Original Article

Serum insulin levels and anthropometric indices in macrosomic neonates; a comparative study between fetuses of diabetic and non-diabetic mothers

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Objective: To measure serum insulin levels and anthropometric indices of the macrosomic neonates and to associate them with maternal glycemic factors.

Methodology: This multi-center cross-sectional study was conducted in various hospitals in Karachi from November 2011 to February 2013 and included 125 macrosomic neonates**.** Mothers were grouped as diabetic and non-diabetics. Anthropometric parameters of baby were measured in addition to blood markers like cord blood insulin.

Results: Comparison of anthropometric indices showed statistically significant higher values of head circumference (p=0.007), chest circumference (p=0.015), abdominal circumference (p<0.010), mid-upper arm (p<0.010) and bi-parietal diameters (p=0.035) in macrosomic neonates of diabetic mothers as compared to macrosomic neonates of non-diabetic mothers. Fetal serum insulin was increased in neonates of diabetic mothers as compared to that of non-diabetics.

Conclusion: Hyperinsulinemia was found in increased frequency in macrosomic infants of diabetic mothers as compared to the non-diabetics. Newborns of diabetic mothers showed significantly higher bi-parietal diameter, head, chest, abdominal and mid upper arm circumference. Abdominal circumference and mid upper arm circumference were significantly high in the macrosomic infants with hyperinsulinemia. (Rawal Med J 202;45:593-597).

Keywords: Macrosomia, hyperinsulinemia, diabetes, anthropometric indices.

INTRODUCTION

Macrosomia is defined as birth weight >90th percentile corrected for gestational age, sex and parity. National Centre for Health Statistics defined that 90th-percentile birth weight at 40 weeks is 4,060gm, most accepted definition is birth weight >4000 gm.[1] In Pakistan, where the mean birth weight is 3.0$\pm$0.5 kg^2, $\geq$ 4.0 were included in the study.

Hyperinsulinemia is an important cause of macrosomia in neonates,[3] a condition with increased serum insulin.[4] Metzger et al analyzed Pedersen hypothesis that linked hyperinsulinemia with macrosomia (fetal overgrowth).[5] Guzmán-Bárcenas et al showed that the growth of fetus is strongly correlated with concentration of insulin of umbilical cord.[6] Maternal hyperglycemia results in fetal hyperglycemia causing hypertrophy of fetal islet tissue with insulin-hypersecretion. This proposal was based primarily on maternal and infant blood glucose concentrations, supported by the findings of pancreatic-islet hypertrophy and beta-cell hyperplasia in the infants.[5]

There is a positive relation between obesity and insulin resistance. The insulin resistance enhances the metabolic stress and hyperglycemia in obese pregnant mothers.[4] Thus, adolescent obesity is related with adolescent type 2 diabetes and gestational Diabetes Mellitus (GDM).[7] Glycemic control during pregnancy decreases the frequency of macrosomic fetuses but still pregnancy with diabetes has 3.5 times higher chances of delivering macrosomic fetus as compared to general population despite proper glycemic control.[8,9] Our study was aimed to evaluate the occurrence of hyperinsulinemia in macrosomic neonates based on mother's glycemic status.

METHODOLOGY

This cross-sectional multicenter study was conducted at Civil Hospital, Mamji and Habib Medical Center from November 2011 to February 2013. Approval from the Institutional review board (IRB) of DUHS (IRB-275/DUHS-11) was obtained. All macrosomic (in Pakistan, where the mean birth weight is 3.0±0.5 kg[2], ≥ 4.0 were included in the study) singleton neonates were consecutively enrolled from these hospitals. Preterm babies (<37 weeks gestation) and multiple pregnancies were excluded. Sample size was calculated by using openepi.com sample size calculator according to the study by Kamana et al Sample size calculated for 95% confidence interval with 5% error for prevalence of at 3% prevalence of macrosomia in our population is 78 but, we included 125 neonates.[10] A total of 125 participants were enrolled which were divided into two groups on the basis of maternal glycemic status, i.e. diabetes and non-diabetes on the basis of HbA1c levels. The diabetic mothers includes both with gestational diabetes and established diabetes.

