

Effect of Glycemic Control on Pregnancy out Come in Diabetic Pregnant Women at Obstetric and Gynecological Department in Tripoli-Libya

Hiyam BenRajab^{@1,2}, Fuad Zekri^{1,2} and Weam Najjar¹

¹Department of Gynecology and Obstetrics, Tripoli University Hospital;

²Department of Gynecology and Obstetrics, Faculty of Medicine, University of Tripoli, Libya

Received 3 October 2019/Accepted 16 December 2019

ABSTRACT

Elevated HbA1c is associated with increased risk of adverse pregnancy outcomes including abortion, stillbirth, and congenital abnormalities. The study conducted to assess the association between hemoglobin A1c (HbA1c) and the risk of adverse pregnancy outcomes in diabetic pregnancies.

A cross sectional study included all pregnant diabetic women (251) in a Tripoli University Hospital from January 2017 to January 2018. HbA1c values from first, second and third trimester were collected, and pregnancy outcome was categorized as good (babies surviving the first month of life without major congenital abnormalities) and adverse (spontaneous and therapeutic abortion, stillbirth, neonatal death, or major congenital abnormalities detected within the first month). The frequency of adverse outcomes was calculated according to HbA1c values.

This study identified 251 diabetic pregnant women in the study period. Twenty-seven women with type 1 diabetes (10.4%), 123 gestational (47.3%) and 101 with type 2 diabetes (38.8%) were included in the study. Mean HbA1c early in pregnancy measured in a central laboratory, was higher in the women with an adverse outcome group ($P=0.009$). Second and third trimester HbA1c and mean HbA1c during pregnancy were higher in the women with an adverse outcome group ($P=0.002$, $P=0.001$ respectively).

Strong correlation between high HbA1c values and pregnancy adverse outcome specific to every trimester, optimizing glycemic control during pregnancy will reduce these adverse effects.

Keywords- HBA1c; Pregnancy; Outcome.

INTRODUCTION

Diabetes mellitus is one of the most common medical complications of pregnancy; up to 5% of diabetic pregnant women have either pre-existing diabetes or gestational diabetes. Of women who have diabetes during pregnancy, it is estimated that approximately 87.5% have gestational diabetes (which may or may not resolve after pregnancy), 7.5% have type 1 diabetes, and the remaining 5% have type 2 diabetes. The prevalence of type 1 diabetes and especially type 2 diabetes has increased in recent years. The incidence of gestational diabetes is also increasing because of higher rates of obesity in the general population and more pregnancies in older women.¹

Diabetes in pregnancy generates a significant risk to the fetus and the mother. Congenital malformations and perinatal morbidity remain commonly happen when compared with the offspring of non-diabetic pregnancies. Diabetic mothers are always at risk of progression of microvascular diabetic complications as well as early pregnancy loss, pre-eclampsia, polyhydramnios and premature labour.²

There are two common classes of Diabetes Mellitus identified in pregnancy. The first is called pre-gestational diabetes mellitus (diabetes present before pregnancy) that antedates pregnancy and referred to as diabetes mellitus and pregnancy.³ Optimize Glycemic Control: Diabetes ante-natal care should be provided in a special hospitals and the team caring for pregnant women should ideally include a Diabetes Nurse Specialist, Dietician, Diabetologist and an Obstetrician.

The main objective of ante-natal care is to Provide and maintain tight glycemic control and also to monitor the mother for diabetes complications. Tighter glycemic control has effect on maternal and fetal complications. Excellent glycemic control should be continued during the pregnancy, fasting glucose levels of <90-99 mg/dl (5.0-5.5 mmol/l), 1-h postprandial glucose levels of <140 mg/dl (7.8 mmol/l), and 2-h postprandial glucose levels of <120-127 mg/dl (6.7-7.1 mmol/l).⁴ The glycated hemoglobin (HbA1c) reference values were 4.5-6.2% (25.7-44.3 mmol/mol).⁵



Elevated HbA1c is associated with increased risk of adverse pregnancy outcomes including abortion, stillbirth, and congenital abnormalities; Glycosylated hemoglobin (HbA1c) is known to correlate with fetal malformations if elevated during organogenesis.⁶women with high HbA1c were at a higher risk of delivering macrosomicbabies.⁷

The current study conducted to assess the association between hemoglobin A1c (HbA1c) and the risk of adverse pregnancy outcomes in diabetic pregnancies.

