

**OBSTETRİCS OUTCOMES AND POSTPARTUM ASSESSMENT OF PATIENTS
WITH RESULTS OF BETWEEN 130-140 mg/dl VALUES in 50-gr OGTT
PERFORMED DURING PREGNANCY***

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Abstract

Objectives: Gestational diabetes mellitus screening tests which is 50-gr OGTT generally recommended in 24th-28th weeks of pregnancy. There are two limited value in results, one of this is 130 mg/dl and the second one is 140 mg/dl. We aimed to compare two grup; first is control group is less than 130mg/dl and the second grup is 130-140md/dl.

Material and Methods: In the study; there are 2 groups which emerge 92 patients according to 50-gr OGTT values in the 24th -28th weeks of pregnancy. The first group contains 46 patients whose OGTT values' are under than 130 mg/dl and the second group contains 46 patients whose OGTT values are between 130mg/dl and 140 mg/dl. 75-gr OGTT is tested to patients whose pregnancy are in the end of the 6 weeks.

Conclusions: There is no international optimal agreement on diagnosis at the moment for GDM and treatments are challenging. All patients must be protected against hyperglycemia even though their screening test results do not exceed threshold levels. Nowadays the complication rates are very low due to early diagnosis and close chasing. These patients should be followed up after pregnancy for the development of Diabetes Mellitus Type 2.

Key words: Gestational diabetes, pregnancy, oral glucose tolerance test

1. INTRODUCTION

Gestational diabetes mellitus (GDM), the most common metabolic disorder of pregnancy, is defined as “the type of glucose intolerance that develops in the second and third trimester of pregnancy, resulting in hyperglycemia of variable severity” (1) True incidence is not known and its prevalence varies with society and diagnosis criteria.(2). The latter rate varies between 1% and 14% in different societies.(3.4). Recent studies suggest that GDM prevalence is on the

rise; the reason of which may be increased prevalence of obesity as well as lower threshold values in diagnosis and tests. The patients in this group were diagnosed postpartum with Type 2 diabetes (2-14%) or impaired glucose tolerance or fasting glucose (3-35%).(5) Various studies indicated that 10 to 50% of this patient group would develop Type 2 Diabetes in 5 years.(6) The clinical and public health relevance of gestational diabetes mellitus (GDM) is widely debated due to its increasing incidence, the resulting negative economic impact, and the potential for severe GDM-related pregnancy complications. Also GDM not only increases the risk for maternal and fetal complications during pregnancy, but it also raises the risk of long term complications in both mother and offspring.(7)

Gestational Diabetes Screening: There is an ongoing debate as regards whether diabetes screening is necessary during pregnancy, which patient groups should be screened, and which screening method should be utilized.(8)

The International Association of Diabetes and Pregnancy Study Group (IADPSG) convened a workshop conference to recommend new diagnostic criteria based on the data emanating from the HAPO study, for the various adverse outcomes was used to define the blood glucose thresholds for the diagnosis of GDM. This association recommended a one-step approach, a universal 75g two hour OGTT between 24 and 28 weeks of gestation, and if any single threshold value on the OGTT was met or exceeded (fasting value, 5.1mmol/L [92mg/dL]; one-hour value, 10.0mmol/L [180mg/dL]; two-hour value, 8.5mmol/L [153mg/dL], GDM is diagnosed. Many institutions, including the WHO and FIGO, have endorsed these criteria. Initially, the American Diabetes Association (ADA) also adopted these guidelines but subsequently reversed its stance and accepted both the one-step approach as advocated by IADPSG and also the two-step approach as supported by many institutions including the American College of Obstetricians and Gynecologists (ACOG)

ACOG endorses their commendations of the National Institute of Child Health and Human Development Consensus Development Conference, which include a two-step method with the 50g glucose challenge test for screening, and a diagnosis of GDM with a 100g OGTT if the screening test is positive.(9)

The 50-g glucose challenge test is a glucose loading test. Women drink containing 50 g of glucose. After 1 hour the venous glucose level is measured. A 75- or 100-g diagnostic oral glucose tolerance test (OGTT) is performed when the blood glucose value is elevated after a

