SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 4.
Issue: 3.
Page N. 116-124
Year: 2020

Original Article www.wjahr.com

CARBOHYDRATE TOLERANCE IN PREGNANCY WOMEN, STATUS OF SERUM IRON AND SERUM PHOSPHORUS LEVELS IN GESTATIONAL DIABETES MELLITUS CASES: A CASE CONTROL STUDY IN A DISTRICT, ANDHRA PRADESH, INDIA

***[1]Dr. D.S.R.S. Prakash and [2]M. Kiran Deedi**

[1]Department of Biotechnology, Adikavi Nannaya University, Rajamahendravaram, East Godavari 533 296, Andhra Pradesh, India.
[2]Department of Biochemistry, GSL Medical College, Rajamahendravaram, East Godavari District 533 296, Andhra Pradesh, India.

Received date: 18 March 2020 **Revised date:** 08 April 2020 **Accepted date:** 29 April 2020

***Corresponding author: Dr. D.S.R.S. Prakash**

Department of Biotechnology, Adikavi Nannaya University, Rajamahendravaram, East Godavari 533 296, Andhra Pradesh, India.

ABSTRACT

Gestational diabetes mellitus is defined as any degree of glucose intolerance with the onset of pregnancy or first recognized during pregnancy (Metzger GE, 1991). Women with gestational diabetes mellitus far exceed the number of pregnant women with pre-existing diabetes, the ratio being approximately 10 to 1.clinical recognition of gestational diabetes is important because it can be associated with increased prenatal mortality and increase birth trauma, and maternal hypertension (Magee MS et al.1993). The present study was done to know the incidence of glucose intolerance in pregnant women and to evaluate the relation with serum iron and serum phosphorous. In 50 pregnant women between 24-28 weeks of gestation oral glucose tolerance test (OGTT) with 75-g glucose without regard to recent meal status was done. In the same cases, serum iron and serum phosphorous were measured.

KEYWORDS: Carbohydrate tolerance, serum iron, serum Phosphorus, Gestational Diabetes Mellitus, Andhra Pradesh.

INTRODUCTION

The present study was undertaken to screen for gestational diabetes mellitus and to correlate the levels of serum iron and phosphorous with gestational diabetes mellitus. Finally, an attempt was made to find out the linear correlation between gestational diabetes mellitus and serum iron levels. It is worth remembering the wise statement of Norbert Frienkel that "No single period in human development provides a greater potential than pregnancy for long range pay off via relatively short range period of enlightened metabolic manipulation." Hence prevention of diabetes, "targeting Gestational Diabetes Mellitus is an important step."

The longitudinal changes in carbohydrate metabolism during gestation are integral to a successful pregnancy outcome for both mother and fetus. So, prevention of any disease particularly non communicable diseases include four steps, primary prevention, post primary prevention, secondary prevention and tertiary prevention. The steps taken after diagnosing some form of abnormal glucose tolerance like impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) is called as post primary prevention. In the prevention of diabetes, most of the published data and success have been in post primary prevention either with life style modification or with drug intervention. What is required is primary prevention; the disease should not develop at all. This may be possible as there are convincing evidences that many of the adult diseases have foetal origin. Hence, for primary prevention the focus should be on intrauterine environment as the preventive medicine starts before birth.

There are two components for the development of any disease, the genetic, and the environmental factors. Of the two, there are evidences to establish the fact that the intra uterine environment plays a vital role in the development of diabetes. Intrauterine exposure to hyperglycemia during the critical period of foetal development programs the development of pancreas relatively and affects insulin secretion function. Further maternal hyperglycemia has a direct effect on the foetal pancreas and is associated with the increased susceptibility to future diabetes in the infant. Women with a history of gestational diabetes mellitus as well as their children are at increased risk of future

diabetes, predominantly type II diabetes (Coustan DR, 1993; Mestman JH et al. 1972).

Pregnancy is a metabolic state often described as a ***"Diabetogenic state"*** due to an increased plasma concentration of glucose and insulin that occur after a meal relative to increases in plasma glucose and insulin concentrations that occur in non-pregnant individuals. Diabetes mellitus complicates about 1-2% of all pregnancies. It is associated with a high perinatal morbidity and mortality. Before the introduction of insulin, perinatal mortality due to pregnancy related diabetes mellitus is about 65%. How ever, the rate has fallen drastically with the introduction of insulin by providing good and tight glycaemic control. During pregnancy, there is a significant alteration in glucose homeostasis secondary to the complex hormonal changes and increased metabolic demands of gravid uterus, its contents, and the mother. The rise in the hormones includes oestrogen, progesterone, human placental lactogen, and cortisol that alters this metabolism is largely responsible for the altered homeostasis.

