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Original Research Article

Birth-weight, insulin levels, and HOMA-IR in new-borns at term

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ABSTRACT

Background: Abnormal birth weight babies are prone to develop adverse metabolic and cardiovascular outcomes later in life. There is dearth of knowledge regarding correlation of birth-weight with hyperinsulinemia and insulin resistance in term newborns.
Methods: Prospective cohort study was done in Institute of Obstetrics and Gynecology, Egmore, Madras Medical College from time period of May 2016 to November 2016. Inclusion criteria were newborns with gestational age between 38 to 41 weeks of normal pregnancies of healthy mothers aged 18 to 39 years. Incomplete/unclear data about mother's health status, diabetes, history of gestational diabetes, hypertension, pre-eclampsia, eclampsia and conditions influencing glucose metabolism were exclusion criteria. In the first phase, cutoff point of HOMA-IR (homeostatic model assessment of insulin resistance) was established in 33 AGA neonates with birth-weight >2500 g and <4000 g. In the second phase, 34 term neonates were enrolled to determine whether LGA/SGA is related with hyperinsulinemia and elevated HOMA-IR. Serum insulin and serum glucose was obtained from cord blood. Hyperinsulinemia was defined by serum insulin levels ≥12.60 µU/mL and HOMA-IR ≥2.34. Multiple logistic regression analysis and Mann Whitney test was used to find association between birth-weight with hyperinsulinemia and HOMA-IR index.
Results: A total of 67 newborns were enrolled; 24, 10, and 33 with SGA, LGA and AGA respectively. Hyperinsulinemia was more prevalent in 16 newborns particularly in SGA (p=0.01), whereas HOMA-IR was noted in 13 neonates (p=0.06). Multiple logistic regression analysis revealed LGA had a strong association with hyperinsulinemia (p=0.02) and HOMA-IR (p=0.02).
Conclusions: Study revealed term LGA is associated with hyperinsulinemia and elevated HOMA-IR at birth.

Keywords: Birth weight, Hyperinsulinemia, HOMA-IR, Insulin, Insulin resistance

INTRODUCTION

Impaired insulin secretion and insensitivity of insulin action predisposes to type 2 diabetes by complex mechanism of action.[1] Low birth weight predisposes to obesity and type 2 diabetes in adulthood due to lack of adequate growth of beta cells during intrauterine period.[2] High birth weights also predispose to high risk of obesity and type 2 diabetes later.[3] There is a U-shaped trend between birth-weight and metabolic disorders in adulthood. Genetic, nutritional and environmental factors also play a determinate role in development of metabolic disorders. Increase in cytokines and decrease serum adiponectin during pregnancy also has an impact on birth-weight.[4] For regulation of intrauterine growth insulin plays a key role. Insulin's effect on birth-weight is mediated by leptin particularly in LGA. Risk factors that modify insulin concentration during fetal life alters

normal development of endocrine system, predisposing later to insulin resistance.[5] As there is dearth of knowledge regarding correlation of birth-weight with hyperinsulinemia and insulin resistance in term newborns this prospective cohort study was carried out to find out the correlation of birth-weight with hyperinsulinemia and insulin resistance.

The objective of this study was to find the correlation between birth-weight with hyperinsulinemia and insulin resistance in term newborns.

METHODS

Prospective cohort study was done in Institute of Obstetrics and Gynecology, Egmore, Madras Medical College from time period of May 2016 to November 2016. After obtaining IRB approval and informed consent from parents the study was carried out.

Inclusion criteria were normal newborns with gestational age between 38 and 41 weeks of healthy mothers aged 18 to 39 years.

Exclusion criteria were inadequate data about mother's health, diabetes, history of gestational diabetes, hypertension, pre-eclampsia, eclampsia and risk factors influencing glucose metabolism.