50-g glucose challenge test (the threshold value is often set as 7.2 or 7.8 mmol/l). The OGTT is a glucose loading test in which women ingest a drink containing 75 or 100 g of glucose. The test is performed after overnight fasting. Venous glucose levels are measured both before and at 1 and 2 hours after the ingestion of a glucose load. GDM is diagnosed if blood glucose values after an OGTT are elevated. A number of studies have evaluated the accuracy of the 50-g glucose challenge test as a screening test for GDM, reporting diverse results.(10)

Threshold values of screening and diagnostic tests are not clearly determined. Some studies using the 50 g screening test have taken 130 mg/dl (11,12,13), some studies have taken 135 mg/dl (14,15,16) and some studies have taken 140 mg/dl as the threshold value.(17,18, 19,20,21) And he performed a diagnostic test on the patients who were above the defined limit. There are still some controversial parts in GDM screening. Single-stage scan or two-stage scan? Between which weeks should it be done? Should it be done to all patients?? Which associations are more cost-effective to accept cut-off values?

Despite all these questions, morbidity in pregnancy increases with increasing sugar values during pregnancy. We also evaluated both the obstetric results and postpartum evaluation of the patients who were between the 2 cut-off values (130 mg/dl and 140 mg/dl), which are frequently used in our study. According to some associations, we found that as the blood sugar level increased in patients with normal values, there were significant differences compared to the group with low glucose levels.

2. MATERIAL and METHODS

This was a retrospective study and was approved by the ethics committee of Göztepe Research and Training Hospital and written informed consent form was obtained from each participant. The Ethics committee number is: 17/j and the acceptance date was: 29.11.2011

Protocols: Patients presented to Medeniyet University Göztepe Training and Research Hospital between January 2011 and August 2012 were enrolled in the study. 92 patients according to 50-gr OGTT values in the 24th -28th weeks of pregnancy. There are 2 groups which The first group contains 46 patients whose OGTT values are under than 130 mg/dl. The second group contains 46 patients whose OGTT values are between 130mg/dl and 140 mg/dl. And all for all patient . 75-gr OGTT is tested postpartum 6 weeks. Patient's name, surname, age, height, weight, BMI

(Body Mass Index was calculated as per following formula: $\text{Body Weight (kg)}/\text{Height (m}^2\text{)} = \text{kg/m}^2$), gravida, parity, macrosomia history, abortus, number of living children, previous pregnancy, family diabetes mellitus history, medications in use, birth weeks, birth types, and birth weights of babies were inquired and recorded. Previous birth weight of above 4.000 g was considered positive for macrosomia history.

Definition: Pregnant women presenting to our clinic receive a routine 50-g glucose screening test as antenatal screening test between week 24 and 28. The patient population was divided into two groups as per test results. Patients with 50-g OGTT value of lower than 130 mg/dl comprised the first group, where those with a test result of 130-140 mg/dl were included in the second group. 75-g OGTT was performed in patients, who have completed postpartum 6th week.

Statistical Analysis: The results of all patients were recorded separately in two groups and compared. Statistical Package for Social Sciences (SPSS) 13.0 (Chicago, IL, USA) software was used in statistical analyses performed in computer environment. All values were stated in the form of mean \pm SD. Statistical significance was considered within 95% confidence and $p < 0.05$. Cases with p values lower than < 0.05 were considered significant.

3. RESULTS

The average age of our patients were similar. There was no significant difference with regard to BMI. Both groups enrolled in the study had similar demographic features upon comparison. There was no significant difference between the two groups.

Table 1. Demographic features of all patients enrolled in the study

	All Patients	Group 1 (n: 46) (≤130mg/dl)	Group 2 (n:46) (130-140 mg/dl)
Patient's Age	29.4+/-5.5 years	29.8+/-5.8 years	29.0+/- 5.2 years
BMI	24.75+/-3.97 kg/m ²	23.67+/-3.19 kg/m ²	25.82+/-4.39 kg/m ²
Gravida	2.26+/-1.24	2.17+/-1.49	2.34+/-1.33
Parity	1.83+/-0.86	1.73+/-0.8	1.93+/-0.92
Abortus	1.61(19.56%)	1.77 (19.56%)	1.12 (19.56%)
Average 50-g OGTT	115.86+/- 22.71mg/dl	96.54 + 16,48 mg/dl	135.19+/-2.80 mg/dl
Macrosomic birth history	14.3	%8.69	%19.56

