

# Maternal Serum Insulin in Hypertensive Disorders of Pregnancy and Neonatal Outcome

S. Chhabra\*, A. Tembhare and V. Agrawal

*Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha - 442 102, Maharashtra, India*

**Abstract:** *Background:* Complications of hypertensive disorders, during pregnancy (HDP), labour, postpartum have been recognized for centuries. Focus has shifted from maternal to materno-neonatal outcome, because effects of HDP on maternal metabolism have significant impact on perinatal outcome. Possibility of linkage of hyperinsulinemia leading to hypoglycaemia, growth retardation is real.

*Objective:* Study was conducted to know relation of maternal serum insulin to the severity of hypertensive disorders and its effects on neonatal outcome.

*Material methods:* Case control study was carried out over two years. Fasting blood sugar, insulin, post glucose blood sugar were estimated.

*Results:* Overall 13.32% women who delivered during study period had HDP. Of these 964 women, 609(63.17%) had mild HDP, 12 (1.97%) of them had elevated insulin, 9 (75%) of 12 had LBW, [(2 neonatal deaths, 4(33.33%) still births, 3(25%) admitted to neonatal intensive care NIC)]. Eighty three (8.6%) had severe HDP, 12(14.45%) of them had elevated serum insulin, 8 (66.33%) of 12 had LBW babies (2 NND, 2 still births, one admitted to NIC), significant ( $p<0.001$ ) difference from 71 with severe HDP with normal insulin. One hundred eight (11.2%) had mild preeclampsia, 21(19.44%) with elevated insulin, [17 (81%) of 21 had LBW babies, 4 (19.04%) NND, 3(14.28%) admitted to NIC, one (4.76%) septicemia. 9 (42.85%) still born, perinatal loss significantly higher ( $p<0.001$ ), than 87 with mild preeclampsia and normal insulin. One hundred fifteen (11.9%) women had severe PE, 52(45.21%) had elevated serum insulin, 16(30.76%) LBW babies, 13(25%) still births, 13 (25%) babies admitted to NIC, one of 13 (1.92%)died (LBW), difference (significant ( $p<0.05$ ) from 63 severe PE with normal insulin. Forty nine (5.08%) women had eclampsia, 24 (48.97%) of them had elevated insulin, of them 7 (29.16%) had LBW, 13(54.16%) still births, 13 (54.16%) admitted to NIC, one (4.16%) NND, significantly more than in 25 with normal insulin ( $p<0.02$ ). In HDP maternal insulin levels correlated significantly with perinatal outcome irrespective of severity of HDP.

*Conclusion:* While there was linkage of maternal serum insulin to the severity of HDP, the change in the insulin level affected the perinatal outcome more than the severity of HDP.

**Keywords:** Hyperinsulinemia, Neonatal outcome, Hypertension, Hypoglycaemia, Perinatal outcome.

## INTRODUCTION

Hypertensive disorders of pregnancy (HDP) and their complications during pregnancy, labour, postpartum have been recognized for centuries, but "whys" remain poorly understood [1, 2]. There is now a growing body of evidence linking HDP with insulin resistance [3-7]. A high increase in blood glucose and insulin during pregnancy with HDP could lead to abnormalities of fetal weight, preterm delivery, neonatal hypoglycemia, septicemia and neonatal death [8-12]. All the women with HDP do not have FGR and low birth weight (LBW) babies but quite a few do have [13-15]. It is possible that, insulin plays a role. Looking at the significantly higher incidence of fetal growth restriction (FGR) among women with high insulin levels [16, 17], possibility of hyperinsulinemia leading to hypoglycaemia and thus growth retarded baby seems significant.

## OBJECTIVE

Study was conducted to know the relationship of maternal serum Insulin levels on severity of hypertensive disorders of pregnancy effect on the neonatal outcome.

## MATERIAL AND METHODS

The present case control study was carried out over a period of two years. Women with singleton pregnancy with gestational age more than 20 weeks and hypertensive disorders excluding chronic hypertension, pre-pregnancy diabetes, renal disease, coagulation disorders, epilepsy or any other major medical disorder, were included in the study, after taking informed written consent. Fasting blood sugar, insulin and post glucose blood sugar were estimated and repeated weekly. These women were followed up for maternal-neonatal outcome till delivery and 7 days postpartum, if the baby was admitted in Neonatal Intensive Care Unit (NICU) till the discharge of the baby. Still births (SB), LBW, neonatal deaths (NND), admission to the NICU and the indication for the admission were analyzed.