Anthropometric parameters of baby like weight, crown heel length, head, chest, abdominal, mid upper arm, bi-parietal diameter and skin fold thickness were measured using standard protocols. Cord blood sample was collected at birth and blood samples from mothers, were drawn next morning. The samples were sent to Dow Diagnostic and Research Laboratory (DDRRL). The HbA1c and fetal blood sugar was determined (Hitachi 902 analyzer) and cord blood insulin was determined (IMMULITE 1000 analyzer; Siemens Medical Solutions Diagnostics). Reference values used for fasting cord blood plasma glucose is 45-96 mg/dl , for serum insulin is 3-20 µU/ml whereas reference values for HbA1c is <6%.

Statistical Analysis: Data were analyzed by SPSS version 21. Mean difference was calculated by Mann-Whitney U test for all anthropometric variables. Pearson correlation was applied to determine correlation between all anthropometric parameters and maternal insulin and HbA1c. $p<0.05$ was considered statistically significant.

RESULTS

Of 125 newborns, 83 (66.4%) were males and 42 (33.6%) females (Fig 1). The mean values of neonatal weight were 4.14±0.16 kg, crown heel length were 52.30±2.16cm, subscapular skin fold were 6.54±1.20 cm, triceps skin fold thickness were 5.84±1.11 cm, head circumference were 35.76±0.90 cm, mid upper arm circumference were 13.84±1.13 cm, abdominal circumference were 35.71±1.74cm, chest circumference were 37.81±1.74cm, and bi-parietal diameter were 18.55±2.17 cm.

The mean maternal glucose level (HbA1c) was 5.64±0.72% while maternal insulin level was17.91±3.63 µIU/ml. Maternal diabetes was observed in 22 (18%) patients whereas 103 (82%) mothers had normal glycemic status (Table 1). The fetal insulin level was found to be 20.72 ±6.74 µIU/ml. A significantly higher abdominal circumference (p-value 0.010) and mid-upper arm (p-value 0.010) was found among fetus with hyperinsulinemia as compared to normal fetal insulin level (Table 2).

Table 1. Comparison of anthropometric parameters between study groups on the basis of maternal glycemic status.

Parameter	Groups (N = 125)	N	Mean	Standard Deviation	P-value
Baby weight (kg)	Normal	103	4.13	0.16	0.09
	Diabetic	22	4.2	0.2	
CH Length (cm)	Normal	103	52.11	2.28	0.17
	Diabetic	22	52.96	1.56	
Head Circumference (cm)	Normal	103	37.46	0.95	0.007*
	Diabetic	22	38.05	0.41	
Chest (cm)	Normal	103	37.68	1.79	0.015*
	Diabetic	22	38.46	1.41	
Abdominal circumference (cm)	Normal	103	35.45	1.76	<0.01*
	Diabetic	22	36.96	1	
Mid Upper arm (cm)	Normal	103	13.66	1.08	<0.01*
	Diabetic	22	14.73	1.04	
BPD (cm)	Normal	103	9.45	0.34	0.035*
	Diabetic	22	9.62	0.36	
SS Fold (mm)	Normal	103	5.55	0.71	0.685
	Diabetic	22	5.61	0.57	
TS fold (mm)	Normal	103	5.16	0.58	0.808
	Diabetic	22	5.13	0.57	

*p-value <0.05 considered as significant using Mann-Whitney U test

Table 2. Comparison of anthropometric parameters of the study groups on the basis of fetal insulin level.

Parameter	Fetal Insulin	n	Mean	Standard Deviation	P-value
Baby weight (kg)	Normal insulin levels	51	4.14	0.15	0.87
	Hyperinsulinemia	74	4.14	0.18	
CH Length (cm)	Normal insulin levels	51	52.11	2.28	0.88
	Hyperinsulinemia	74	52.3	2.11	
Head Circumference (cm)	Normal insulin levels	51	37.62	0.86	0.56
	Hyperinsulinemia	74	37.53	0.94	
Chest (cm)	Normal insulin levels	51	37.51	1.58	0.11
	Hyperinsulinemia	74	38.03	1.83	
Abdominal Circumference (cm)	Normal insulin levels	51	35.14	1.14	0.01*
	Hyperinsulinemia	74	36.11	1.98	
Mid upper arm (cm)	Normal insulin levels	51	13.53	0.95	0.01*
	Hyperinsulinemia	74	14.07	1.22	
BPD (cm)	Normal insulin levels	51	9.51	0.32	0.51
	Hyperinsulinemia	74	9.47	0.36	
SS fold (mm)	Normal insulin levels	51	5.52	0.67	0.63
	Hyperinsulinemia	74	5.58	0.69	
TS fold (mm)	Normal insulin levels	51	5.04	0.55	0.06
	Hyperinsulinemia	74	5.24	0.59	

*p-value<0.05 considered as significant using Mann-Whitney U test

Table 3. Correlation of anthropometric measurements with HbA1c and maternal serum insulin.