Anthropometric characteristics of mother and newborn and blood samples were obtained immediately after delivery. In the first phase, cutoff point of HOMA-IR was established in 33 AGA (Appropriate for gestational age) neonates with birth-weight >2500 g and <4000 g. In the second phase, 34 term neonates were enrolled to determine if LGA (Large for gestational age)/SGA (small for gestational age) is related with hyperinsulinemia and elevated HOMA-IR in newborns. Serum insulin and glucose was obtained from cord blood. Hyperinsulinemia was defined by serum insulin levels ≥12.60 µU/mL and HOMA-IR ≥2.34. Multiple logistic regression analysis and Mann Whitney test was used to find association between birth-weight with hyperinsulinemia and insulin resistance (HOMA-IR). The HOMA-IR index (homeostatic model assessment of insulin resistance) was calculated using the formula: fasting insulin (µU/mL) × fasting glucose (mmol/L)/22.5.[6]

RESULTS

The characteristics of the mothers and newborns enrolled in the first phase of the study are shown in Table 1.

Family history of diabetes was present in 38 (56.75%)neonates; more predominant in LGA neonates. Mean parity was 1.61±1.02. Mean birth weight during pregnancy was 67.88±11.58 kg and the average weight was 82.5±11.65 kg which was more in LGA neonates. Newborns birth weight was more in LGA neonates (4.08±0.11 kg). Male (71.64%) sex predominated in the present study. The mother's weight and BMI before pregnancy was significantly lower in the mothers of AGA newborns as compared with mothers of SGA and LGA newborns (Table 1).

Table 1: Maternal and neonatal characteristics.

Characteristics	N (67)	AGA (33)	LGA (10)	SGA (24)
Family h/o diabetes	38 (56.75%)	8	18	12
Parity	1.61±1.02	1.45±0.68	2.2±1.88	1.58±0.86
Mother's age	25.07±3.88	25.67±3.89	23.9±2.62	24.75±4.25
Weight during pregnancy (kg)	67.88±11.58	63.24±9.09	82.5±11.65	66.5±6.52
Gestational age, weeks	38±1.26	38.25±1.24	38.4±0.91	36.3±2.35
New-born's birth weight, kg	2.66±0.81	2.77±0.56	4.08±0.11	1.96±0.21
Sex (males)	71.64%	33%	20%	25%

AGA: Appropriate for gestational age; SGA: Small for gestational age; LGA: Large for gestational age

Table 2: Pattern of distribution of insulin and insulin resistance in AGA, LGA and SGA neonates.

	N	SGA	LGA	AGA
Total	67	24	10	33
Hyper insulinemia	16	8	5	3
Insulin resistance	13	5	5	3

AGA: Appropriate for gestational age; SGA: Small for gestational age; LGA: Large for gestational age

A total of 67 newborns were enrolled; 24, 10, and 33 with SGA, LGA, and AGA, respectively. Hyperinsulinemia was identified in 16 neonates: 8 (50%), 5 (31.2%), and 3 (18.8%) with SGA, LGA, and AGA (p=0.01), whereas HOMA-IR was noted in 13 neonates: 5 (38.4%), 5 (38.4%), and 3 (31.2%) newborns with SGA, LGA and AGA (p=0.06) (Table 2).

90th percentile of distribution for insulin levels was 12.60µU/mL and the fourth quartile of HOMA-IR index 2.34.

Mann Whitney test showed significant statistical significance in LGA between birth weight and insulin (p - 0.003) and HOMA-IR (p- 0.000) whereas in SGA babies

no significance was noted between birth weight and insulin(p-0.225) and insulin resistance (p-0.06) (Table 3 and 4).

Table 3: Mann Whitney test between mean levels of insulin, glucose and HOMA-IR in LGA and AGA neonates.