\*Address correspondence to this author at the Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha - 442 102, Maharashtra, India;  
Tel: 07152-284342; Fax: 07152-284286;  
E-mail: chhabra\_s@rediffmail.com, schhabra@mgims.ac.in

## RESULTS

During the study period of two years, there were 7233 women delivered, 964 (13.32%) had HDP, [686 (71.2%) rural, 278 (28.8 %) urban], rural significantly more than 60% overall rural ( $p < 0.005$ ), 58 (6%) were in their teens, significantly more than 4% overall teenage cases ( $P$  value  $< 0.005$ ), however majority of the women with HDP (768 (79.6%)) were of 20-24 years and 138  $\geq$  25 yrs (13.1 %). Primigravida [777 (80.6 %)] were highly significantly more than overall 42% primigravida during the study period ( $P$  value  $< 0.005$ ). Of the 964 women, 634 (65.7 %) were term ( $\geq$  37 weeks) and 330 (34.30%) preterm ( $< 37$  weeks) at admission with HDP.

Of the total 964 study subjects, 609(63.17%) had **mild HDP**, 12 (1.97%) of them had elevated serum insulin, 9 (75%) of these 12 had LBW babies, [2 NND, (one due to septicemia, one preterm), 4(33.33%) SB and 3(25%) babies were admitted to NICU] compared to 117 (19.5%) LBW babies, 10 (1.67%) stillbirths, 6 (1%) NND and 21 (3.51%) admissions to NIC ( $p < 0.001$ ) amongst 597 cases of mild PIH with normal insulin levels. Among babies admitted to NIC, 28.57% died out of the cases with normal insulin levels compared to 66.66% NND amongst babies in NIC of the mothers with elevated insulin levels.

Of all the study subjects, 83 (8.6%) had **severe HDP**, 12(14.45%) of them had elevated serum insulin. Eight (66.33%) of these 12 had LBW babies (2 NND and 2 SB, one baby was admitted to NIC, well on discharge), significant ( $p < 0.001$ ) difference from the 71 women with severe PIH but normal insulin, 10 (14.08%) LBW babies, 5(7.04%) NICU admissions and 2 NND (2.81%). Among NICU admissions 2 NND occurred in babies of mothers with normal insulin but in the elevated serum insulin cases 2 NND occurred in the babies who didn't get admitted to NIC at birth, suggesting that maternal insulin levels affected the babies' health in the absence of other neonatal problems.

Of the total 964 cases, 108 (11.2%) women had **mild preeclampsia** (PE), 21(19.44%) of them had elevated insulin. Of these 21 babies, 17 (81%) were LBW, 4 (19.04%) NND, 3(14.28%) admitted to NIC and one (4.76%) septicemia. 9(42.85%) SB (5 preterm), significantly higher ( $p < 0.001$ ) than 8 (9.2%) LBW babies, 8(9.2%) SB, 10 (1.5%) admissions to NICU, of which 2 (2.3%) NND amongst the 87 women with mild preeclampsia and normal insulin.

One hundred fifteen (11.9%) women were of **severe PE**, 52(45.21%) of them had elevated serum insulin, 16(30.76%) of them had LBW, 13(25%) SB, 13 (25%) babies were admitted to NICU and one (1.92%) NND (LBW) occurred, significantly more ( $p < 0.05$ ) than 63 women with severe PE with normal insulin levels, 11 (17.46%) SB, 14 (22.22%) LBW babies, (all preterm) and 8 babies (12.69%) were admitted to NICU, of which 7 (11.11%) died.

Of the 964 cases with hypertensive disorders, 49(5.08%) had **eclampsia**, 24 (48.97%) of them had elevated insulin. Of them 7 (29.16%) had LBW, 13(54.16%) SB, 13 (54.16%) were admitted to NICU and one (4.16%) died. Of the 25 women of eclampsia with normal insulin, 6 (24%) had SB, 4(16%) LBW babies, 3(12%) NND occurred, 3(12%) were admitted to the NICU, later died, significant difference ( $P$  value  $< 0.02$ ).

