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Metformin Compared with Diet or Insulin in Management of Gestational Diabetes in Clinical Practice

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Abstract: The aim was to investigate the maternal and neonatal outcomes in women suffering from gestational diabetes mellitus who have undergone different treatment modalities such as dietary management, metformin, and insulin. We examined the grooming of databases gathered from the aforementioned source and recommended that every future prospective data collection should only involve women who had gestational diabetes and delivered within the time span between March 2013 and July 2014. Starting in March 2013, women in require of medicine were given with the option to choose between metformin and insulin treatment, with the exception of those with foetal abdominal circumference under the 10th percentile who did not receive treatment with metformin. Gestational diabetes was identified in 150 women. Three groups, each containing 50 patients, were randomized to receive metformin, insulin, or diet. Upon diagnosis, the fasting glucose levels of the insulin plus metformin group were much greater than those of the diet group ($p < 0.001$). There was a significant connection among insulin medication and increased incidence of Caesarean section compared to both diet and metformin (45.6% insulin, 37 percent metformin, and 34% diet; $P = 0.02$). Furthermore, they displayed increased proportions for customized LGA (18.5% for first infants on insulin; 12.5% for first infants using Metformin; 12.4% for diets); however, this difference was statistically significant (P=0.02). There were also higher proportions of admissions within neonatology departments (18.7% in cases who used Insulin; 12.7% if metformin was used;14.0% in dietary), preterm births (19.2% IN CASES WHO have used Insulin before delivery compared to 12.5% who did it through methasone alone) and receiving neonatal intravenous dextrose (11%.5% babies born with dextrose on their inside compared to five percent plus seven percent plus ten percent respectively). The outcomes of newborns treated using diet were similar to those treated using metformin. The treatment of gestational diabetes with metformin was related to less bad outcomes than using insulin only in clinical practice, though treatment groups' baseline differences might have played a role in this.

Keywords: Metformin; Diet; Gestational Diabetes; Pre-eclampsia; and Preterm.

INTRODUCTION

Starting from the 12th week of pregnancy, blood sugar levels in the fetus stimulate the production of insulin by the fetus; it is a strong in-utero growth promoter [Dabelea, D. *et al*., 2005]. The prevalence of gestational diabetes (GDM) is increasing as maternal age and obesity are on the rise, too. The way the body works during pregnancy allows for easy movement of glucose from the mother to the placenta and then to her baby-this happens most after meals [Hunt, K. J. *et al*., 2007; American Diabetes Association, 2010]. In pregnancies complicated with diabetes, glucose from the mother's blood is sent to her unborn child instead of being accumulated in her belly or thighs as it should be done normally. Gestational diabetes mellitus (GDM): [Alwan, N. *et al*., 2009] It is any glucose intolerance that manifests for the first time during pregnancy or is detected there. This condition is widely prevalent and affects around 3-6% of all pregnancies [Cunningham, F. G. *et al*., 2010]. Thus, during the initial stages of pregnancy, particularly fasting, hyperglycemia is practically always a sign of evident diabetes. The greatest danger after birth is infant macrosomia, a name for a child with a very high birth weight. Macrosomia diagnosis for a baby can only be made through weighing upon birth, which implies that it is determined after giving birth. The condition of fetal macrosomia may occur in as much as ten percent of all deliveries [Reece, E. A. *et al*., 2008 – American Diabetes Association, 2004]. The most prevalent medical complication of pregnancy is associated with various adverse outcomes both in the short and long term for mothers and their unborn children [Agarwal, M. M. *et al*., 2007]. Among these, women with uncontrolled GDM have more chances of experiencing pregnancy-related problems such as preterm labor, septic complications, hydramnios, and hypertension-related disorders. [Pennison, E. H. *et al*., 2001] In addition to these, there are also GDM's associated effects on the fetus, which include fetal macrosomia, fetal distress, metabolic disorders, growth imbalance, and hyperbilirubinemia, among others, all of which have lasting consequences [Carpenter, M. W. *et al*., 1982]. The advantages associated with GDM screening and clinical care have been discovered for the prenatal periods,

