & DISCUSSION

The anthropometric variables at birth of infants of women with uncomplicated normal pregnancies, PIH and GDM are shown in Table 1. Though PIH was expected to result in lower birth weights and GDM higher birth weights, there was no significant difference in birth weights between PIH, GDM and normal pregnancy groups.

Table 1: Anthropometric variables of infants at birth

	Normal (N=15)	PIH (N=15)	GDM (N=15)	P value
Weight (Kg)	2.915 ± 0.077	2.787 ± 0.131	3.076 ± 0.125	0.1646
Length (cm)	52.00 ± 0.525	51.53 ± 0.716	51.47 ± 0.844	0.9078
CC (cm)	31.75 ± 0.350	31.37 ± 0.437	32.33 ± 0.482	0.4552
HC (cm)	33.00 ± 0.425	33.47 ± 0.388	33.80 ± 0.438	0.5421

CC = Chest circumference HC = Head circumference

Cord blood and maternal blood IGF-II levels (percentile distribution) in three studied groups are shown in Fig 1. Cord or maternal blood IGF-II did not differ between the three studied groups. A previous study reported that significantly lower cord IGF-II levels were found in intrauterine growth retardation compared to normal. They did not find any significant difference in cord blood IGF-II between LGA and normal infants (Guidice et al, 1995). In contrast, Hall et al (1986) reported higher cord serum IGF-II in newborns of diabetic mothers. In our study, no significant difference in cord blood IGF-II levels in PIH and in GDM groups, compared to normal pregnancies may result from the fact that there were only five low birth weight infants in PIH and three high birth weight infants in GDM groups. The fact that the total sample size was small may also have contributed.

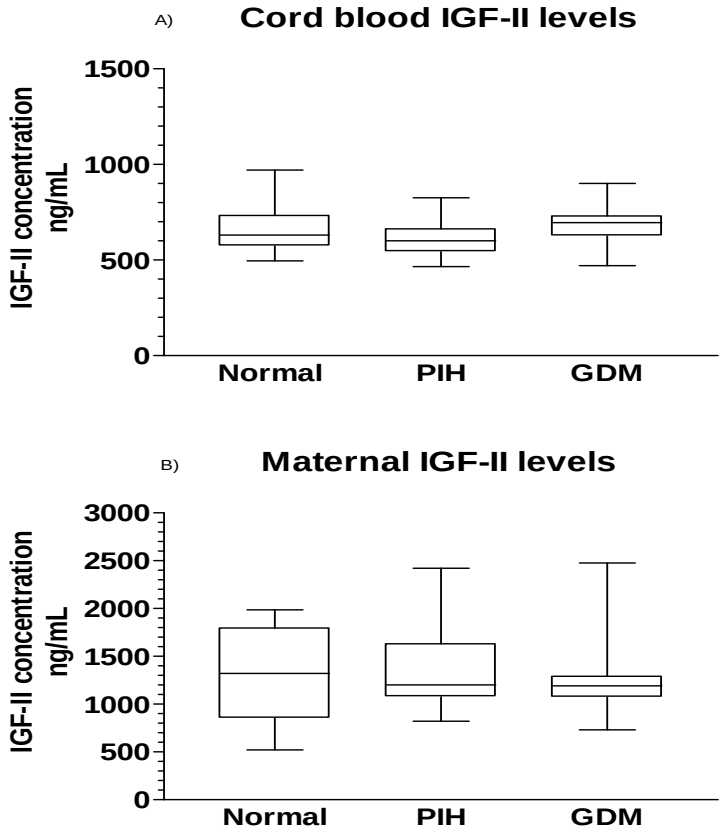

Fig 1: Percentile distribution of Cord (A) and maternal blood (B) IGF-II in normal pregnancies (n=15), pregnancy induced hypertension (PIH, n=15) and gestational diabetes mellitus (GDM, n=15). Line inside the box represents the median (50 th percentile) and the box represents the interquartile range (25 th to 75 th percentile). Whiskers indicate the lower and upper quartiles.