Of all patients, 21.78% had family diabetes history, with 28.26% in the first group and 41% in the second group. There was significant difference between the two groups. The second group had more prevalent family diabetes history. A comparison between the two groups suggested that there were significant differences as regards macrosomic birth history and family (1st degree relatives) diabetes history. The group with higher OGTT values (Group 2) had higher incidence of macrosomic birth and family diabetes history. There was no statistical difference (p>0.05) as regards the birth weeks of the patients

Table 2. Comparison between the group with OGTT values below 130 mg/dl and with that of 130-140 mg/dl with regard to macrosomic birth, gestational diabetes history, and family diabetes history

	Below 130 mg/dl(n)	130-140 mg/dl	P<0.05 Significance
Macrosomic Birth	%8.69	%19.56	P<0.05 Significant
GDM History	No GDM	Only one patient with GDM	Significance not examined
Family DM History	%28.26	%41	P<0.05 Significant

A comparison between the two groups suggested that there were significant differences as regards macrosomic birth history and family (1st degree relatives) diabetes history. The group with higher OGTT values (Group 2) had higher incidence of macrosomic birth and family diabetes history. There was no statistical difference ($p>0.05$) as regards the birth weeks of the patients.

Considering the birth types, of all patients, It was found that rate of birth with cesarean section was significantly higher in the group 2. (67% - 73.92%) The average birth weight in were statistically compared between the two groups, and there found a significant difference. The average birth weight in the group 2 was significantly higher.

75-g OGTT administration following postpartum 6th week. Only one patient (2.3%), who received 75-g OGTT, was diagnosed with overt diabetes. The patient was provided with recommendations and referred to diabetes polyclinics. 50-g OGTT value of the patient at 24th week of pregnancy, who was diagnosed with diabetes, had been 139 mg/dl with a family diabetes history. There was no statistically significant difference between the two groups as regards blood glucose level. Nevertheless there found significant difference in 1-hour and 2-hour glucose values ($p<0.05$). The group, Gestational Diabetes Screening test results of which were 130-140 mg/dl, had significantly higher results compared to the other group.

4. DISCUSSION

Women with pregestational diabetes mellitus should go under strict metabolic control before conception or during the first antenatal examination. This is a widely accepted approach to prevent from complications associated with pregnancy.(22) The most widely adopted screening and the frequently applied approach in Turkey is the two-step approach. This approach provides that each pregnant presenting between weeks 24-28 of pregnancy should have 50-gr OGTT and that pregnant women considered to have positive results should go under 100-gr OGTT upon preparation of suitable conditions.(22, 23) Almost everywhere in the world, pregnant women with high 50-g OGTT values but normal 100-g OGTT values are considered to have normal glucose tolerance and are excluded from monitored for gestational diabetes. Only a few studies described those cases as “borderline glucose intolerance,” or “mild gestational diabetes.”(24,25). There are no adequate number of studies suggesting how those groups should be monitored and how the perinatal results would be.

We have compared the patient group, which had 50-g OGTT screening test results below 130 mg/dl, with the patient group, which had 130-140 mg/dl therefrom, during the 24th and 28th weeks of pregnancy. Our aim was to find how the increased glucose levels affected pregnancy, pregnancy results, and postpartum 75-g OGTT values in patients not diagnosed with gestational diabetes. And we found that accordance with the literature, there are significant differences in the form of macrosomia and related delivery, in line with the literature.

Schmidt *et al.* suggested that GDM increased macrosomia risk by 50-70%. It was seen based on WHO criteria that 4% macrosomia developed only when such actors associated with GDM as mother’s age, height, pre-pregnancy BMI, ethnic traits, weight gain etc. were removed..(27) We found in our study found consistent with literature that increased hyperglycemia in patients’ OGTT values was associated with increase in macrosomic birth history. There was no elevated blood pressure in any of the cases involved in the study.

The groups were compared as regards family DM history and previous birth weight of above 4,000 g. It was seen that those risks were more prevalent in the group with 50-g OGTT results of >130 mg/dl compared to the other, and that the difference was statistically significant ($p < 0.05$). These patients had significantly higher results in 75-g OGTT, 1-hour, and 2-hour values. Literature suggests that GDM prevalence and abnormal glucose intolerance are higher in cases with family DM history, GDM history, and macrosomic baby anamnesis (28, 29, 30, 31).

