Clinical assessment of neonatal complications in infants born to diabetic mothers in Qena Governorate

Khaled A.Abdelbaseer[a],Heba M.Qubaisy[a],Mona M. Aboalabass[a]

[a]Pediatrics Department, Qena Faculty of Medicine South Valley University.

Back ground: Diabetes is one of the commonest and important metabolic disorders that affect the health of pregnant women and infant. About 3-10% of all pregnancies complicated by diabetes mellitus. There are two types of diabetes that occur in pregnancy, first is gestational diabetes that first diagnosed during pregnancy and pre-gestational diabetes which starts before pregnancy. Adverse outcome are not confined to pre-gestational diabetes alone. Maternal and infant morbidity and mortality are also high amongst gestational diabetes.

Objective: To detect relative frequency of various neonatal complications in infants born to diabetic mothers at Qena University Hospital and other hospitals inside Qena Governorate.

Patients and methods: This is a cohort prospective study of neonates admitted at NICU department or attended the outpatient clinic of nursery of Qena University Hospital and other hospital inside Qena Governorate between April 2018 to March 2019.

Results: In this cohort prospective study that included all patients who were either admitted at NICU department or attended the outpatients clinic of nursery at Qena University Hospital and other hospitals inside Qena Governorate between April 2018 to March 2019. Clinical evaluation were done on 220 cases during the period of the study. The age of the patients ranged with a mean andSD1.2 $\pm$ .7days, 164 infants have complications in our study with different presentations as difficult breathing (54.5%), cyanosis(16.8%), jitterness(14.5%), yellowish discoloration(16.8%). The relative frequency of complications were, respiratory(54.5%), metabolic(39.5%), cardiac(16.8%), jaundice(16.8%), macrosomia(12.3%), skeletal(9.5%), hematological(8.6%) and neurological(5%).

Conclusion: Bothmaternal diabetes ,gestational and pre-gestational diabetes mellitus lead to complications in infants born to those mothers. Respiratory complications were the most common complications among the cases. Cardiac, macrosomia and neurological complications were higher in pre-gestational diabetes than gestational diabetes.

Keyword, Diabetes mellitus, pregnancy, infants, complications.

Introduction

Maternal diabetes causes complications in the embryo/fetus that start in the uterus or present immediately after birth and could last a lifetime. Women with type 1 diabetes or type 2 diabetes diagnosed before or during the first trimester of pregnancy are at greatest risk of fetal congenital anomalies and spontaneous abortion. This risk associated with both frequent and sever hyperglycemia before conception and during organogenesis. The more sever the maternal hyperglycemia, the greater is the risk for fetal abnormalities(**Pearson et al., 2007**)

All types of diabetes mellitus in pregnancy, pre-gestational diabetes mellitus and gestational diabetes mellitus are associated with a significantly increased risk of short and long term maternal, fetal and neonatal adverse outcomes(**Wahlberg et al., 2016)**

Patients and Methods

This is acohort prospective study of neonates admitted at NICU of Qena University Hospital and other Hospitals inside Qena Governorate between April 2018 and March 2019.

Patients

Inculsion criteria of all neonates born to diabetic mothers attending Neonatal Intensive Care Unit and outpatient clinic of nursery,Qena University Hospital, South Valley University and other hospitals in Qena Governorate, during the study period .Patients were classified according to presence or absence of complications

Methodology

Detailed medical history was taken focusing on age of patients, sex ,residence, single or multiple,gestational age, type of delivery and family history of consanguinity, maternal diseases, type of diabetes mellitus, duration of diabetes, type of treatment for DM and presence of abortion or sibling death.Full clinical examinations was done for them focusing on general examination, anthropometric measures, vital signs, presence of jaundice or cyanosis, chest, cardiac,abdominal, neurological and skeletal examination. Investigations were done for them,random blood glucose as routine, complete blood picture, serum calcium in cases with convulsions or jitterness,serum bilirubin in jaundiced patients, X-ray in cases with cyanosis or respiratory distress, echocardiography if congenital heart disease was suspected.

Results

This is an analytical cohort prospective study that included all patients who were either admitted to NICU or attended the outpatient clinic of nursery at Qena University Hospital of South Valley University and other Hospitals at Qena Governorate within one year starting from April 2018 to March 2019. Clinical evaluation were done on 220 cases during the period of the study.