Cord IGF-II levels in normal uncomplicated pregnancies, but not in PIH and GDM groups significantly correlated with birth weight(r = 0.5676, P = 0.0273). There were no significant correlations between cord blood IGF-II and other anthropometric variables in any of the three groups.

Conflicting results have been reported on the relation between IGF-II and fetal growth in previous studies. Ong et al., (2000) reported that cord IGF-II positively correlated with birth weight. Others have shown a weakly correlation or no correlation with birth weight (Susa et al., 1984; Hall et al., 1986; Samman et al., 1990; Lassarrec et al., 1991; Fant et al., 1993; Verhaeghe et al., 1993; Osorio et al., 1996; Klauwer et al., 1997).

IGF-II is the primary growth factor during early embryonic development where differentiation and proliferation of tissues and organogenesis take place (Daughday and Rotwein, 1989). It is also an angiogenic growth factor (Herr et al., 2003) increases placental function primarily by increasing placental (uterine and umbilical) blood flows, associated with increased placental vascularity and the migration of trophoblast cells. Therefore, transfer of glucose is increased and stimulates fetal insulin gene family

including IGF-I and IGF-II subsequently increasing fetal size.

The associations between maternal IGF-II levels and fetal growth or infant birth size are inconsistence. (Wiznitzer et al, 1989, Olausson et al, 2008, McIntyre et al, 2000, Zhong et al, 2012). However, we found Maternal IGF-II did not correlate with neonatal anthropometry in normal uncomplicated pregnancies, PIH or GDM groups.

CONCLUSION & SUGGESTION

We have observed correlation between cord blood IGF-II and birth weight in uncomplicated normal pregnancy. To refute or confirm these observations the present investigation should be expanded to include a larger number of subjects.