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postnatal periods, and peri-natal outcomes [Fraser, R. *et al*., 2007]. All in all, GDM screening, therapy, and management are aimed at reducing large-for-gestational-age deliveries as well as averting stillbirths in order to reduce maternal and neonatal morbidity and mortality eventually [Dabelea, D. *et al*., 2000]. During the last two decades, there has been a remarkable decline in stillbirth rates despite preventive insulin therapy introduction, while there is no change on increases in C-section rates and large-for-gestational-age birth weights among women with GDMs [HAPO Study Cooperative Research Group, 2008]. Insulin-insensitive and insulin-dependent effects are present in metformin, that works on opposing insulin resistance. Glycaemic control, along with other metabolic parameters, are enhanced by the use of metformin, while some parameters concerning vascular function are also improved to lower atherosclerotic risk [Langer, O. *et al*., 2005]. Numerous studies show that mothers can breastfeed their newborns safely. Weight-normalized maternal doses were found to be between 0.65% and 0.11% of the mean baby exposure to the drug. This is less of a concern than 10% in relation to nursing [Crowther, C. A. *et al*., 2005; Langer, O. *et al*., 1988]. Furthermore, four hours after feeding, the serum blood glucose concentrations in the newborns, which ranged from 47 to 77 mg/dL, were within limits for normality [Jimenez-Moleon, J. J. *et al*., 2002 – Swaminathan, K. *et al*., 2009]

PATIENTS AND METHODS

The Committee on Obstetrics and gynaecology of the Arab Board for Medical Specialisation approved the protocol for this prospective study that involved all women with gestational diabetes who gave birth after 24 weeks of gestation at Baghdad Teaching Hospital between March 2013 and July 2014. During this time, it was instructed that screening for gestational diabetes should be performed during gestation weeks 24 – 28 using a 50-g glucose screen. Women whose plasma glucose levels were 7.8 mmol/L or greater following one hour underwent a 100-gram oral glucose tolerance test for diagnostic purposes.

When blood glucose levels after two hours were ≥9.0 mmol ⁄ l or ≥155 mg/dl [for this, it was diagnosed as having gestational diabetes], it is advisable for women with multiple or extreme risk factors to undertake earlier testing for gestational diabetes at the time of booking. If a woman satisfied one of the following criteria, she had an increased chance of developing GDM: she was over 40 years old, overweight (BMI > 25kg/m2), experience glucosuria, previously having GDM, previously giving birth to a baby with macrosomia (birth weight >4500g) or having suspicion of fetal macrosomia in current pregnancy.

After being diagnosed with gestational diabetes mellitus, the women had consultations regarding their lifestyle and were given four sets of capillary glucose readings on a daily basis (during fasting hours and two hours following each meal). Typically, those whose average levels of glucose during fasting were over 5.0 mmol/l, along with values for postprandial glucose readings after a span of two hours over 6.0mmol/l or 6.5mmol/l based on some other medical factors like the number of elevated indices, etc., were often recommended to take medications generally within two weeks.

From March 2013 onwards, women who were diagnosed with GDM during a singleton pregnancy were invited for participation in the study after reaching 24 weeks of gestation. Those who gave consent to use insulin or metformin medications. Each woman was provided with written information on each of the medications, explaining that metformin crosses the placenta. All this information was given to every woman without preferentiality to any one drug. Normal liver and kidney function were established by GHbA1c measurement and serum concentrations of transaminases, electrolytes, and creatinine after an overnight fast before treatment could start. The exclusion criteria included the history of substance abuse, major fetal deformities, fetal growth restriction (anticipated fetal growth below the fifth percentile for gestational age), and systemic diseases (cardiovascular, renal, hepatic, or autoimmune). It was not possible to blind treatment since drugs were given through different routes. A dosage of 500mg was given once each day for a week to commence metformin therapy in individuals with T2DM who had never been treated before. Following that, Dosage increments were made such that in the second week, it reached 2500 mg daily (sometimes even 3000mg/day if there were issues of obesity), and this pattern persisted through three weeks until glycaemic control was achieved. In severe cases of adverse reactions like diarrhea, withdrawal from treatment ensued.