## DISCUSSION

Relationship between hyperinsulinemia and high blood pressure affecting maternal and fetoneonatal outcome has been reported [18-21]. In pregnancy, the alterations in the metabolism of carbohydrate and insulin may be playing a role in the etiology and effects of hypertensive disorders of pregnancy. Many features of the insulin resistance syndrome have been associated with HDP, hyperinsulinemia, glucose intolerance, obesity, and lipid abnormalities [22-24]. The documentation of these features before the onset of hypertension in pregnancy suggests that insulin resistance or associated abnormalities may have a role in this disorder [25-27]. Insulin resistance is a physiologic phenomenon in normal pregnancy. In predisposed individuals this could lead to hyperinsulinemia with the development of gestational hypertension, gestational diabetes mellitus, or both. Elevated second-trimester insulin levels characterize the subsequent development of preeclampsia which supports the hypothesis that hyperinsulinemia and insulin resistance may contribute to the pathogenesis of preeclampsia [28]. Maternal mean blood-glucose and serum insulin in pregnancy correlated significantly with neonatal weight, It has been studied that maternal insulin sensitivity had stronger correlation with fetoplacental growth in comparison with maternal demographic or morphometric factors [29-31]. Whether the elevated insulin by way of causing hypoglycaemia leads to growth restriction or is it the higher insulin levels with severe disease that gives rise to higher percentage of LBW babies is not well understood.

In the present study of 609 women with mild PIH, 12(1.64%) had hyperinsulinemia. Of 83 women with severe PIH, 12(17.39%) had elevated insulin levels. Twenty one (19.4%) of 108 women with mild PE had elevated insulin. Of 115 women with severe PE, 52(45.2%) had elevated insulin and of 49 women with eclampsia, 24(48.97%) had hyperinsulinemia. As the severity of HDP increased the derangements in the insulin increased, suggesting a positive relationship between the severity of the disease and serum hyperinsulinemia. Further to this elevation of insulin women with similar severity of HDP, the perinatal outcome was poorer in cases with hyperinsulinemia. Other researchers have also reported poor perinatal outcome in the women with HDP with elevated insulin levels compared to normal insulin levels in women with HDP [32, 33].

Pregnancy is a physiological state which has significant alterations in glucose and insulin metabolism [34-36]. HDP affect maternal glucose metabolism, which further has impact on perinatal outcome [37]. Many factors play a role in the pathogenesis of FGR, including the maternal blood glucose level and serum insulin [38]. The principle modulator of this hyperinsulinemia in pregnancy is hyperoestrogenaemia.

All women with hypertensive disorders do not have hyperinsulinemia and growth restriction. In the present study details of babies were recorded in mild and severe cases in relation to hyperinsulinemia. There was clear difference in cases with hyperinsulinemia, with similar severity of HDP. It was revealed that women with elevated insulin levels have a higher percentage of LBW babies and poorer perinatal outcome compared to women with normal insulin levels in women with similar severity of disease. Other researchers have also reported more perinatal deaths among women with hyperinsulinemia and suggested that more research is needed about carbohydrate

metabolism in HDP for further understanding of the patho-physiology involved [39, 40].

In the present study of hypertensive disorders of the 609 women with mild PIH, 12 had elevated insulin levels of whom one had preterm delivery, 3 were appropriate for gestational age (AGA), 3 had SB, 9 were LBW, compared to 119 (19.5 %) FGR babies, 20 (3.3 %) perinatal deaths. Of the 12 women with severe PIH and elevated insulin levels, 3 (25%) had FGR compared to 10 (14.49%) of 69 women with severe PIH with normal insulin levels. There were 12 (17.39%) perinatal deaths in women with severe PIH with elevated insulin compared to 7 of 14 (50%) neonatal deaths in the women with severe PIH with normal insulin levels. Of the 21 women with mild preeclampsia and elevated insulin levels, 6 (28.5 %) had FGR compared to 8 (9.2%) of the 87 of mild preeclampsia with normal insulin levels and perinatal deaths were 14(16.09 %) compared **10 (11.49%) perinatal deaths among the women with HDP with normal insulin levels**. Twenty two (35.4 %) of 62 women with severe preeclampsia and elevated insulin had FGR compared to 14 (26.4%) cases of FGR amongst of the 53 with severe preeclampsia with normal insulin. Thirteen (41.9%) of the 31 women with eclampsia with elevated insulin had FGR compared to 4 (22.2%) of the 18 eclamptic women with normal insulin (P value <0.001). Researchers have also reported that alterations in glucose and insulin in pregnancy have critical impact on the birth outcome and later the growth of the offspring [41-43]. Perinatal outcome was affected by serum insulin in women with hypertensive disorders. There are not many studies from resource poor countries and more research is needed.