MATERIALS AND METHODS

A cross sectional study included all pregnant diabetic women (251) in a Tripoli university hospital (TUH) from January 2017 to January 2018. HbA1c was measured in a central laboratory; values from first, second and third trimester were collected, and pregnancy outcome was categorized as good (babies surviving the first month of life without major congenital abnormalities) and adverse (spontaneous and therapeutic abortion, stillbirth, neonatal death, or major congenital abnormalities detected within the first month). The frequency of adverse outcomes was calculated according to HbA1c values; variables were including Type of diabetes (gestational diabetes /type 1 diabetes / type 2 diabetes), A1c values in the first, second and third trimester of pregnancy, mode of delivery, baby weight, adverse out come and good outcome. Pregnancy outcomes were divided into good (babies surviving the 1st month of life without detected congenital abnormalities) and adverse (composed of stillbirth, neonatal death, major or minor congenital abnormalities detected within the 1st month of life). Data was analyzed using SPSS program version 16. Descriptive statistics including means, standard deviation, frequencies, and percentages were obtained for all variables as appropriate. *P* value < 0.05 considered significant.

Verbal informed consent was obtained from all participants during their follow up at the clinic and data confidentiality was maintained throughout the study and any resulting publication anonymously.

RESULTS

A total 251 diabetic pregnant women were enrolled in present the study. The results showed that 27 (11%) women were with type 1 diabetes, 123(49%) women with gestational diabetes, and 101 women with type 2 diabetes (40%) (Figure 1).

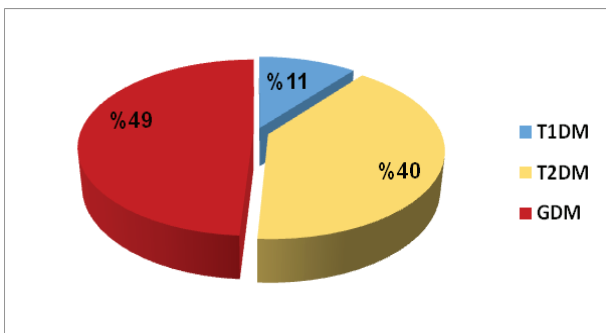


Figure 1: Distribution of patients according to the type of diabetes, TUH, 2016.

The results showed that, 169 cases were in good outcome group, normal vaginal delivery was performed in 79(31.5%) and 172(68.5%) of cases were underwent cesarean section. There was ahiger percentage of caesarian section in both groups. No significant differences were determined between both groups regarding mode of deliver (Table 2).

Table 2: Relation between mode of delivery and pregnancy outcome at TUH 2016

Mode of delivery	Good outcome Group No. (%)	Adverse outcome Group No. (%)
Normal vaginal delivery	59 (35%)	20 (24.4%)
Caesarian section	110 (65%)	62 (75.6%)
Total	169 (100%)	82(100%)

The mean of birth weight of 241 infants was 3677± 711 grams and 162(56.1%) of infants were macrosomic. There were 133 women in first trimester; the mean HbA1c level in First trimester was higher in the women with an adverse outcome group; HbA1c> 7 reported in 76.5% of adverse outcome group. There was a significant difference between HbA1c level and pregnancy outcome (*P* = 0.009) (Table 3).

Table 3: HbA1c value during first trimester and pregnancy outcome at TUH, 2016

HbA1c	Good outcome No. (%)	Adverse outcome No. (%)	Total No. (%)
≤ 6	22 (33.8%)	7(10.3%)	29 (21.8%)
6.1-7	11(17%)	9 (13.2%)	20 (15%)
7.1-8	13 (20%)	18(26.5%)	31(23.3%)
8.1-9	10 (15.4%)	14 (20.6%)	24 (18%)
≥ 9.1	9 (13.8%)	20 (29.4%)	29 (21.8%)
Total	65 (100%)	68 (100%)	133 (100%)

Table 4 showed 78 out of 175 pregnancies in second trimester had adverse outcome; 37% out of them with HbA1c ≤ 7, on other hand 63 % with HbA1c> 7 and HbA1c in Second trimester was higher in the women with an adverse outcome group (*P* = 0.002).

Table 4: HbA1c value during second trimester and pregnancy outcome at TUH, 2016

HbA1c	Good outcome No. (%)	Adverse outcome No. (%)	Total No. (%)
≤ 6	33(34%)	12 (15.4%)	45 (25.7%)
6.1-7	29 (29.9%)	17 (21.8%)	46 (26.3%)
7.1-8	19 (19.6%)	17 (21.8%)	36 (20.6%)
8.1-9	9 (9.3%)	19 (24.3%)	28 (16%)
≥ 9.1	7 (7.2%)	13 (16.7%)	20 (11.4%)
Total	97 (100%)	78 (100%)	175 (100%)

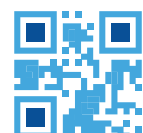


Table 5 showed that HbA1c in third trimester was higher in the women with an adverse outcome group ($P = 0.001$); 100 out of 229 pregnancy had adverse outcome; 54% out of them with $HbA1c \leq 7$ on other hand 46% with $HbA1c > 7$.