The women who had low-level appropriate sugar levels on the second week of using metformin or

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those whose glucose level was consistently above these figures after two weeks of taking a maximum daily dose of the drug were allowed to use other necessary types of insulin as per prescription as well as any woman receiving metformin through prescription whose other benefits also accrued to this group for analysis. Insulin was given according to the glucose profile of the patient, aiming at similar glucose targets like in women treated with metformin. For women preferring insulin, therapy comprised of intermediate-acting isophane insulin solo before sleeping to adjust the fast serum level and premeal short-acting insulin analogue in order to reduce postprandial blood sugar levels. Moreover, if the traditional ultrasound assessment showed that a fetus's abdomen circumference was below the 10th percentile, indicating placental insufficiency or in some unique maternal contraindications, metformin was not provided for women.

The women took to monitoring the capillary glucose levels regularly and conveyed the outcomes to the clinics that provide prenatal care. Starting from 36 weeks of pregnancy, they were monitored at the outpatient clinics for expectant mothers in the hospitals that offered both inpatient and outpatient services once or twice a week. Between 24 and 32 weeks of pregnancy, the mothers visited the outpatient labor and delivery units every 4 weeks for their check-ups while appraising visits were scheduled for 2-week intervals from 32 to 36 weeks gestation. One of these routine check-ups also involved ultrasound examinations for assessing fetal growth and polyhydramnios as well as gaining weight by the mom. A gauge of glycosylated hemoglobin was determined at baseline trial involvement time, two weeks post commencement of treatment, and every month thereafter till delivery date was reached; through finally, a postpartum visit was scheduled after 7-8 weeks after giving birth. Macrosomia was the primary endpoint. Other secondary outcomes included incidence of preterm birth before 37 weeks gestation, birth injuries (clavicular fracture or brachial plexus injury), and neonatal complications (NICU admission; IV glucose-treated hypoglycemia; phototherapy administered hyperbilirubinemia). Measurements for both umbilical cords, artery pH values, and Apgar scores were also recorded. One outcome in mothers was that the metformin group had a higher need for insulin.2. Polyhydramniosis implies a gestational age of 60 percent or more. 3. Issues regarding hypertension during pregnancy and delivery. Macrosomia is two to four times more likely in untreated GDM than in women without diabetes or after successful therapy for GDM.

Defining large for gestational age required customized birth weights over the 90th percentile, while tiny ones were determined by birth weights below the 10th percentile. The analysis was conducted using Stata version 9.2 (Stata Corp, College Station, TX, USA). Comparisons of frequency values were made through v2-tests and presented as n (%). The number of women in each group was 50 as the sample size. Continuous data is presented in the form of the mean (standard deviation), and comparison was done using a one-way analysis of variance for comparison among three groups, the Bonferroni test for multiple comparisons, and the student's t-test for comparison between two groups, including t-test for unequal variance when applicable. As long as they were not available, the demographics of absence figures were left out of this study. Missing outcome data are seen as suggestions for the absence of results.

RESULTS

In a study, 205 ladies were drawn to outpatient clinics because they had GDM. Out of a total of 153 people who agreed, 50 were put on a diet only, while another 50 took insulin, and the last 53 had metformin treatment. However, two women withdrew from study before starting the treatment, and one was excluded because her liver function tests were abnormal, in which case the metformin group had only 50 women left. Women's baseline characteristics are displayed in **Table 1.** The findings showed that fasting glucose levels in diet-treated women were lower than those of their medication-treated counterparts. There was no significant difference in the baseline characteristics of the women within the study groups.

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Table 1: Enroll basics characteristics of Maternal.