## CONCLUSION

Perinatal outcome was affected by serum insulin in women with hypertensive disorders. While there was linkage of maternal serum insulin to the severity of HDP, the change in the insulin level affected the

**Table 1: Severity of Hypertensive Disorders and Fasting Serum Insulin in Pregnant Women**

Insulin	MPIH	SPIH	MPE	SPE	ECL
Normal	597	71	87	63	25
Elevated	12(1.64%)	12(17.39%)	21(19.4%)	52(45.21%)	24(48.97%)
Total	609	83	108	115	49

PIH- Pregnancy Induced Hypertension, MPIH=Mild PIH, SPIH=Severe PIH, MPE= Mild preeclampsia, SPE= Severe preeclampsia, ECL= Eclampsia

**Table 2: Parity/ Gestational Age and Serum Insulin in hypertensive Women**

P	I	MPIH(609)			SPIH(83)			MPE(108)			SPE(115)			ECL(49)		
		A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
P0	I<27	17	116	404	0	9	33	2	16	36	2	23	15	0	5	6
	I>27	0	2	6	0	2	7	0	4	6	2	21	22	3	12	6
<b>Total</b>		<b>17</b>	<b>118</b>	<b>410</b>	<b>0</b>	<b>11</b>	<b>40</b>	<b>2</b>	<b>20</b>	<b>42</b>	<b>4</b>	<b>44</b>	<b>37</b>	<b>3</b>	<b>17</b>	<b>12</b>
P1+	I<27	3	19	40	1	10	17	1	13	18	4	6	3	0	4	3
	I>27	0	1	1	0	4	1	2	4	5	3	10	4	1	8	1
<b>Total</b>		<b>3</b>	<b>20</b>	<b>41</b>	<b>1</b>	<b>14</b>	<b>18</b>	<b>3</b>	<b>17</b>	<b>23</b>	<b>7</b>	<b>16</b>	<b>7</b>	<b>1</b>	<b>12</b>	<b>4</b>
<b>Grand Total</b>		<b>20</b>	<b>138</b>	<b>451</b>	<b>1</b>	<b>25</b>	<b>58</b>	<b>5</b>	<b>37</b>	<b>65</b>	<b>11</b>	<b>60</b>	<b>44</b>	<b>4</b>	<b>29</b>	<b>16</b>

P= Parity, I= Serum Insulin Level, MPIH- Mild PIH, SPIH- Severe PIH, MPE- Mild Preeclampsia, SPE- Severe Preeclampsia, ECL- Eclampsia,  $\leq 27$  ml, I  $> 27$  mlU/ml, P-parity T-Total, GT-Grand Total

A-Gestation <28 weeks, B-29-37weeks, C  $\geq 37$  weeks, I -Insulin

**Table 3: Severity of Hypertensive Disorders, Fasting Serum Insulin Levels, Neonatal Outcome**

HDP	Serum Insulin	Preterm Delivery	Septicemia	NICU	NND	LBW	SB	TOTAL
MPIH (609)	NI	00	00	21	06	117	10	597
	EI	01	01	03	02	09	03	12
	<b>Total</b>	01	01	24	07	126	13	609
SPIH (83)	NI	00	00	05	02	10	05	69
	EI	00	00	06	02	08	02	12
	<b>Total</b>	00	00	11	04	18	07	81
MPE (108)	NI	00	00	10	02	08	08	87
	EI	00	01	03	04	17	09	21
	<b>Total</b>	00	01	13	06	25	17	108
SPE (115)	NI	00	00	08	07	14	11	53
	EI	00	00	13	01	26	13	52
	<b>Total</b>	00	00	21	08	40	24	115
ECL (49)	NI	00	00	03	03	04	06	18
	EI	00	00	13	01	16	04	24
	<b>Total</b>	00	00	16	04	20	10	49
<b>TOTAL (964)</b>		<b>01</b>	<b>02</b>	<b>65</b>	<b>40</b>	<b>229</b>	<b>72</b>	<b>964</b>

HDP- Hypertensive disorders of pregnancy, SB= still birth, LBW= low birth weight, NND= Neo natal death, NICU= neonate admitted to NICU, AGA= Appropriate for gestational age, NI=Normal Insulin level, EI=Elevated Insulin, TW=Total

perinatal outcome more than the severity of HDP. There are not many studies from resource poor countries and more research is needed.