Some studies examined the GDM prediction sensitivity of 50-g glucose screening test at different threshold levels in their study as conducted in 2005, in Turkey. Uludağ S. *et al* found that GDM prediction sensitivity as per threshold levels increased by increased hyperglycemia. For 1-hour values between 135-144 mg/dl, 155-164 mg/dl, and above 185 mg/dl, GDM prediction sensitivity was 14.6%, 28.6%, and almost 100%, respectively.(26)

In our study, average OGTT values of patients with such diabetic risk factors, as macrosomic birth and positive family history, were significantly higher. This suggests that such patients must be carefully monitored although they were not diagnosed with GDM.

HAPO study as conducted in 9 countries, 15 centers during 2000-2006 found that high blood glucose levels were directly associated with increased pregnancy risks. Furthermore, it was found that there were complications directly associated with GDM such as LGA, first cesarean section, and clinical neonatal hypoglycemia, and indirect complications as premature birth, shoulder dystocia or birth injuries, neonatal intensive care requirement, hyperbilirubinemia, and preeclampsia. Assessment of the groups in our study as per birth types suggested that there was a statistical difference between the groups ($p < 0,05$).

Increase in glucose levels is associated with increase in cesarean section rates. Regardless of complications associated with diabetes, Monique M. Hedderson *et al*. found that glucose intolerance of different levels were associated with spontaneous premature birth. In our study we did not see any premature birth as considered an indirect complication by HAPO study. Statistical assessment suggested that there is no statistically significant difference as regards the birth weeks of the patients and that all births occurred between 38th-42nd pregnancy weeks. This may be attributed to the fact that our hospital is a multidisciplinary tertiary hospital, and that we conduct regular antenatal monitoring and early hospitalization.

As for the birth types, it was found in our study that the group 2 had a significantly higher rate of cesarean section ($p < 0.05$). Only the data from patients with previously normal birth history were included in the calculation of increase in cesarean section rate. It seems that cesarean section became the more preferred option considering all the labor and delivery complications. Our study found that cesarean section rates significantly increased in patients by increase in hyperglycemia.

A comparison as regards neonatal weight indicated that there was a significant difference between the first and the second groups. It was seen that the neonatal weight was higher in the second group. Although macrosomia is not solely associated with diabetes mellitus and attributed to multifactorial causes, increase in 50-g OGTT values seems to have been associated with macrosomic fetus.

Patients on insulin during pregnancy will probably develop DM in the forthcoming years as early as the first year following GDM. A study found that 63% of the cases retook insulin after Type I Diabetes diagnosis during the first year (32, 33). 9 patients out of 63 as monitored by Buschard continued insulin and 37 patients (63%) required insulin treatment after an average of 256 days.(33) Therefore there are studies, which recommend that patients with GDM should be followed up to postpartum five years..

Postpartum assessment of our patients included 75-g OGTT control at postpartum 6th week. The number of patients diagnosed with post-pregnancy diabetes was one among those agreed to take the test. There was no difference as regards fasting glucose values between the two groups upon postpartum 75-g OGTT. Still there was significant difference between 1-hour and 2-hour glucose values. The results of the patient, group2 during their pregnancy, were significantly higher than the control group. This suggests that postpartum OGTT values increase as hyperglycemia increases. On the grounds that the number of patients involved in the study was limited and that this test was performed only once during the early period, our results must be reassessed in longer periods.

Gestational diabetes mellitus is among the risk factors of Type 2 Diabetes in the later periods of life. Therefore early and accurate diagnosis of postpartum DM and associated risk factors is important. Maternal and fetal complications may be decreased in women exposed to GDM risk by information of patients, appropriate pre-conceptional anamnesis, and examination before pregnancy. Patients with 50-g OGTT values that are considered normal will not be diagnosed with gestational diabetes. However these patients should be closely monitored in case they have the risk factors. The antenatal follow-up of such patients should be performed in a multidisciplinary approach at polyclinics. Pregnancy outcomes are expected to be better when fetal and maternal condition is monitored.