	Diet n=50	**insulin n=50**	**Metformin n=50**	**P-value**
Age (years)	34.2 ± 5.2	33.9 ± 5.0	34.2 ± 5.2	P = 0.67
OGTT (mmol/l)	4.4 (0.7)	5.3 (1.1)	5.2 (0.8)	< 0.0001
- **Fasting glucose (mmol/l)**	9.5 (1.1)	9.9 (2.1)	9.4 (1.6)	0.0008
- **2-h glucose (mmol/l)**				
HbA1c (%) at randomization	5.5± 0.7	5.7 ± 0.9	5.5± 0.7	P = 0.08

Table 2: Determine maternal outcomes and neonatal outcomes.

	Metformin alone n = 40	**Metformin + insulin n = 10**	**P-value**
OGTT (mmol/l)			
- Fasting glucose (mmol/l)	4.9 (0.6)	5.6 (0.9)	< 0.0001
- 2-h glucose (mmol/l)	9.4 (1.4)	9.3 (1.9)	0.6
Hypertension			
- Chronic	2.4	8.8	0.004
- Gestational	6	10.2	
- Pre-eclampsia	2.8	3.7	
Mode of birth			
- Vaginal	63.8	62	0.5
- El LSCS	17.3	21.3	
- Em LSCS	18.9	16.7	
Preterm < 37 weeks			
- Iatrogenic	12.2	12.7	0.8
- Spontaneous	8.3	7.3	
	4.3	5.5	
Preterm < 32 weeks	0	0.8	0.13
Birth weight (g)	3204 (489)	3241 (596)	0.5
SGA	9.5	7.8	0.5
LGA	11.5	13.8	0.5
NICU admission§	10.3	15.6	0.08
NICU + 2 days§	8.3	14.7	0.03
Intravenous dextrose	3.2	7.3	0.04
Glucose < 2.3 mmol/l	13	10.1	0.32

Maternal outcomes are represented in **Table 3**. No differences existed between the three groups about hypertensive issues. Insulin-treated mothers had higher rates of Caesarean section as compared to metformin or diet therapy; however, they experienced polyhydramnios to a slightly greater extent but not significantly.

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Table 3: Identify outcomes of maternal participants.

		Diet n=50%	Insulin n=50%	Metformin n=50%	P-value
Hypertension					0.3
-	Chronic	3.5	6.5	5.4	
-	Gestational	5.7	5.3	8	
al		3.8	4	3.4	
-	Pre-				
eclampsia					
Mode of birth		66	54.4	63	0.02
-	Vaginal	15.4	22.3	19.1	
-	El LSCS	18.6	23.3	17.9	
-	Em LSCS				
polyhydramnios		13	18	13	0.37

In but in the metformin group, there were higher rates of gestational hypertension on women treated with insulin as compared to those treated with metformin alone (p = 0.004) **Table 2**. **Table 4** presents the neonatal outcomes. Outcome measures were comparable for diet and metfomin treatment groups [except for more preterm births < 32 weeks in the diet group). In comparison to those on metfomin and diets, however, the insulin group had more infants with large-for-gestational-age, premature deliveries, neotatal admissions, as well as administration of intravenous glucose to the infant. Increase in premature deliveries was ascribed to iatrogenic premature deliveries; there was no change in the rates of spontaneous premature births. Between-group comparisons did not show a significant difference between the Apgar score at 5 minutes, neonatal Hyperbilirubinemia, and cord artery Blood pH.

Table 4: Identification of Neonatal Outcomes.

	Diet n=50	Insulin n=50	Metformin n=50	P-value
Preterm < 37 weeks	12	19.1	12.4	0.005
Iatrogenic	8.9	15	7.6	
Spontaneous	3.1	4.1	4.8	
Preterm < 32 weeks	2.9	3	0.4	
Birthweight (g)	3168 (635)	3176 (701)	3221 (541)	0.4
SGA	11.8	11.8	8.7	0.22
LGA	12.4	18.5	12.5	0.02
NICU admission §	14	18.7	12.7	0.04
NICU + 2 days §	12.4	17.7	11.3	0.014
Intravenous dextrose	7.4	11.1	5.1	0.004
Glucose < 2.3 mmol/l	10	14.3	11.7	0.18
Neonatal hyperbilirubinemia	13(27.9)	18 (36.0)	13 (27.7)	0.379
Cord artery pH	7.25+-0.09	7.25 ± 0.09	7.25 ± 0.09	0.976
Apgar score at 5 minutes	9.0+-0.7	8.9 ± 0.7	9.0 ± 0.8	0.617