#### ACKNOWLEDGEMENT

We thank all the patients for their consent and cooperation.

#### REFERENCES

- [1] Ellen W, Seely and Care G. Solomon. Insulin Resistance and Its Potential Role in Pregnancy –Induced Hypertension. J Clin Endocrinol Metab. 2003; 88(6): 2393-8. <https://doi.org/10.1210/jc.2003-030241>
- [2] Lowe SA, Brown MA, Dekker GA, Gatt S, McLintock CK, McMahon LP, *et al.* Guidelines for the management of hypertensive disorders of pregnancy 2008. Aust NZ J Obstet Gynaecol 2009; 49(3): 242-6. <https://doi.org/10.1111/j.1479-828X.2009.01003.x>

- [3] Martinez AE, Gonzalez OM, Quinones GA, Ferrarini E. Hyperinsulinemia in glucose-tolerant women with preeclampsia. A controlled study. *Am J Hypertens* 1996; 9: 610-614. [https://doi.org/10.1016/0895-7061\(95\)00448-3](https://doi.org/10.1016/0895-7061(95)00448-3)
- [4] Grobman WA, Kazar RR, Serum insulin, insulin like growth factor-1 and insulin like growth factor binding protein -1 in women who develop preeclampsia. *Obstet Gynaecol* 2001; 97: 521-526. <https://doi.org/10.1097/00006250-200104000-00008>
- [5] Bartha JL, Romero R, Torrejon R, Comino D. Insulin, insulin like growth factor 1, insulin resistance in women with pregnancy-induced hypertension. *Am J Obstet Gynaecol* 2002; 187(3): 735-740. <https://doi.org/10.1067/mob.2002.126283>
- [6] Albuquerque I, Mhaskar A. The assessment of hyperinsulinemia in hypertensive disorders in pregnancy. *J Obstet Gynaecol Ind* 2003; 53: 342-344.
- [7] Bernard N, Girouard J, Forest JC, Giguère Y. The combination of ApoC III, hepatic lipase and hormone sensitive lipase gene polymorphisms suggests an association with susceptibility to gestational hypertension. *J Hum Genet* 2007; 52(3): 244-54. <https://doi.org/10.1007/s10038-006-0106-1>
- [8] Green D, Stephen M. Fetal maternal metabolism relationship. *J Obstet Gynaecol* 2002; 33: 11-18.
- [9] Afolabi Mark AB. Association of essential hypertension and insulin resistance. *J Obstet Gynaecol* 2007; 196: 39.
- [10] Mark AB. Association of essential hypertension and insulin resistance. *J Obstet Gynaecol* 2007; 196: 39.
- [11] C N Ekhatior and M I Ebomoyi Blood glucose and serum lipid profiles during pregnancy. *African Journal of Diabetes Medicine*. 2012; 20(1): 16-19.
- [12] Nahar L, Nahar K, Hossain MI, Yasmin H, Annur BM. Placental changes in pregnancy induced hypertension and its impacts on fetal outcome. *Mymensingh Med J* 2015; 24(1): 9-17.
- [13] Piper JM, Langer O, Xenakis EM, McFarland M, Elliott BD, Berkus MD. Perinatal outcome in growth-restricted fetuses: do hypertensive and normotensive pregnancies differ? *Obstet Gynecol* 1996; 88(2): 194-9. [https://doi.org/10.1016/0029-7844\(96\)02169-2](https://doi.org/10.1016/0029-7844(96)02169-2)
- [14] Maulik D. Fetal growth restriction: the etiology. *Clin Obstet Gynecol* 2006 Jun; 49(2): 228-35. <https://doi.org/10.1097/00003081-200606000-00006>
- [15] Beukers F, Cranendonk A, de Vries JI, Wolf H, Lafeber HN, Vriesendorp HC, et al. Catch-up growth in children born growth restricted to mothers with hypertensive disorders of pregnancy. *Arch Dis Child* 2013; 98(1): 30-5. <https://doi.org/10.1136/archdischild-2012-302510>
- [16] Zhao J, Wu LF. [Study of the causes of fetal growth restriction with unclear etiologies]. *Zhonghua Fu Chan Ke Za Zhi* 2004 May; 39(5): 329-33.
- [17] Dalfrà MG, Pacini G, Parretti E, Ragazzi E, Mello G, Lapolla A. Elevated insulin sensitivity and  $\beta$ -cell function during pregnancy in mothers of growth-restricted newborns. *Am J Physiol Endocrinol Metab*. 2011 Jul; 301(1): E25-30. Epub 2011 Apr 5. <https://doi.org/10.1152/ajpendo.00024.2011>
- [18] Ferrannini E, Natali A, Capaldo B, Lehtovirta M, Jacob S, Yki-Järvinen H. Insulin resistance, hyperinsulinemia, and blood pressure: role of age and obesity. European Group for the Study of Insulin Resistance (EGIR). *Hypertension* 1997; 30(5): 1144-9. <https://doi.org/10.1161/01.HYP.30.5.1144>