REFERENCE

1. *Daughaday WH and Rotwein P. (1989). Insulin-like growth factors I and II Peptide, messenger ribonucleicacid and gene structures, serum, and tissue concentrations. Endocrine Review. 10, 68 - 91.*
2. *Jones JI and Clemmons DR. (1995). Insulin-like growth factors and their binding proteins: biological actions. Endocrine Review 16, 3 - 34.*
3. *Lauszus FF[1], Klebe JG, Flyvbjerg A. (2001). Macrosomia associated with maternal serum insulin-like growth factor-I and -II in diabetic pregnancy. Obstetrics & Gynecology 97:734-41.*
4. *DeChiara T, Efstratiadis A and Robertson EA. (1990). Growth-deficient phenotype in heterozygous mice carrying an insulin-like growth factor II gene disruption by targeting. Nature, 345, 78 – 80.*
5. *Lala PK and Chakraborty C. (2003). Factors regulating trophoblast migration and invasiveness; possible derangements contributing to pre-eclampsia and fetal injury. Placenta, 24, 575 – 587.*
6. *Cambel S and Lees C. (2000). Obsteric by Ten Teachers, 17th edition, ELSI imprint, UK.*
7. *Giudice LC, Martina NA, Crystal RA, Tazuke S and Druzin M. (1997). Insulin-like growth factor binding protein- 1 at the maternal–fetal interface and insulin-like growth factor I, insulin-like growth factor II, and insulinlike growth factor binding protein 1 in the circulation of women with severe pre-eclampsia. American Journal of Obstetrics and Gynecology, 176, 751–757.*
8. *Hall K, Hannson U and Lundin G. (1986). Serum levels of somatomedins and somatomedin binding protein in pregnant womenwith type-I or gestational diabetes and their infants. The Journal of Clinical Endocrinology and Metabolism. 63, 1300 – 1305.*
9. *Ong K, Kratzsch J, Kiess W, Costello M, Scott C and Dunger D. (2000). Size at Birth and Cord Blood Levels of Insulin, Insulin-Like Growth Factor I (IGF-I), IGF-II, IGF-Binding Protein-1 (IGFBP-1), IGFBP-3, and the Soluble IGF-II/Mannose-6-Phosphate Receptor in Term Human Infants. The Journal of Clinical Endocrinology and Metabolism, 85, 4266 -4269.*
10. *Susa JB, Widness JA, Hintz R, Liu F, Sehgal P, Schwartz R. (1984). Somatomedins and insulin in diabetic pregnancies: effects of fetal macrosomia in the human and rhesus monkey. The Journal of Clinical Endocrinology and Metabolism, 58, 1099 – 1105.*
11. *Samman NA, Schultz PN, Pham FK. (1990). Insulin-like growth factor –II and nonsuppressible insulin-like activity levels in newborns. American Journal of Obstetrics and Gynecology. 163, 1836 – 1839.*
12. *Lassarre C, Hardouin S, Daffos F, Forestier F, Frankenne F, Binoux M. (1991). Serum insulin-like growth factors and insulin-like growth factor binding proteins in the human fetus. Relationships with growth in normal subjects and in subjects with intrauterine growth retardation. Pediatric Research, 29, 219 – 225.*
13. *Fant M, Salafia C and Baxter RC. (1993). Circulating levels of IGFs and IGF binding proteins in human cord serum: relationships to intrauterine growth. Regulation Peptide, 48, 29 – 39.*
14. *Verhaeghe J, Van Bree R, Van Herck E, Laureys J, Bouillon R and Van Assche FA (1993). C-peptide, insulin-like growth factors I and II, and insulin-like growth factor binding protein 1 in umbilical cord serum: correlations with birth weight. American Journal of Obstetrics and Gynecology, 169, 89 – 97.*
15. *Osorio M, Torres J, and Moya F. (1996). Insulin-like growth factors (**IGF**s) and **IGF** binding proteins-1, -2, and -3 in newborn serum: relationships to fetoplacental growth at term. Early Human Development, 46, 15 – 26.*
16. *Klauwer D, Blum WF, Hanitsch S, Rascher W, Lee PD and Kiess W. (1997). IGF-**I,** -II, free IGF-I and IGFBP-1,-2 and-3 levels in venous cord blood: relationship to birth weight, length and gestational age in healthy newborns. Acta Paediatric, 86, 826 – 833.*
17. *Herr F, Liang OD, Herrero J, Lang U, Preissner KT, Han VK, Zygmunt M. (2003). Possible angiogenic roles of insulin-like growth factor II and its receptors in uterine vascular adaptation to pregnancy. J Clin Endocrinol Metab 88: 4811–4817.*
18. *Wiznitzer A , Reece EA , Homko C , Furman B , Mazor M , Levy J 1998 Insulin-like growth factors, their binding proteins, and fetal macrosomia in offspring of nondiabetic pregnant women. Am J Perinatol 15:23–28.*
19. *Olausson H , Lof M , Brismar K , Lewitt M , Forsum E , Sohlstrom A 2008 Longitudinal study of the maternal insulin-like growth factor system before, during and after pregnancy in relation to fetal and infant weight. Horm Res 69:99–106.*
20. *McIntyre HD , Serek R , Crane DI , Veveris-Lowe T , Parry A , Johnson S , Leung KC , Ho KK , Bougoussa M , Hennen G , Igout A , Chan FY , Cowley D , Cotterill A ,*

Barnard R 2000 Placental growth hormone (GH), GH-binding protein, and insulin-like growth factor axis in normal, growth-retarded, and diabetic pregnancies: correlations with fetal growth. J Clin Endocrinol Metab 85:1143–1150.

21. *Zhong CL, Anne MN, Edgard D, Francois A, Isabelle G, Bryna S, Anik C, Jocelyne C, Anissa D, Cheri D, Emile L, Yuquan W, Pierre J, William DF 2012 Maternal and Fetal IGF-I and IGF-II Levels, Fetal Growth, and Gestational Diabetes. J Clin Endocrinol Metab 97: 1720–1728.*
22. *Zhong CL, Anne MN, Edgard D, Francois A, Isabelle G, Bryna S, Anik C, Jocelyne C, Anissa D, Cheri D, Emile L, Yuquan W, Pierre J, William DF 2012 Maternal and Fetal IGF-I and IGF-II Levels, Fetal Growth, and Gestational Diabetes. J Clin Endocrinol Metab 97: 1720–1728.*