In the metformin group, the individuals receiving additional insulin were more likely to have babies who needed intravenous dextrose and stayed for at least two days in a neonatal intensive care unit, as opposed to those treated with metformin exclusively. On the diagnostic oral glucose tolerance test, women receiving both types of therapy had lower 2-hour glucose (9.3 vs. 9.9 mmol / L, P = 0.009) but higher fasting glucose (5.6 vs. 5.3 mmol / L, P = 0.008) compared to those receiving insulin alone as shown in Table 1. The metformin + insulin group delivered fewer babies through Caesarean section (38.0 vs. 45.6%) than the insulin-treated group, though this was not significant (P = 0.05). According to data, women treated with metformin plus insulin had less incidences of early labor (12.7 versus 19.1% P = 0.04) compared to those who were on insulin alone. The rates of small for their age at birth (7.8 versus 11.8%, P = 0.12), large for their age at birth (13.8 versus 18.5%, P = 0.13), neonates hospitalized (15.6 versus 18.7%, P = 0.3) or who

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needed intravenous dextrose (7.3 versus 11.1%, P=0.13) did not significantly differ between groups. There were two deaths before birth. One was among some female individuals undergoing nutrition therapy who appeared at 26 weeks suffering from antepartum haemorrhage accompanied by premature labour. In the course of the other instance, despite a Crash Caesarian section due to a massive placental abruption in labour at 39 weeks treated with insulin, severe neonatal hypoxia claimed the life of this infant.

In the attempt of this surrogate mothering, however, a random analysis was validated following the exclusion of birth weight-decreased infants. The research findings indicated that although there was still a slightly higher percentage of premature births among the insulin group, the difference is not statistically significant (insulin = 15.8%, metformin = 12%, diet = 10.7%, P = 0.10). Hence, there were no longer any significant differences between the treatment groups when it concerned rates of admission to the neonatal unit (insulin = 15.4%, metformin = 10.9%, diet = 11.3%, P = 0.13) and stays more than two days (insulin = 14.3%, metformin = 9.8%, diet = 9.9%, P = 0.09). However, the insulin group continued to be given intravenous dextrose significantly more often as compared to other groups (insulin = 8.4%, metformin = 4.0%, diet = 6.3%, P = 0.03).

DISCUSSION

It was demonstrated by this study that metformin is an appropriate and secure choice whilst treating GDM [Balani, J. *et al*., 2009]. Comparing the instances of unfavorable pregnancy or newborn outcomes, metformin did not raise them in women taking it in contrast to those who were administered on insulin. At the same time, it is particularly ideal for treating postprandial hyperglycemia during the late stages of gestation [Jovanovic, L. *et al*., 1999]. This is one of the pioneering studies documenting results in women having gestational diabetes who have received medication either through dieting, metformin, or insulin, with a percentage approximating 70% of them requiring the drugs. Metfomin-treated women showed similar outcomes on various scales that were assessed when compared to their counterparts that only followed a weight reduction diet except for reduced occurrences of premature deliveries before 32 weeks, which were common among them.

In contrast, they experienced significantly reduced levels of rates related to preterm delivery, caesarean section rate, large-for-gestational-age babies' occurrence, and neonatal transfers, as well as a number of infants placed under intravenous dextrose therapy [Hyer, S. L. *et al*., 2005 – Tertti, K. *et al*., 2008]. The women's glucose level was suboptimal for a more extended period, which should accelerate fetal development prior to attaining normal glycaemia levels. These are observational data, so although they point towards greater success with a combination of metformin and more insulin as needed when compared to using insulin alone, there is also a chance that other factors played some roles in those outcomes [DeFronzo, R. A. *et al*., 1948; Asche, C. V. *et al*., 2008]. It was shown that hypoglycemia is more severe in the newborns who were treated with insulin than those treated using metfomin, which is similar to our research. Usually, compared to insulin, metfomin therapy does not increase the risk of problems for infants; on the contrary, it can reduce hypoglycemia in newborn babies [ACOG, 2001]. In regard to women with metformin who managed to attain normoglycemia, we had on our trial insulin-requiring patients that showed significantly elevated fasting blood sugar levels during OGTTs as well as earlier medical attention demand, which shows they faced a worse case of insulin resistance.