- [19] Sierra-Laguado J, García RG, Celedón J, Arenas-Mantilla M, Pradilla LP, Camacho PA, López-Jaramillo P. Determination of insulin resistance using the homeostatic model assessment (HOMA) and its relation with the risk of developing pregnancy-induced hypertension. *Am J Hypertens* 2007; 20(4): 437-42. <https://doi.org/10.1016/j.amjhyper.2006.10.009>
- [20] Kayemba-Kay's S, Peters C, Geary MP, Hill NR, Mathews DR, Hindmarsh PC. Maternal hyperinsulinism and glycaemic status in the first trimester of pregnancy are associated with the development of pregnancy-induced hypertension and gestational diabetes. *Eur J Endocrinol* 2013; 168(3): 413-8. <https://doi.org/10.1530/EJE-12-0609>
- [21] Correia-Costa L, Santos AC, Severo M, Guerra A, Schaefer F, Caldas Afonso A, Barros H, Azevedo A. Sex-Specific Mediating Role of Insulin Resistance and Inflammation in the Effect of Adiposity on Blood Pressure of Prepubertal Children. *PLoS One* 2015; 10(6): e0132097. <https://doi.org/10.1371/journal.pone.0132097>
- [22] Katsiki N, Athyros VG, Karagiannis A, Mikhailidis DP. Metabolic Syndrome and Non-Cardiac Vascular Diseases: an Update from Human Studies. *Curr Pharm Des* 2013 Dec 5.
- [23] Liu YH, Zhao TY, Hou LQ. Change and correlated factors of fasting level of the plasma endotoxin in subjects with different glucose tolerances and body mass indices. *Sichuan Da Xue Xue Bao Yi Xue Ban* 2013; 44(5): 769-73, 778.
- [24] Singla R, Goyal A, Bedi GK, Rao HK. Study of serum insulin levels in patients of euglycemic essential hypertension: A cross sectional study in North Indian population. *Diabetes Metab Syndr*. 2013; 7(4): 202-5. <https://doi.org/10.1016/j.dsx.2013.10.018>
- [25] Sowers JR, Saleh AA, Sokol RJ. Hyperinsulinemia and insulin resistance are associated with preeclampsia in African-Americans. *Am J Hypertens* 1995; 8(1): 1-4. [https://doi.org/10.1016/0895-7061\(94\)00166-9](https://doi.org/10.1016/0895-7061(94)00166-9)
- [26] Ellen W, Seely and Care G. Solomon. Insulin Resistance and Its Potential Role in Pregnancy -Induced Hypertension. *J Clin Endocrinol Metab* 2003; 88(6): 2393-8. <https://doi.org/10.1210/jc.2003-030241>
- [27] Mastrogiannis DS, Spiliopoulos M, Mulla W, Homko CJ. Insulin resistance: the possible link between gestational diabetes mellitus and hypertensive disorders of pregnancy. *Curr Diab Rep* 2009; 9(4): 296-302. <https://doi.org/10.1007/s11892-009-0046-1>
- [28] Sowers JR, Saleh AA, Sokol RJ. Hyperinsulinemia and insulin resistance are associated with preeclampsia in African-Americans. *Am J Hypertens* 1995; 8(1): 1-4. [https://doi.org/10.1016/0895-7061\(94\)00166-9](https://doi.org/10.1016/0895-7061(94)00166-9)
- [29] Catalano PM, Thomas AJ, Huston LP, Fung CM. Effects of maternal metabolism on fetal growth and body composition. *Diabetes Care* 1998; 21(2): B85-90.
- [30] Tanvig M. Offspring body size and metabolic profile. Effects of lifestyle intervention in obese pregnant women. *Dan Med J* 2014; 61(7): B4893.
- [31] Cade WT, Tinius RA, Reeds DN, Patterson BW, Cahill AG. Maternal glucose and fatty acid kinetics and infant birth weight in obese women with Type 2 Diabetes. *Diabetes* 2016, 9. pii: db151061.
- [32] Fadl HE, Gärdefors S, Hjertberg R, Nord E, Persson B, Schwarcz E et al. Randomized controlled study in pregnancy on treatment of marked hyperglycemia that is short of overt diabetes. *Acta Obstet Gynecol Scand*. 2015; 29. <https://doi.org/10.1111/aogs.12717>
- [33] Henriksson P, Löf M, Forsum E. Glucose Homeostasis Variables in Pregnancy versus Maternal and Infant Body Composition. *Nutrients* 2015; 7(7): 5615-27. <https://doi.org/10.3390/nu7075243>
- [34] Catalano PM, Tyzbit ED, Wolfe R, et al. Longitudinal changes in basal hepatic glucose production and suppression during insulin infusion in normal pregnant women. *Am J Obstet Gynecol* 1992; 167: 913-19. [https://doi.org/10.1016/S0002-9378\(12\)80011-1](https://doi.org/10.1016/S0002-9378(12)80011-1)