	AGA	LGA	P value
Glucose	7.71±6.11	3.89±1.23	0.003
Insulin	3.84±4.15	8.84±3.42	
Glucose	7.71±6.11	3.89±1.23	0.000
HOMA-IR	1.41±1.75	1.53±0.74	

AGA: Appropriate for gestational age; LGA: Large for gestational age

Table 4: Mann Whitney test between mean levels of insulin, glucose and HOMA-IR in SGA and AGA neonates.

	AGA	SGA	P value
Glucose	7.71±6.11	5.73±2.46	0.225
Insulin	3.84±4.15	8.11±5.90	
Glucose	7.71±6.11	5.73±2.46	0.06
HOMA-IR	1.41±1.75	2.16±2.10	

AGA: Appropriate for gestational age; SGA: Small for gestational age

Multivariate logistic regression analysis showed LGA neonates had a strong association with hyperinsulinemia (p=0.01) and HOMA-IR (p=0.02); whereas SGA showed association with hyperinsulinemia (p=0.02) and was not associated with HOMA-IR (p=0.641) (Table 5).

Table 5: Multivariate logistic regression analysis to find out significance between birth weight, insulin and insulin resistance (HOMA-IR).

S. No	Variables	Odds ratio	95% confidence interval	P value
LGA	Hyperinsulinism	5.02	1.15-22.3	0.002
	HOMA-IR	5.6	1.17-26.72	0.002
SGA	Hyperinsulinism	5.95	1.16-21.50	0.002
	HOMA-IR	1.4	0.37-5.79	0.641

DISCUSSION

Results of this study suggest that LGA newborns have higher insulin levels and HOMA-IR than AGA and SGA newborns. Association between LGA and insulin resistance indicates late onset of maternal diabetes.[7]

A total of 67 newborns were enrolled; 24, 10, and 33 with SGA, LGA and AGA respectively. Hyperinsulinemia was identified in 16 neonates and insulin resistance in 13 neonates more in low birth weight neonates without statistical significance compared to study done by Sahasrabuddhe A et al where insulin levels were high in low birth weight and low in high birth weight babies.[8]

Mann Whitney test showed significant statistical significance in LGA between birth weight and insulin levels (p - 0.003), insulin resistance (p - 0.000) whereas in SGA babies no significance was noted between birth weight and hyperinsulisim (p - 0.225) and insulin resistance (p - 0.06) contrary to study done by Sahasrabuddhe A et al which revealed increased insulin levels in low birth weight neonates.

Multivariate logistic regression analysis showed LGA neonates had a strong association with hyperinsulinemia (p=0.01) and HOMA-IR (p=0.02); whereas SGA showed association with hyperinsulinemia (p=0.02) and was not associated with HOMA-IR (p=0.641) compared to the study done by Simental-Mendía LE et al which revealed that LGA newborns have higher insulin levels and HOMA-IR than AGA and SGA newborns.[9]

However, the increase of insulin levels, according to birth-weight class, in the study by Simental-Mendía LE et al showed the same sequence as compared with our results (AGA<SGA<LGA); reason attributed to differences in birth-weight of the LGA newborns, which were heavier compared to birth-weight of SGA newborns which were lighter in the present study.

LGA neonates at birth have impaired insulin sensitivity which increases insulin secretion by compensatory mechanism to maintain normoglycemia. Fetal insulin resistance is directly proportional to fetal adiposity suggesting birth weight plays a major role in the development of hyperinsulinemia and elevated HOMA-IR in the newborns as said by Catalano et al.[10] In the present study SGA neonates exhibited low HOMA-IR, probably due to increase in leptin levels and decreased adiponectin levels.[11]

Interestingly we were able to arrive at reference values of cord insulin levels and HOMA-IR in AGA newborns so that we were able to compare with LGA and SGA neonates and confounders were eliminated from the study.

Limitations of the present study were

- Small sample size of LGA/SGA neonates that could be a source of bias.
- Second, the cause-effect relationship cannot be established.

CONCLUSION

In conclusion, present results suggest that LGA is associated with hyperinsulinemia and elevated HOMA-IR at birth.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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