Meanwhile, when we compared the average birth weights of infants born from the supplemental insulin group to those whose mothers only took metfomin, it was obvious that normoglycemia could be achieved through higher doses of insulin in comparison to their counterparts. In reality, owing to the limited sample size, the LGA rates of 13.8 percent in the extra insulin group and 11.5 % in the metformin-only group were not statistically significant [Kjos, S. L. *et al*., 1995; Caplan, R. H. *et al*., 1982]. In our study, women who were prescribed metfomin had less postprandial glucose levels than those treated with insulin, similar to what occurred in the Mig trial. In addition, control of glucose level was attained earlier in those who were assigned metfomin, whereas the postprandial glucose concentrations during treatment were much lower. Since other researchers have also noted that poor outcome could be attributed to late presentation by women whose duration of treatment before delivery was short. The group under consideration consisted of women who were prescribed metfomin plus insulin and was compared against women treated with only insulin

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[Boulvain, M. *et al*., 2001 – Kim, C. *et al*., 2007]. At baseline, these two groups differed significantly such that those on combination therapy had higher fasting glucose levels at diagnosis [Knowler, W. C. *et al*., 2002]. These combined therapies led to reduced pre-term births (the reduction was significant) while there was a small decrease in case of caesarean sections (P=0.05), but other than that, the outcomes were similar between the two groups. Similar to the ease of use and acceptance of metformin among women in pregnancy as compared to its alternative, there is better compliance with the prescribed therapeutic regimen. [Briggs, G. G. *et al*., 2005 – Rowan, J. A. *et al*., 2008] At the initiation of therapy, they do not demand much educational guidance because it is easier to administer them. The occurrence of maternal hypoglycaemia, which is a distressing state for most females during pregnancy, is minimized to a very great extent. Insulin, on the other hand, is more costly, requires a specific temperature to store it, overloads unrich countries and can be difficult to handle as well as uncomfortable by itself.

CONCLUSION

It has been demonstrated that clinically, among women with gestational diabetes requiring medications, the provision of insulin or metformin results in less incidence of preterm births and improved neonatal outcomes for the group using metformin. Nonetheless, it is possible that some of these results were influenced by the differences in the initial conditions of treatment groups.