Table 5: HbA1c value during third trimester and pregnancy outcome at TUH, 2016

HbA1c	Good outcome No. (%)	Adverse outcome No. (%)	Total No. (%)
≤ 6	61(47.3%)	32 (32%)	93 (40.6%)
6.1-7	44 (34.1%)	22 (22%)	66 (28.8%)
7.1-8	14 (10.8%)	21 (21%)	35 (15.3%)
8.1-9	8 (6.2%)	14 (14%)	22 (9.6%)
≥ 9.1	2 (1.6%)	11 (11%)	13 (5.7%)
Total	129 (100%)	100 (100%)	229 (100%)

By the end of pregnancy, there were 52 pregnancies recorded with adverse outcome, stillbirth reported in 10(19.2%) of neonates, and neonatal deaths in 3(5.8%) of pregnancies, 19(36.5%) had major congenital anomalies and 20(38.5%) of them had minor congenital anomalies (Table 6).

Table 6: Neonatal out come at TUH, 2016

Complication	No.	%
Still birth	10	19.2 %
Neonatal death	3	5.8 %
Major congenital anomalies	19	36.5%
Minor congenital anomalies	20	38.5%
Total	52	100%

DISCUSSION

This study report most of patients had gestational diabetes followed by T 2 diabetes and minority have T1 diabetes this supported with Indian study which was carried on 2016 included 325 patients, 54.5% had gestational diabetes, 29.23% had T 2 diabetes and only 16.3% was T1 diabetes.⁵ We noticed more than sixty percent of diabetic women included in our study delivered by cesarean section with no difference in adverse and good out come in relation to mode of delivery; this going with study in Bahrain 2017 which showed rate of elective caesarean section increased from 12.5% in non-diabetic mothers to 50% in patients with pre-existing diabetes. In cases of allowing a trial of Labour, approximately 70% of patients with pre-existing diabetes had successful vaginal delivery with minimal morbidity.⁸ Macrosomia of infants is one of complications in uncontrolled diabetes in pregnancy, in present study more than 50% were macrosomic. González-Quintero et al.⁹ found that 15.7% women with uncontrolled blood glucose delivered macrosomic babies. In Royal Infirmary, Edinburgh, Scotland, U.K. one study conclude Glycaemic

control in the immediate pre-conception period and early first trimester appears to have a greater influence on birth weight than does glycaemic control during the later weeks of pregnancy.¹⁰

A significant relation between high HbA1c and adverse pregnancy out come in first, second and third trimesters (P value; 0.009, 0.002, 0.001 respectively) was found in current study, similarly; González-Quintero et al.⁹ found that women with suboptimal glycaemic control had significantly higher rates of adverse neonatal outcome, higher rate of caesarean delivery and higher level of nursery admission. Mane. L et al¹¹ from Barcelona-Spain; they found in a multiethnic population study, an early $HbA1c \geq 5.9\%$ measurement in first trimester identifies women at high risk for poorer pregnancy outcomes independently of gestational diabetes mellitus diagnosis later in pregnancy. Also supported by Capula et al.¹² in Italy showed that HbA1c at diagnosis and before delivery resulted a good predictor of adverse pregnancy outcome. On the other hand, a studies conducted by Nielsen et al^{6,13} reported that, relative risk calculations indicated a highly significant and consistent correlation between HbA1c values above 6.6% and adverse fetal outcome in the first trimester of pregnancy of type 1 mothers, without any indication of a cut-off level below which further improvement in HbA1c was of minor importance.

Our results not supported with Kerksen A. et al¹⁴ study, which proved that although glycaemic control contributes to birthweight in women with type 1 diabetes, the birthweight of an earlier born infant appears to be a much better predictor of the birthweight of a subsequent infant than HbA1c levels during pregnancy. It may, therefore, be used to identify patients at risk of giving birth to a macrosomic infant; so daily home monitoring of glucose levels, rather than HbA1c levels, should be used for assessment of maternal glycaemia during pregnancy. This also supported with USA study¹⁵, which conclude that on the basis of associations with adverse outcomes; HbA1c measurement is not a useful alternative to an oral glucose tolerance test (OGTT) in pregnant women.