Gestational diabetes mellitus is the most common metabolic abnormality of carbohydrate metabolism of pregnancy occurring in 1-14% of the patients depending a population described and criteria used for diagnosis *(WHO, 1985).* Gestational diabetes mellitus is defined as carbohydrate intolerance of any degree with onset or first recognition during pregnancy *(Metzger BE, 1991).* Diagnosis of gestational diabetes mellitus is important to identify both infants at risk of adverse outcomes and women at risk of subsequent development of diabetes. In addition to foetal demise, gestational diabetes mellitus has been linked to the complications of large for gestational age, macrosomia, birth trauma such as increased maternal lacerations and neonatal shoulder dystocia, increased need for operative interference (Sermer M et al. 1995; Coustan DR et al. 1984) and neonatal metabolic disorders such as hypoglycaemia, hyperbilurubinemia and disordered calcium balance. The occurrence of gestational diabetes mellitus may go unrecognized throughout pregnancy unless complications arise and some of these may occur very late. Because gestational diabetes mellitus is associated with adverse effects on the pregnancy and a significant number of patients subsequently develop overt diabetes, it is important to screen for the condition.

The most common cause of anemia is iron deficiency. Iron is needed to form hemoglobin. Iron is mostly stored in the body in the hemoglobin. About 30 percent of iron is also stored as ferritin and hemosiderin in the bone marrow, spleen, and liver. Iron is obtained from foods in our diet, however, only 1 mg of iron is absorbed for every 10 to 20 mg of iron ingested. A person unable to have a balanced iron-rich diet may suffer from some degree of iron-deficiency anemia. An increased iron requirement and increased red blood cell production is required when the body is going through changes such as growth spurts in children and adolescents, or during pregnancy and lactation. Malabsorption of iron is common after some forms of gastrointestinal surgeries. Most of the iron taken in by foods is absorbed in the upper small intestine. Any abnormalities in the gastrointestinal (GI) tract could alter iron absorption and result in iron-deficiency anaemia. Loss of blood can cause a decrease of iron and result in iron-deficiency anemia. Sources of blood loss may include GI bleeding, menstrual bleeding, or injury. Transitional metals especially iron, which are particularly abundant in the placenta, are important in the production of free radicals. Antioxidants as well as avoidance of iron excess ameliorate maternal and early foetal damage. Most of the body's phosphorus is combined with calcium in the bones, but about 15% exists - as phosphate (PO4) ions - in the blood and other soft tissues and body fluids. Dietary phosphorus is efficiently absorbed, so a low phosphate level caused by dietary deficiency is unlikely in those on a normal diet unless the person has a malabsorption syndrome (inadequate absorption of nutrients in the intestinal tract). Phosphate levels are controlled by parathyroid hormone and 1, 25-dihydroxy vitamin D. The 1, 25-dihydroxy vitamin D increases absorption of calcium and phosphate in the intestines. **Parathyroid hormone-** Increases calcium and PO4 release from bone, decreases loss of calcium and increases loss of PO4 in the urine and Increases conversion of 25-hydroxy vitamin D to 1,25- dihydroxy vitamin D in the kidneys

MATERIALS AND METHODS

In the present study, Oral glucose tolerance test was done in about 50 sample of antenatal cases between 24-28 weeks of gestation who attended the antenatal clinic in G.S.L.Hospital, Rajahmundry. Along with oral glucose tolerance test serum iron, serum phosphorous and hemoglobin were estimated in the same patients. Oral glucose tolerance test is a well-standardized test, and is highly useful to diagnose diabetes mellitus. Patient was kept on fasting after 8pm previous night and a sample of blood is collected in the fasting state. Then the patient is asked to drink 75-g of glucose solution. After 2-hr post glucose samples of blood was taken.

Blood samples (2 mL) were collected under medical supervision from the subjects with an informed consent at diabetic care unit, GSL general hospital, Rajahmundry, AP, India.

RESULTS AND DISCUSSION

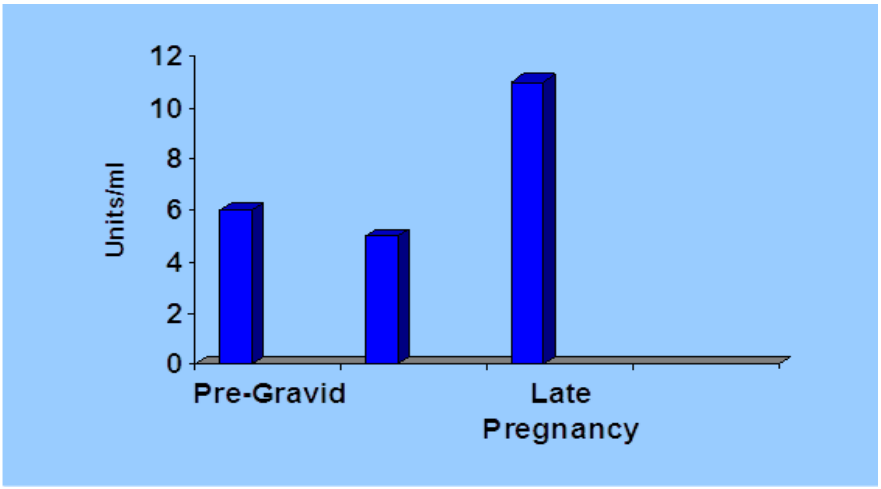

Fig. 1: Changes In Fasting Insulin Concentrations.