REFERENCES

1. Dabelea, D., Snell-Bergeon, J. K., Hartsfield, C. L., Bischoff, K. J., Hamman, R. F. & McDuffie, R. S. "Increasing prevalence of gestational diabetes mellitus (GDM) over time and by birth cohort." *Diabetes Care*, 28.3 (2005): 579-584.
2. Hunt, K. J. & Schuller, K. L. "The increasing prevalence of diabetes in pregnancy." *Obstetrics and Gynecology Clinics of North America*, 34.2 (2007): 173-199.
3. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2010; 33 (Suppl 1): S62–S69.
4. Alwan, N., Tuffnell, D. J. & West, J. "Treatments for gestational diabetes." *Cochrane Database of Systematic Reviews*, 2009.3 (2009): CD003395.
5. Cunningham, F. G., Leveno, K. J., Bloom, S. L., Hauth, J. C., Rouse, D. J. & Spong, C. Y. *Williams Obstetrics*. 23rd ed., New York: McGraw-Hill, 2010: 1104–1121.
6. Reece, E. A. & Homko, C. J. "Diabetes mellitus and pregnancy." In: Gibbs, R. S., Karlan, B. Y., Haney, A. F. & Nygaard, I. E. *Danforth's Obstetrics and Gynecology*. 10th ed., Philadelphia: Lippincott Williams and Wilkins, 2008: 247–251.
7. Martin, J. A., Hamilton, B. E., Sutton, P. D., Ventura, S. J., Menacker, F. & Kirmeyer, S. "Births: final data for 2004." *National Vital Statistics Reports*, 55.1 (2006): 1-101.
8. Metzger, B. E., Buchanan, T. A., Coustan, D. R., et al. "Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus." *Diabetes Care*, 30.suppl 2 (2007): S251-S260.
9. Metzger, B. E. & Coustan, D. R. "Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. The Organizing Committee." *Diabetes Care*, 21. 2 (1998): B161-B167.
10. American Diabetes Association. Gestational diabetes mellitus. DiabetesCare.2004;27 (suppl 1): S88-S90.
11. Agarwal, M. M., Dhatt, G. S., Punnose, J. & Zayed, R. "Gestational diabetes: Fasting and postprandial glucose as first prenatal screening tests in a high-risk population." *Journal of Reproductive Medicine*, 52.4 (2007): 299-305.
12. Pennison, E. H. & Egerman, R. S. "Perinatal outcomes in gestational diabetes: A comparison of criteria for diagnosis." *American Journal of Obstetrics and Gynecology*, 184.6 (2001): 1118-1121.
13. Carpenter, M. W. & Coustan, D. R. "Criteria for screening tests for gestational diabetes." *American Journal of Obstetrics and Gynecology*, 144.7 (1982): 768-773.
14. Fraser, R. & Heller, S. R. "Gestational diabetes: Etiology and management." *Obstetrics and Gynecology Reports in Medicine*, 17.12 (2007): 345-348.
15. Dabelea, D., Hanson, R. L., Lindsay, R. S., Pettitt, D. J., Imperatore, G., Gabir, M. M., et al. "Intrauterine exposure to diabetes conveys risks for type 2 diabetes and obesity: A study of discordant sibships." *Diabetes*, 49.12 (2000): 2208-2211.
16. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, Hadden DR, McCance DR, Hod M, McIntyre HD, Oats JJ, Persson B, Rogers MS, Sacks DA.