5. CONCLUSION

There is no international optimal agreement on diagnosis at the moment. Gestational diabetes is not merely a simple macrosomic delivery problem but an issue that should be considered in a more complex manner. Several studies suggested that glucose metabolism of pregnant with gestational diabetes have abnormalities that are precursors of Type 2 Diabetes. Therefore these patients should be monitored well both during pregnancy and in the postpartum period. We used 50-g OGTT screening test in the patients involved in our study. We concluded upon statistical analyses that 50-g OGTT values of patients with previous macrosomic birth history were significantly higher. Furthermore patients, who had previous cesarean section and with positive family history, had higher OGTT values. The pregnancy results of patients suggested that cesarean rate and birth weight were higher in the group 2. Diabetes incidence was 2% in the short-term screening with postpartum 75 gr OGTT and that it was consistent with the literature. It was seen that increase in 50-gr OGTT values was associated with increase in postpartum 75-gr 1-hour and 2-hour glucose values. All patients must be protected against hyperglycemia even though their screening test results do not exceed threshold levels. In conclusion, we found, as with HAPO study, that increased blood glucose levels were directly associated with increased pregnancy risks. However the present study should be repeated in the long run. The limited number of cases requires assessment of the results in itself. Therefore further studies should be conducted for longer periods and wider patient groups.

Referances

- 1- Classification and diagnosis of diabetes. *Diabetes Care*. American Diabetes Association (2016) Jan;39 Suppl 1:S13-22 DOI: 10.2337/dc16-S005
- 2-Turok DK, Ratcliffe SD, Baxley AG. Management of gestational diabetes mellitus. *Am Fam Physician* 2003;68: 1769–72.
- 3-Dornhorst A, Paterson CM, Nicholls JS, Wadsworth J, Chiu DC, Elkeles RS, et al. High prevalence of gestational diabetes in women from ethnic minority groups. *Diabet Med* 1992;9: 820–825.
- 4-Marquette GP, Klein VR, Niebyl JR. Efficacy of screening for gestational diabetes. *Am J Perinatol* 1985;2: 7–9.

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- 5-Kim C, Tabaei BP, Burke R, McEwen LN, Lash RW, Johnson SL, et al. Missed opportunities for type 2 diabetes mellitus screening among women with a history of gestational diabetes mellitus. *Am J Public Health* 2006;96: 1643-8.
- 6-Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of Type 2 diabetes: a systematic review. *Diabetes Care* 2002;25:1862-8.
- 7- Chiefari B, Arcidiacono D, Foti A, Brunetti Gestational diabetes mellitus: an updated overview E. *Italian Society of Endocrinology (SIE)* 2017; Sep;40(9):899-909.
- 8-Kjos SL, Buchanan TA. Gestational diabetes mellitus. *N Engl J Med* 1999;341:1749-1756.
- 9- Bharat Bassawa, Horace Fletcher. Screening for gestational diabetes mellitus: *J Obstet Gynaecol* 2018 Nov;38(8):1035-1038.
- 10- M vanLeeuwen, a MD Louwse, Glucose challenge test for detecting gestational diabetes mellitus: a systematic review *BJOG* 2012 Mar;119(4):393-401.
- 11- [W.Juntarat](#), [W.Rueangchainikhom](#), 50-grams glucose challenge test for screening of gestational diabetes mellitus in high risk pregnancy *J Med Assoc Thai* . 2007 Apr;90(4):617-23.
- 12- [YarivYogev](#) · The association between glucose challenge test, obesity and pregnancy outcome in 6390 non-diabetic women *J Matern Fetal Neonatal Med* 2005 jan;17(1):29-34
- 13-K. Feldman Gestational Diabetes Screening: The International Association of the Diabetes and Pregnancy Study Groups Compared With Carpenter-Coustan Screening *Obstet Gynecol* 2016 . Jan;127(1):10-17.
- 14-K.P.Fuller and A. F. Borgida, “Gestational diabetes mellitus screening using the one-step versus two-step method in a high risk practice,” *Clinical Diabetes*, vol.32, no.4, pp.148–150, 2014.
- 15-Y.-M. Wei, H.-X. Yang, W.-W. Zhu, H.-Y. Yang, H.-X. Li, and .Kapur, “Effects of intervention to mild GDM on outcomes,” *Journal of Maternal-Fetal and Neonatal Medicine*, vol.28, no.8, pp.928–931, 2015.
- 16-J.K.Ethridge, P.M.Catalano, “Perinatal outcomes associated with the diagnosis of gestational diabetes made by the international association of the diabetes and pregnancy study groups criteria,” *Obstetrics and Gynecology*, vol.124, no.3, pp.571–578, 2014.