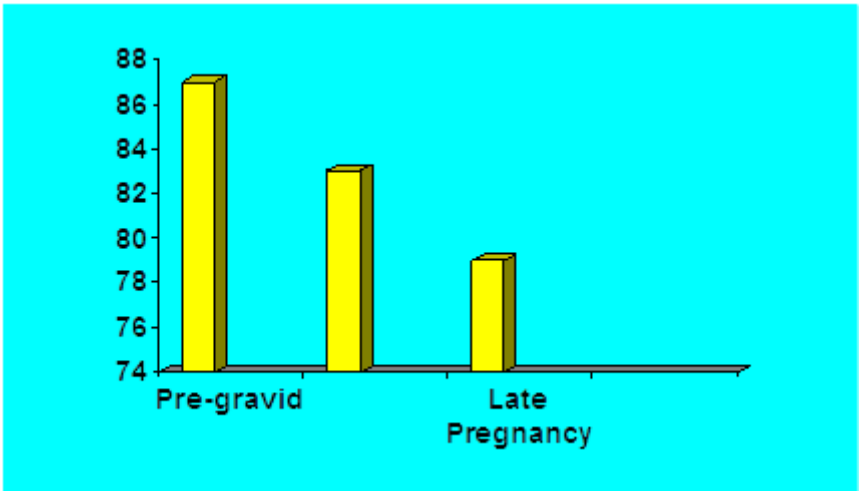

Fig. 2: Changes in Fasting Glucose Concentrations.

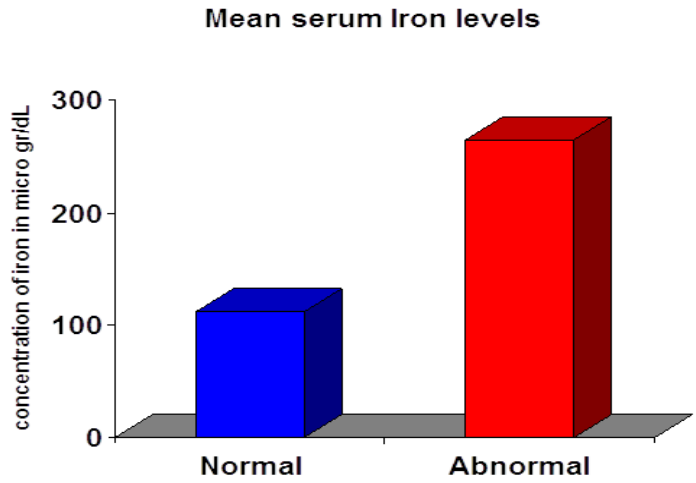

Fig. 3:

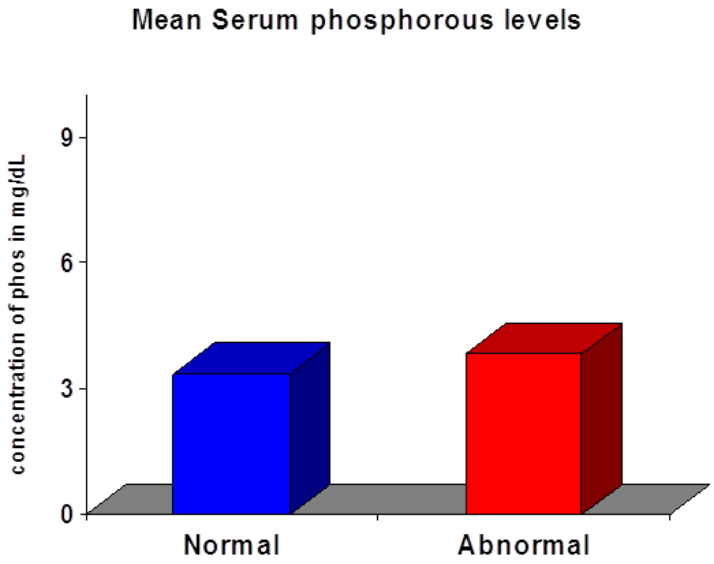

Fig. 4:

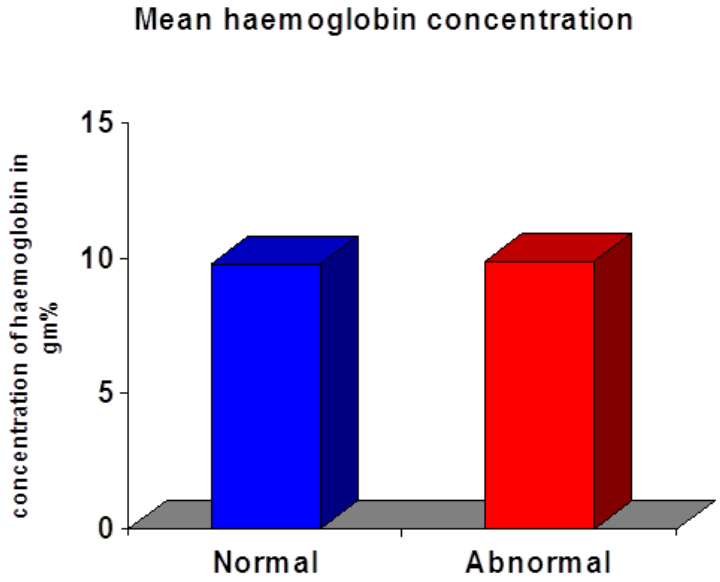

Fig. 5:

Table 1: Comparative study of cases with normal and abnormal glucose tolerance.

	Normal glucose tolerance (Mean+-S.D)	Abnormal glucose tolerance Mean+-S.D)	Significance
Fasting plasma glucose (mg/dL)	76.78 +/- 9.94	107.25 +/- 14.68	< 0.001
Post load plasma glucose (mg/dL)	102.22 +/- 24.43	147 +/- 4.76	< 0.001
Serum iron (µg/dL)	111.35 +/- 53.08	264 +/- 33.8	< 0.001
Serum phosphorous (mg/dL)	3.367 +/- 0.58	3.82 +/- 0.63	Not significant
Haemoglobin (Gm%)	9.776 +/- 1.41	9.925 +/- 1.58	Not significant

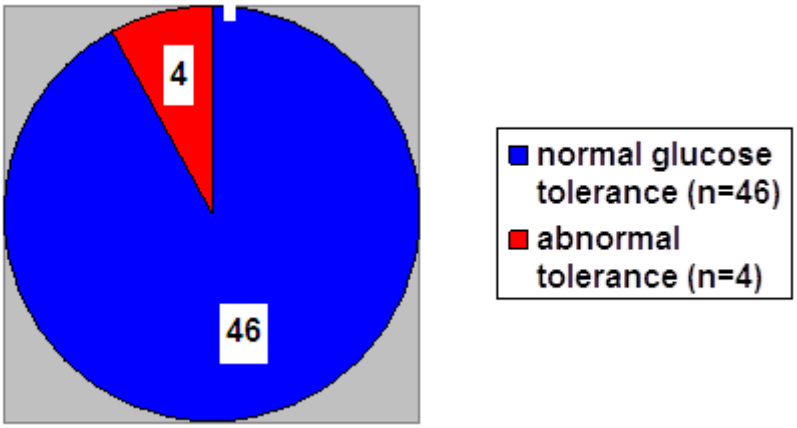

Fig. 6:

Distribution of Cases (Normal Vs abnormal glucose tolerance)

Gestational diabetes mellitus is defined as any degree of glucose intolerance with the onset of pregnancy or first recognised during pregnancy (Metzger GE, 1991). Women with gestational diabetes mellitus far exceed the number of pregnant women with pre-existing diabetes, the ratio being approximately 10 to 1. Clinical recognition of gestational diabetes is important because it can be associated with increased prenatal mortality and increase birth trauma, and maternal hypertension (Magee MS et al.1993).

The present study was done to know the incidence of glucose intolerance in pregnant women and to evaluate the relation with serum iron and serum phosphorous. In 50 pregnant women between 24-28 weeks of gestation oral glucose tolerance test (OGTT) with 75-g glucose without regard to recent meal status was done. In the same cases, serum iron and serum phosphorous were measured. The criteria for the diagnosis of gestational diabetes mellitus according to the recommendations of World Health Organization (de Veciana M, Major CA, Morgan et al. 1995).

Fasting blood sugar >99mg/dL,
Post glucose blood sugar >144 mg/dL were taken.

The prevalence of gestational diabetes mellitus was 8% which is comparable to the world wide prevalence (Joslin's Diabetes Mellitus, 2005). The frequency of gestational diabetes mellitus depends on the both the population studied and the diagnostic criteria used resulting in the range of prevalence between 1% and 14% (Joslin's Diabetes Mellitus, 2005). The prevalence of gestational diabetes tends to be higher in populations with high rate of type 2 diabetes. The prevalence in the general United States populations is about 4% (Eugelgan MM et al. 1988).

Screening of women between 24-28 weeks gestation with serum glucose levels obtained after 120 min. following 75 –g glucose load test administered at any time of the day without regard to the time since the last meal has become a well validated and widely applied screening procedure. A value of 140 mg/dL or higher identifies 80% women with gestational diabetes mellitus, and a value of 130mg/dL or higher increases the sensitivity to 90% (Coustan DR et al . 1989).