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Hyperglycaemia and adverse pregnancy outcomes. N Engl J Med. 2008;358 (19):1991–2002.
17. Langer, O., Yogev, Y., Most, O. & Xenakis, E. M. "Gestational diabetes: The consequences of not treating." *American Journal of Obstetrics and Gynecology*, 192.4 (2005): 989-997.
18. Crowther, C. A., Hiller, J. E., Moss, J. R., McPhee, A. J., Jeffries, W. S. & Robinson, J. S. "Effect of treatment of gestational diabetes on outcomes." *New England Journal of Medicine*, 352.24 (2005): 2477-2486.
19. Langer, O. & Mazze, R. "The relationship between large-for-gestational-age infants and glycemic control in women with gestational diabetes." *American Journal of Obstetrics and Gynecology*, 159.6 (1988): 1478-1483.
20. Jimenez-Moleon, J. J., Bueno-Cavanillas, A., Luna-del-Castillo, J., Gracia-Martin, M., Lardelli-Claret, P. & Galvez-Vargas, R. "Impact of different levels of carbohydrate intolerance on neonatal outcomes classically associated with gestational diabetes mellitus." *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 102.1 (2002): 36-41.
21. Landon, M. B., Spong, C. Y., Thom, E., et al. "A multicenter, randomized trial of treatment for mild gestational diabetes." *New England Journal of Medicine*, 361.14 (2009): 1339-1348.
22. Cheung, N. W. "The management of gestational diabetes." *Vascular Health and Risk Management*, 5 (2009): 153-164.
23. Swaminathan, K., Howlett, H. C. & Campbell, I. W. "Metformin in diabetic pregnancy." *Journal of the Royal College of Physicians of Edinburgh*, 39 (2009): 10-14.
24. Balani, J., Hyer, S. L., Rodin, D. A. & Shehata, H. "Pregnancy outcomes in women with gestational diabetes treated with Metformin or insulin: A case-control study." *Diabetic Medicine*, 26.8 (2009): 798-802.
25. Jovanovic, L., Ilic, S., Pettitt, D. J., et al. "Metabolic and immunologic effects of insulin lispro in gestational diabetes." *Diabetes Care*, 22.9 (1999): 1422-1427.
26. Hyer, S. L. & Shehata, H. A. "Gestational diabetes mellitus." *Current Obstetrics and Gynaecology*, 15.6 (2005): 368-374.
27. Kirpichnikov, D., McFarlane, S. I. & Sowers, J. R. "Metformin: An update." *Annals of Internal Medicine*, 137.1 (2002): 25-33.
28. Tertti, K., Ekblad, U., Vahlberg, T. & Rönnemaa, T. "Comparison of Metformin and insulin in the treatment of gestational diabetes: A retrospective, case-control study." *Review of Diabetic Studies*, 5.2 (2008): 95-101.
29. DeFronzo, R. A. & Simonson, D. C. "Oral sulfonylurea agents suppress hepatic glucose production in non-insulin-dependent diabetic individuals." *Diabetes Care*, 7.1 (1984): 72-80.
30. Asche, C. V., McAdam-Marx, C., Shane-McWhorter, L., et al. "Association between oral antidiabetic use, adverse events, and outcomes in patients with type 2 diabetes." *Diabetes, Obesity and Metabolism*, 10.8 (2008): 638-645.
31. American College of Obstetricians and Gynecologists Committee on Practice Bulletins–Obstretrics. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-Gynecologists. Number 30, September 2001 (replaces Technical Bulletin Number 200, December 1994). Gestational diabetes. Obstet Gynecol.2001;98 (3):525-38.
32. Kjos, S. L., Leung, A., Henry, O. A., Victor, M. R., Paul, R. H. & Medearis, A. L. "Antepartum surveillance in diabetic pregnancies: Predictors of fetal distress in labor." *American Journal of Obstetrics and Gynecology*, 173.5 (1995): 1532-1539.
33. Caplan, R. H., Pagliara, A. S., Beguin, E. A., et al. "Constant intravenous insulin infusion during labor and delivery in diabetes mellitus." *Diabetes Care*, 5.1 (1982): 6-10.
34. Boulvain, M., Stan, C. & Irion, O. "Elective delivery in diabetic pregnant women." *Cochrane Database of Systematic Reviews*, 2001.2 (2001): CD001997.
35. Rouse, D. J., Owen, J., Goldenberg, R. L. & Cliver, S. P. "The effectiveness and costs of elective cesarean delivery for fetal macrosomia diagnosed by ultrasound." *JAMA*, 276.18 (1996): 1480-1486.
36. Kim, C., Newton, K. M. & Knopp, R. H. "Gestational diabetes and the incidence of type 2 diabetes: A systematic review." *Diabetes Care*, 25.10 (2002): 1862-1868.
37. Kim, C., Herman, W. H. & Vijan, S. "Efficacy and cost of postpartum screening strategies for diabetes among women with histories of gestational diabetes mellitus." *Diabetes Care*, 30.5 (2007): 1102-1106.
38. Knowler, W. C., Barrett-Connor, E., Fowler, S. E., *et al*. "Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin." *New England Journal of Medicine*, 346.6 (2002): 393-403.

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39. Briggs, G. G., Ambrose, P. J., Nageotte, M. P., et al. "Excretion of metformin into breast milk and the effect on nursing infants." *Obstetrics and Gynecology*, 105.6 (2005): 1437-1441.
40. Langer, O., Yogev, Y., Most, O. & Xenakis, E. M. "Gestational diabetes: The consequences of not treating." *American Journal of Obstetrics and Gynecology*, 192 (2005): 989-997.
41. Rowan, J. A., Hague, W. M., Gao, W., Battin, M. R. & Moore, M. P.; MiG Trial Investigators. "Metformin versus insulin for the treatment of gestational diabetes." *New England Journal of Medicine*, 358.19 (2008): 2003-2015.

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