- [35] Connolly CC, Holste LC, Aglione LN, *et al.* Alterations in basal glucose metabolism during late pregnancy in the conscious dog. *Am J Physiol Endocrinol Metab* 2000; 279: E1166-77.
- [36] Henriksson P, Löf M, Forsum E. Glucose Homeostasis Variables in Pregnancy versus Maternal and Infant Body Composition. *Nutrients*. 2015; 7(7): 5615-27. <https://doi.org/10.3390/nu7075243>
- [37] Nahar L, Nahar K, Hossain MI, Yasmin H, Annur BM. Placental changes in pregnancy induced hypertension and its impacts on fetal outcome. *Mymensingh Med J* 2015; 24(1): 9-17.
- [38] Fadl HE, Gärdefors S, Hjertberg R, Nord E, Persson B, Schwarcz E *et al.* Randomized controlled study in pregnancy on treatment of marked hyperglycemia that is short of overt diabetes. *Acta Obstet Gynecol Scand* 2015 Jul 29. [Epub ahead of print] <https://doi.org/10.1111/aogs.12717>
- [39] Ken K Ong and David B Dunger Birth weight, infant growth and insulin resistance. *Eur Journal of Endocrinology* 2004; 151: U131-9. <https://doi.org/10.1530/eje.0.151U131>
- [40] Xiong X, Buekens P, Pridjian G, Fraser WD. Pregnancy-induced hypertension and perinatal mortality. *J Reprod Med* 2007; 52(5): 402-6.
- [41] Biendicho J, Pérez-González J, Fabre E. Intrauterine growth in gestational diabetes. *An Esp Pediatr* 1988; 29(1): 26-30.
- [42] Catalano PM, Drago NM, Amini SB. Maternal carbohydrate metabolism and its relationship to fetal growth and body composition. *Am J Obstet Gynecol* 1995; 172(5): 1464-70. [https://doi.org/10.1016/0002-9378\(95\)90479-4](https://doi.org/10.1016/0002-9378(95)90479-4)
- [43] Ong KK, Diderholm B, Salzano G, Wingate D, Hughes IA, MacDougall J *et al.* Pregnancy insulin, glucose, and BMI contribute to birth outcomes in nondiabetic mothers. *Diabetes Care* 2008; 31(11): 2193-7. <https://doi.org/10.2337/dc08-1111>

---

Received on 12-10-2016

Accepted on 24-11-2016

Published on 30-11-2016

<http://dx.doi.org/10.15379/2408-9761.2016.03.03.04>© 2016 Chhabra *et al.*; Licensee Cosmos Scholars Publishing House.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>), which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.