In present study, cases with abnormal glucose tolerance (gestational diabetes mellitus) have-

Mean fasting plasma glucose	107.25 ± 14.68
Mean post plasma glucose	147 ± 4.76
Mean serum iron	264 ± 33.8
Mean serum phosphorous	3.82 ± 0.63
Mean haemoglobin	9.925 ± 1.58

In cases with normal glucose tolerance have-

Mean fasting plasma glucose	76.78 ± 9.94
Mean post plasma glucose	102.22 ± 24.43
Mean serum iron	111.35 ± 53.08
Mean serum phosphorous	3.367 ± 0.58
Mean haemoglobin	9.776 ± 1.41

Both fasting plasma glucose and post load plasma glucose levels are significantly higher in cases with abnormal glucose tolerance when compared with cases of normal glucose tolerance ($p<0.001$).

Serum iron concentration is significantly higher in cases with abnormal glucose tolerance when compared with cases of normal glucose tolerance. It is well established that people with haemochromatosis, a genetic condition that causes extremely high levels of iron in the body are at increased risk for developing diabetes. But a new study suggests even a moderately elevated iron levels may be associated with diabetes (Am J of Clin nutr, 2004). Recently, a prospective study in New Jersey, showed pregnant women who developed gestational diabetes mellitus had higher concentrations of serum ferritin than women who did not develop gestational diabetes mellitus (Diabetes Care, 2006). In another prospective study done in University of Hong Kong to determine whether non-anaemic women with gestational

diabetes mellitus have evidence of increased iron stores. The concentrations of serum ferritin, iron, transferrin saturation and postnatal haemoglobin were significantly higher in gestational diabetes mellitus patients, but there was no difference in the weight, BMI, third trimester haemoglobin and they concluded that there was an association between increased iron stores and glucose intolerance at the third trimester in non-anaemic women. The role of iron excess in the pathogenesis of gestational diabetes mellitus needs to be examined (Diabetic Medicine, 2001).

In our present study, the haemoglobin concentration was also estimated but no significance was noted in the concentration of haemoglobin when compared with normal and abnormal glucose tolerance cases. However, recently a case control study in Chinese women was done to examine the relationship between high haemoglobin concentration and occurrence of gestational diabetes mellitus. Women with BMI >26 kg/m2 has shown that who developed WHO category of impaired glucose tolerance, with the 2-hr glucose values of the 75-g OGTT between 144 mg to 196 mg/dL (WHO, 1980) during pregnancy has significantly increased haemoglobin concentration compared with BMI matched controls (Lao TT, Ho LF, 2000). There is no significant change in Serum phosphorous and haemoglobin concentrations in both the groups.

CONCLUSION

In the modern era, the prevalence of Gestational Diabetes Mellitus is increasing due to various factors like nutrition, modified life-style, delayed conception, increasing incidence of diabetes mellitus and etc. Screening of gestational diabetes mellitus is essential to reduce the prenatal mortality and morbidity and maternal morbidity.

In the present study, the prevalence of Gestational Diabetes Mellitus is 8% in cases attending the antenatal clinic in G.S.L.General Hospital. Both fasting and post load plasma glucose levels are significantly high in cases of Gestational Diabetes Mellitus. Serum iron is significantly high in cases of Gestational Diabetes Mellitus. However, the studies to link excess serum iron to gestational diabetes mellitus are under trial. Our study showed elevated serum iron correlates with development of Gestational Diabetes Mellitus. Serum phosphorous and haemoglobin concentrations have not shown significant variation.

ACKNOWLEDGEMENTS

Authors express their sincere gratitude for giving support to publish this paper to Prof. M. Jagannadha Rao, Vice Chancellor, Adikavi Nannaya University, Rajamahendravaram, East Godavari District, Andhra Pradesh, India.