17- S. Liao, J. Mei, W. Song et al., “The impact of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) fasting glucose diagnostic criterion on the prevalence and outcomes of gestational diabetes mellitus in Han Chinese women,” *Diabetic Medicine*, vol.31,no.3,pp.341–351, 2014.

18- K. Benhalima, M. Hanssens, R. Devlieger, J. Verhaeghe, and C. Mathieu, “Analysis of pregnancy outcomes using the new IADPSG recommendation compared with the carpenter and coustan criteria in an area with a low prevalence of gestational diabetes,” *International Journal of Endocrinology*, vol. 2013, ArticleID248121,2013.

19- A. Lapolla, M. G. Dalfr`a, E. Ragazzi, A. P. De Cata, and D. Fedele, “New International Association of the Diabetes and Pregnancy Study Groups(IADPSG) recommendations for diagnosing gestational diabetes compared with former criteria. Retrospective study on pregnancy outcome,” *Diabetic Medicine*, vol. 28,no.9,pp.1074–1077,2011.

20- C. Assaf-Balut, E. Bordi`u, L. Del Valle et al., “The impact of switching to the one-step method for GDM diagnosis on the rates of postpartum screening at tendance and glucose disorder BioMed Research International in women with prior GDM. The San Carlos Gestational Study,” *Journal of Diabetes and Its Complications*, vol.30,no.7,pp.1360–1364,2016.

21- J. M. Kong, K. Lim, and D. M. Thompson, “Evaluation of the International Association of the Diabetes in Pregnancy Study Group New Criteria: gestational diabetes project,” *Canadian Journal of Diabetes*, vol.39,no.2,pp.128–132,2015.

22-Metzger BE. Summary and recommendations of the Third International Workshop: Conference on Gestational Diyabetes Mellitus. *Diyabetes* 1991;40(Suppl 2):197-201.

23-American Diyabetes Association. Diagnosis and Classification of Diyabetes Mellitus. *Diyabetes Care* 2004; 27 suppl: 5-10.

24-Bonomo M, Corica D, Mion E, et al. Evaluating the therapeutic approach in pregnancies complicated by borderline glucose intolerance. A randomized clinical trial. *Diabet Med* 2005;22:1536-41.

25-Weijers RNM, Bekedam DJ, Simulders YM. Determinants of mild gestational hyperglycemia and gestational diabetes mellitus in a large Dutch multiethnic cohort. *Diabetes Care* 2002;25:72-7.

26-Uludağ S, Gezer A. Gebelik Diabeti. *Türk Jinekoloji ve Obstetrik Derneği, Uzmanlık Sonrası Güncel Gelişmeler Dergisi*. 2005;1(2):55-61

27-Schmidt MI, Duncan BB, Reichelt AJ, Branchtein L, Matos MC ve ark. Gestational Diabetes Mellitus Diagnosed With a 2-h 75-g Oral Glucose Tolerance Test and Adverse Pregnancy Outcomes. *Diabetes Care* 2001; 24:1151-1155.

28-Langer O, Brustman L, Anyaegbuman A, Mazze R. The significance of one abnormal glucose tolerance test value on adverse outcome in pregnancy. *Am J Obstet Gynecol* 1987;157:758-763.

29-Forsbach G, Contreras-Soto JJ, Fong G, Flores G, Moreno O. Prevalence of gestational diabetes and macrosomic newborns in a Mexican population. *Diabetes Care* 1988;11:235-238.

30-Aberg A, Westbom L, Kallen B. Congenital malformations among infants whose mothers had gestational diabetes or preexisting diabetes. *Early Hum Dev* 2001;61:85-95.

31-Gerardo Forsbach-Sánchez, Hector E. Tamez-Peréz, Julia Vazquez-Lara. Diabetes and Pregnancy. *Archives of Medical Research*, 2005;36(3):291-299.

32-Fougner KJ, Vanky , Carlsen SM. Metformin has no major effects on glucose homeostasis in pregnant women with PCOS: results of a randomized double-blind study. *Scand J Clin Lab Invest*. 2008 Jul 24: 1-6. (Epub ahead of print)

33-Buschard, I Buch, M Molsted-Pederson, P Hougaard, C Koni: Increased incidence of true type I diabetes acquired during pregnancy. *British Med J* 294:275,1987