In women with preexisting diabetes, early pregnancy HbA1c directly correlates with pregnancy outcomes. Our results showed adverse out come as still birth, neonatal death, major and minor congenital anomalies correlate with high HbA1c, this agreed by Jensen DM. et al¹⁶ study which found congenital malformation rate increased significantly at A1C above 10.4%, whereas perinatal mortality was increased even at HbA1C below 6.9%.

CONCLUSION

Strong association between high HbA1C values and pregnancy adverse outcome specific to every trimester, optimizing glycaemic control during pregnancy will reduce these adverse effects.

RECOMMENDATIONS

We recommend more studies to express more the correlation between glycaemic control and pregnancy adverse outcome in terms of HbA1c and blood glucose values in pregnant women.



REFERENCES

1. National Institute for health and Care Excellence (2015) Diabetes in pregnancy: management Diabetes in pregnancy: management from preconception to the postnatal from preconception to the postnatal period. *NICE guideline*.pp.55 available at: nice.org.uk/guidance/ng3
2. Abourawi F (2006) Diabetes mellitus and pregnancy, *Libyan J Med.* **1**(1), 28-41.
3. Buchanan TA and Xiang A (2005) Gestational diabetes mellitus, *J Clin Invest.* **115**(3), 485-491.
4. Metzger BE, Buchanan TA, Coustan DR, De Leiva A, Dunger DB, Hadden DR, et al. (2007) Summary and recommendations of the fifth international workshop-conference on gestational diabetes mellitus, *Diabetes Care* **30**(2), S251-260.
5. Buhary BM, Almohareb O, Aljohani N, Alzahrani SH, Elkaissi S, Sherbeeni S, et al. (2016) Glycemic control and pregnancy outcomes in patients with diabetes in pregnancy, *Indian J Endocrinol Metab.* **20**(4), 481-490.
6. Nielsen GL, Møller M, and Sørensen HT (2006) HbA1c in Early Diabetic Pregnancy and Pregnancy Outcomes, *Diabetes Care* **29**(12), 2612-2616.
7. Bhavadharini B, Mahalakshmi M M, Deepa M, Harish R, Malanda B, Kayal A, et al. (2017) Elevated glycated haemoglobin predicts macrosomia among Asian Indian pregnant women, *Indian J Endocrinol Metab.* **21**(1), 184-189.
8. Alomran BS, Alammari FH and Dayoub NM (2017) Pregnancy outcomes in relation to different types of diabetes mellitus and modes of delivery in macrosomic fetuses in Bahrain, *Journal of Taibah University Medical Sciences* **12**(1), 55-59.
9. González-Quintero V, Istwan NB, Rhea DJ, Rodriguez LI, Cotter A, Carter J, et al. (2007) The impact of glycemic control on neonatal outcome in singleton pregnancies complicated by gestational diabetes, *Diabetes Care* **30**(3), 467-470.
10. Gold AE, Reilly R, Little J, Walker JD.(1998) The effect of glycaemic control in the pre-conception period and early pregnancy on birth weight in women with IDDM, *Diabetes Care* **21**(4),535-538.
11. Mane. L, Flores-Le Roux J, Benaiges D, Rodriguez M, Marcelo I, Chillaron J, et al. (2017) Role of first-trimester HbA1c as a predictor of adverse obstetric outcomes in a multiethnic cohort, *J Clin Endocrinol Metab.* **102**(2), 390-397.
12. Capula C, Mazza T, Vero R and Costante G (2013) HbA1c levels in patients with gestational diabetes mellitus: relationship with pre-pregnancy BMI and pregnancy outcome, *J Endocrinol Invest.* **36**(11),1038-1045.
13. Nielsen GL, Sørensen HT, Nielsen PH, Sabroe S and Olsen J. (1997) Glycosylated hemoglobin as predictor of adverse fetal outcome in type 1 diabetic pregnancies, *Acta Diabetol.* **34**(3), 217-222.
14. Kerksen A, de Valk HW and Visser GHA (2005) Sibling birth weight as a predictor of macrosomia in women with type 1 diabetes, *Diabetologia* **48**,1743-174.
15. Lowe LP, Metzger BE, Dyer AR, Lowe J, McCance DR, Lappin TR, et al. (2012) Hyperglycemia and adverse pregnancy outcome (HAPO) study: associations of maternal A1C and glucose with pregnancy outcomes, *Diabetes Care* **35**(3), 574-580.
16. Jensen DM, Korsholm L, Ovesen P, Beck-Nielsen H, Moelsted-Pedersen L and Westergaard JG (2009) Periconceptional A1C and risk of serious adverse pregnancy outcome in 933 women with type 1 diabetes, *Diabetes Care* **32**(6),1046-1048.