BIBLIOGRAPHY

1. ADA Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, Report of the Expert Committee on the Diagnosis and the Classification of Diabetes Mellitus, Clinical practice Recommendations 2000. Diabetes Care, 2000; (Suppl1): S4-S19.
2. American College Of Obstetricians and Gynecologists: Diabetes and Pregnancy. Technical Bulletin NO.200, December, 1994.
3. Am. J Clin nutr, 2004.
4. Barden TP, Knowles HC. Diagnosis of diabetes in pregnancy. Clin Obstet Gynecol, 1981; 24: 3-19.
5. Battaglia FC, Meschia G. Principal substrates of foetal metabolism, Physiol Rev., 1978; 24: 3-19.
6. Bergman RN, Beard JC, Chen M. The minimal model method: Assessment of insulin sensitivity and ß cell function in vivo. In:Clark WL, Larner J, Pohl SL. Methods in Diabetes Research. Vol 2. Clinical Methods. Newyork: John Wiley & Sons, 1986; 15-34.
7. Bergmayer H.V, "Methods of Enzymatic Analysis", A.P.,N.Y., 1974; 1196.
8. British Diabetic Association, 1988.
9. Buchanan TA, Xiang A, Kjos SL et al. Gestational diabetes:antepartum characteristics that postpartum glucose intolerance and type 2 diabetes in Latino women. Diabetes, 1998; 47: 1302-10.
10. Buchanan TA, Xiang Ah, Peters RK et al. Response of pancreatic beta cells to improved insulin sensitivity in women at high risk for type 2 diabetes. Diabetes, 2000; 49: 782-88.
11. Calles-Escadon J, Robbins DC. Loss of early phase of insulin release in humans impairs glucose tolerance and blunts thermic effect of glucose. Diabetes, 1987; 36: 1167-1172.
12. Carpenter MW, Coustan DR: Criteria for screening tests for gestational diabetes.Am J Obstet Gynecol, 1982; 144: 768-773.
13. Carraga MT, Skikne BS, Finley B, Cook JD: Serum transferrin receptor for the detection of iron deficiency in pregnancy. Am J Clin Nutr, 1991; 54: 1077.
14. Catalano PM, Tyzbir ED, Roman NM, Amini SB, Sims EAH. Longitudinal changes in insulin release and insulin resistance in nonobese pregnant women. Am J Obstet Gynecol, 1991; 165: 1667-1672.
15. Catalano PM, Calles J, Roman NM, Tyzbir ED, Amini SB, Wolfe RR, Sims EAH. Longitudinal changes in body composition, energy expenditure and route of glucose disposal in pregnant control subjects and women with gestational diabetes. Presented at the 40th annual meeting of the Society for Gynaecologic Investigation: March 31-April 3, Toronto, Canada, 1993; S114.
16. Catalano PM, Tyzbir ED, Wolfe RR, Roman NM, Amini SB, Sims EAH. Longitudinal changes in basal hepatic glucose production and suppression during insulin infusion in normal pregnant women. Am J Obstet Gynecol, 1992; 167: 913-919.