	Maternal HbA1c	Maternal insulin
Variables	**R**	**r**
Baby weight (Kg)	-0.20	0.90**
CH Length (cm)	0.28	0.32
SS Fold (mm)	0.64**	0.1
TS fold (mm)	0.48*	0.23
Head Circumference (cm)	-0.02	0.36
Mid Upper arm circumference (cm)	0.06	-0.13
Abdominal circumference (cm)	0.33	-0.11
Chest circumference (cm)	0.78**	0.22
Bi-parietal diameter (cm)	-0.13	0.58**

A significantly positive correlation of maternal insulin was observed with baby weight (r=0.90, p<0.01) and Bi-parietal diameter(r=0.58, p<=0.01) whereas maternal HbA1c showed significantly positive correlation with subscapular skin-fold (r= 0.64, p<0.01) and chest circumference (r=0.78, p<0.01) (Table 3).

DISCUSSION

Fetal macrosomia is considered as one of the causative factor of obesity and type 2 diabetes in adult hood.[11] When anthropometric indices were compared according to fetal insulin levels in diabetic and non-diabetic mothers, only abdominal and mid upper arm circumference showed significant differences. A previous study analyzing the differences in anthropometric parameters (birth weight, head circumference, crown-heel length and skin fold thicknesses) of normal and diabetic mothers concluded that birth weight, length, head circumference and skin fold thicknesses of macrosomic infants were more as compared to the babies with normal birth weight.[12]

Magnus et al found that father's birth weight had more impact on that of fetus as compared to mothers.[13] But, Grifith et al reported results in contrast.[14] Modified Pedersen hypothesis states that in addition to maternal glucose, fetal macrosomia could also be caused by other macronutrients.[15] In our study, most of the macrosomic infants were born to mothers with normal glycemic control. It has been reported that 8-14% fetuses born to normoglycemic mothers were macrosomic.[16] In

order to explain this birth rate of macrosomic fetuses in non-diabetics, another study suggested the role of unidentified spells of hyperglycemia during pregnancy.[17] The other explanation was the development of impaired glucose metabolism after the screening period and hence, goes undiagnosed.[18]
A study conducted on 50 infants of hyperglycemic and 52 neonates of normoglycemic mothers, analyzed different physical indices and concluded that in macrosomic babies, there were more shoulder and extremity circumferences and less head-to-shoulder ratio and body fat and upper limb skin folds were more in fetuses with high birth weight.[19] One study concluded that if the mother has uncontrolled diabetes, the skin fold thickness and anthropometric parameters are significantly high in fetuses besides fetal crown-heel length and head circumferences.[20]
Center for Disease Control and Prevention's Pediatric Nutrition Surveillance did a correlational study and found that high fetal birth weight caused higher incidence of childhood obesity.[21] Macrosomia increases the risk of obesity in adolescence, which can lead to metabolic syndrome and cardiovascular disease in these individuals.[22]
In our study, we found significant positive correlation of maternal insulin with baby weight and Bi-parietal diameter. Mother's HbA1c presented significant positive correlation with SS fold and chest circumference. Statistically significant positive correlation was found between Maternal HbA1c and TS fold. Kamana et al also noticed increased birth weight and hyperinsulinemia in infants of diabetic mothers.[10]

CONCLUSION

Hyperinsulinemia was found in increased frequency in macrosomic infants of diabetic mothers as compared to the normoglycemic ones. Abdominal circumference, mid upper arm circumference and triceps skin fold were distinctly conspicuous being significantly high in the macrosomic infants with hyperinsulinemia. However, macrosomic infants born to the mothers with normal glycemic status were in increase frequency indicating involvement of certain factors other than glycemic status responsible for excessive fetal weight

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