17. Catalano PM, Tyzbir ED, Wolfe RR et al. Carbohydrate metabolism during pregnancy in control subjects and women with gestational diabetes. Am J Physiol, 1993; 264: E60-E67.
18. Catalano PM, Huston L, Amini SB, Kalhan SC. Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. Am J Obstet Gynecol, 1999; 180: 903-16.
19. Chan SP, Gelding SV, McManus RJ et al. Abnormalities of intermediate metabolism following gestational diabetic pregnancy.Clin Endocrinol, 1992; 36: 417-20.
20. Coburn JW and Salusky IB, "Control of Serum Phosphorus in Uremia," N Engl J Med, 1989; 320(17): 1140-2. (editorial).
21. Cousins L, Rigg L, Hollingsworth D et al. The 24-hour excursion and diurnal rhythm of glucose, insulin, and C-peptide in normal pregnancy. Am J Obstet Gynecol, 1980; 136: 483-88.
22. Cousins L. Insulin sensitivity in pregnancy. Diabetes, 1991; 40(Suppl.2): 39-43.
23. Coustan DR, Imrah J. Prophylactic insulin treatment of gestational diabetes reduces the incidence of macrosomia, operative delivery, and birth trauma. Am J Obstet Gynecol, 1984; 150: 836-842.
24. Coustan DR, Felig P. Diabetes Mellitus. In:Burrow GN, Ferris TF,eds. Medical complications during pregnancy. Philadelphia:WB Saunders, 1988; 44.
25. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: A method for quantifying insulin secretion and resistance. Am J Physiol, 1979; 237: E214-E223.
26. DeFronzo RA and Lang R, "Hypophosphatemia and Glucose Intolerance: Evidence for Tissue Insensitivity to Insulin," N Engl J Med, 1980; 303(22): 1259-63.
27. DeFronzo RA. Lilly Lecture, 1987. the triumvirate: ß cell, muscle, liver: A collusion responsible for NIDDM. Diabetes, 1988; 37: 667-687.
28. Delmez JA, Fallon MD, Harter HR, et al, "Does Strict Phosphorus Control Precipitate Renal Osteomalacia?" J Clin Endocrinol Metab, 1986; 62(4): 747-52 (review).
29. de Veciana M, Major CA, Morgan MA et al. Post prandial verses preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy, N Engl Med, 1995; 333: 1237-41.
30. Diabetes Care, 2006; 29: 1077-1082.
31. Diabetic Medicine, 2001; 18: 218-223.
32. Dineen S, Gerich J, Rizza R. Carbohydrate metabolism in non-insulin dependent diabetes mellitus. N Engl J Med., 1992; 327: 707-713.
33. Dornhost A, Bailey PC, Anyaoku et al. Abnormalities of glucose tolerance following gestational diabetes. Q J Med, 1990; 284: 1219-28.
34. Dornhost A, Edwards SMG, Nicholls JSD et al. A defect in in sulin release in women at risk of future non-insulin dependent diabetes. Clin Sci., 1991; 81: 195-99.
35. Exton J. Park C. Interaction of insulin and glucagons in the control of liver metabolism. In:Steiner D, Freinkel N. eds. Handbook of Physiology , Section 7, Endocrine Pancreas. Baltimore: William & Wilkins, 1972; 437-455.
36. Fisher J, Magid N, Kallman C, et al, "Respiratory Illness and Hypophosphatemia," Chest, 1983; 83(3): 504-8.
37. Freinkel N. Banting Lecture. Of pregnancy and progeny. Diabetes, 1980; 29: 1023-35.
38. Gabbe SG, Mestman JH, Freeman RK, Anderson GV, Lowehsohn RI. Management and outcome of class A diabetes mellitus. Am J Obstet Gynecol, 1977: 127: 465-469.
39. Hakim RM and Lazarus JM, "Biochemical Parameters in Chronic Renal Failure," Am J Kidney Dis, 1988, 11(3): 238-47.
40. Halevy J and Bulvik S, "Severe Hypophosphatemia in Hospitalized Patients," Arch Intern Med, 1988; 148(1): 153-5.
41. Handwerger S. Clinical counterpoint:the physiology of placental lactogen in human pregnancy. Endocr Rev, 1991; 12: 329-36.
42. Insogna KL, Bordley DR, Caro JF, et al, "Osteomalacia and Weakness From Excessive Antacid Ingestion," JAMA, 1980; 244(27): 2544-6.
43. Jacobs ML, Verhoog S, van de Linden WH et al. Glucagon stimulation test:assessment of ß-cell function in gestational diabetes. Eur J Obstet Gynecol Reprod Biol, 1994; 56: 27-30.
44. Johnstone FD, Nasrat AA, Prescott RJ: The effect of established and gestational diabetes on pregnancy outcome. Br J Obstet Gynecol, 1990; 97: 1009.
45. Kalkhoff RH, Kissebah AH, Kim HJ. Carbohydrate and lipid metabolism during normal pregnancy: Relationship to gestational hormone action. In: Merkatz IR, Adam PA eds. The Diabetic Pregnancy: A perinatal Prospective . Newyork: Grune and Stration, 1979; 3-21.
46. Kautzky-Willer A, Prager R, Waldhaust W et al. Pronounced insulin resistance and inadequate ß-cell secretion characterizes lean gestational diabetes during and after pregnancy. Diabetes Care, 1997; 20: 1717-23.
47. Klebanoff MA, Shiono PH, Selby JV, Trachtenberg AI, Graubard BI: Anaemia and spontaneous preterm birth. Am J Obstet Gynecol, 1991; 164: 59.
48. Knochel JP, "The Pathophysiology and Clinical Characteristics of Severe Hypophosphatemia," Arch Intern Med, 1977; 137(2): 203-20.
49. Lao TT, Ho LF. Impaired glucose tolerance and pregnancy outcome in Chinese women with high body mass index. Hum Reprod, 2000; 15: 1826-9.
50. Lichtman MA, Miller DR, Cohen J, et al, "Reduced Red Cell Glycolysis, 2,3-Diphosphoglycerate and Adenosine Triphosphate Concentration, and Increased Hemoglobin-Oxygen Affinity Caused by

Hypophosphatemia," Ann Intern Med, 1971; 74(4): 562-8.
51. Lind T. Metabolic changes in pregnancy relevant to diabetes mellitus. Postgrad Med J, 1979; 55: 353-57.
52. Lind T, Billewicz WZ, Brown G. A serial study of changes occurring in the oral glucose tolerance test during pregnancy. J Obstet Gynecol Br Commonw, 1973; 80: 1033-39.
53. Lucas MJ, Lowe TW, Bowe L, Melntire DD: Class A1 gestational diabetes: A meaningful diagnosis? Obstet Gynecol, 1993; 82: 260.
54. Magee MS, Walden CE, Benedetti TJ. Influence of diagnostic criteria on the incidence of gestational diabetes and perinatal morbidity. JAMA, 1993; 269: 609.
55. . Martin JW, Friesen HG. Effect of human placental lactogen on the isolated islets Langerhans. Endocrinology, 1969; 84: 619-22.
56. Mayne PD and Kovar IZ, "Calcium and Phosphorus Metabolism in the Premature Infant," Ann Clin Biochem, 1991; 28(Pt 2): 131-42.
57. Mestman JH, Anderson GV, Guadalupe V. Follow-up study of 360 subjects with abnormal carbohydrate metabolism during pregnancy. Obstet Gynecol, 1972; 39: 421-425.
58. Metzger BE, Coustan DR. Summary and recommendations of the fourth International workshop-conference on gestational diabetes mellitus. Diabetes Care, 1998; 21(suppl2): B161-B167.
59. Metzger BE, Freinkel N. Accelerated starvation in pregnancy:implications for dietary treatment of obesity and gestational diabetes mellitus. Biol Neonate, 1987; 51: 78-85.
60. Metzger BE, Phelps RL, Frienkel N, Navakas IA. Effects of gestational diabetes on diurnal profiles of plasma glucose, lipids and individual amino acids. Diabetes Care, 1980; 3: 402-09.
61. Mills JL, Jovanovic L, Knopp R et al. Physiological reduction in fasting plasma glucose concentration in the first trimester of normal pregnancy. Diabetes in early pregnancy study. Metab Clin Exp, 1998; 47: 1140-44.
62. Murphy JF, O'Riordan J, Newcombe RG, Coles EC, Pearson JF: Relation of haemoglobin levels in first and second trimester to outcome of pregnancy. Lancet 1992, 1986.
63. Nicholls JS, Ali DK, Gray IP et al. Increased maternal fasting proinsulin as a predictor of insulin requirement in women with gestational diabetes. Diabetes Med, 1994; 11: 57-61.
64. O'Sullivan JB, Mahan CM: Criteria for the oral glucose tolerance test in pregnancy. Diabetes, 1964; 13: 278.
65. Pacini G.Bergman RN. MINMOD: A computer programme to calculate insulin sensitivity and pancreatic responsitivity from the frequently sampled intravenous glucose tolerance test. Computer methods Programs Biomed, 1986; 23: 113-122.
66. Pritchard JA: Hereditary hypo chromic microcytic anaemia in obstetrics and gynecology. Am J Obstet Gynecol, 1962; 83: 1193.
67. Pritchard JA, Scott DE: Iron demands in pregnancy. In Hallberg L, Harwerth HG, Vanotti A (eds): Iron Deficiency Pathogenesis, Clinical Aspects, Therapy. Newyork, Academic Press, 1970.
68. Reece EA, Hobbins JC: Diabetic embryopathy:Pathogenesis, prenatal diagnosis, and prevention. Obstet Gynecol Surv, 1986; 41: 325.
69. Ryan EA, Enns L. Role of gestational hormones in the induction of insulin resistance. J Clin Endocrinol Metab, 1998; 67: 341-47.
70. Sakamaki H, Yamasaki H, Matsumoto K et al. No deterioration in insulin sensitivity, but impairment of both pancreatic beta cell function and glucose sensitivity, in Japanese women with former gestational diabetes mellitus. Diabet Med, 1998; 15: 1039-44.
71. Scott DE, Pritchard JA: Iron deficiency in healthy young college women. JAMA, 1967; 199: 147.
72. Sebastian A, Hernandez RE, Portale AA, et al, "Dietary Potassium Influences Kidney Maintenance of Serum Phosphorus Concentration," Kidney Int, 1990; 37(5): 1341-9.
73. Silverstone FA, Solomons E, Rubricius J. The rapid intravenous glucose tolerance test in pregnancy. J Clin Invest., 1961; 40: 2180-2189.
74. Sivan E, Chen X, Homko CJ, Reece EA, Boden G. Longitudinal study of carbohydrate metabolism in healthy obese pregnant women. Diabetes care, 1997; 20: 1470-75.
75. Sivan E, Homko CJ, Chen X, Reece EA, Boden G. Free fatty acids and insulin resistance during pregnancy. J Clin Endocrinol Metab, 1998; 83: 2338-42.
76. Sluiter WJ, Erkelens DW, Terpstra P, Reistma WD, Dooreenbos H. Glucose tolerance and insulin release, A mathematical approach: Approximation of the peripheral insulin resistance after oral glucose loading. Diabetes., 1976: 25: 245-249.
77. Spellacy WN, Goetz FC, Greenberg BZ, Ells J. Plasma insulin in normal "early" pregnancy. Obstet GYnecol, 1965; 25: 862-865.
78. Summary and Recommendations of the Second International Workshop Conference on Gestational Diabetes Mellitus, 1985; 34(suppl 2): 123-126.
79. Trinder P. Annals. Clin. Biochem, 1969; 6: 24.
80. Van Assche FA, Aerts L, De Prins F. A morphological study of the endocrine pancreas in human pregnancy. Br J Obstet Gynecol, 1978; 85: 818-20.
81. Weiss PAM, Haeusler M, Kainer F, Purstner P, Hass J: Toward universal criteria for gestational diabetes:Relationships between seventy-five and one hundred gram glucose loads and between capillary and venous concentrations. Am J Obstet Gynecol, 1998; 178: 830.

82. Wolfe RR. Tracers in metabolic research: Radioisotope and stable isotope /mass spectrometry methods. Newyork: Alan R.Liss, 1984; 113-130.
83. World Health Organization: Diabetes Mellitus: Report of a WHO study Group, Geneva: WHO. Technical Report Series No.727., 1985.
84. World Health Organization Expert Committee on Diabetes Mellitus. Diabetes Mellitus: report of a WHO study group. Geneva: WHO, 1985.
85. Young D.S et al.Clinical Chemistry, 1975.