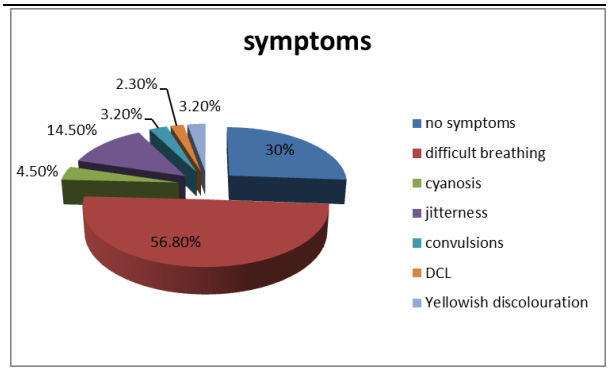
Table (1): The demographic data of the complicatedversus non-complicated cases

		Complicated group(A) (N=164)		**Non complicated group(B) (N=56)**		**P.**
		N.	**%**	**N.**	**%**	
Age	**Mean±SD**	**1.2±.8**		**1±0**		**.05**
Sex	Male	82	50	31	55.4%	.5
	Female	82	50	25	44.6	
Residence	Urban	84	51.2	31	55.4	0.2
	Rural	80	48.8	25	44.6	
Single or multiple	Single	157	95.7	52	92.9	.4
	multiple	7	4.3	4	7.1	
GA	FT	133	81.9	55	18.1	.002
	PT	31	68.2	1	2.2	
DM duration	<6years	72	43.9	18	32.1	.02
	>6years	11	6.7	0	0	
	GDM	81	49.4	38	67.9	
Type of delivery	NVD	2	1.2	9	16.1	0.000
	CS	162	98.8	47	83.9	
Other maternal diseases		12	7.3	1	1.8	.13
Treat	Diet	21	12.	41	73.	0.0

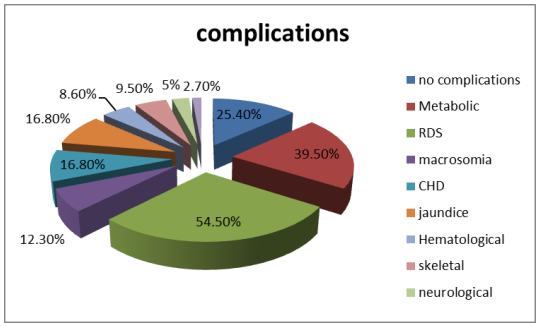
ment recei ved			8		2	00
	Oral hypo glyc emic	22	12. 4	11	19. 6	
	Insul in	121	73. 8	4	7.1	
Cons angui nity		62	37. 8	26	44. 6	,13 9
Abor tion		24	14. 6	5	8.9	.3
Siblin g death	0	155	94. 5	56	5.5	.07 3
	1-2	9	5.5	0	0	

GA: Gestational age, CS: Cesaeran section, FT: Fullterm, NVD: Normal vaginal delivery, PT: Preterm, DM: diabetes mellitus, GDM: Gestational diabetes mellitus.

Table 1: showing that the complicated group was 164 case while the non-complicated was 56 case. As regard age with a mean and SD 1.2±.8days in group (A), in group (B) age was in a mean and SD1±0 days. The male sex was 50% in group (A), while group (B) the male sex was 55.4%. No significant difference in the residence and single or multiple fetus pregnancy between two groups. Gestational age have a significance difference in complicated than non-complicated group. Duration of DM have a significance difference in complicated than non-complicated group. Type of delivery have high significance in complicated than non-complicated group. Also treatment received have a high significance difference in complicated than non-complicated group. Positive consanguinity in group (A) was 37.8%, while 44.6% in group (B). Incidence of abortion was 14.6% in group (A) while 8.9% was in group (B). Siblings death was 5.5% in group(A) ,in group (B) was 0%.



Figure(1) Distribution of symptoms in the studied cases.



Figure(2) Distribution of complications in the studied cases.

Table (2): The distribution of complications in gestational and pre-gestational DM.

Complications		Gestational N=132		Pre-gestational N=88		P value
		N.	%	N.	%	
No complications		42	31.1	14	17	.007
Respiratory	TTN RDS Congenital pneumonia	62 50 74	47 37.8 5.33	58 42 12 5	65.9 47.7 13.6 5.6	.006 .5 .03 .3
Metabol		47	35.	40	45	.0

ic	Hypoglycemia Hypocalcemia	416	629.54.5	391	.5422.3	7.07.03
Cardiac 1-CHD 2-Cardiomyopathy	VSD ASD TGA Associated CHD with primary lesions	1483114 5	10.66.12.3.810.6 3.8	2311661 4 7	26.112.56.86.8 15.9 8	.003.1.1.01.1 .2
Jaundice		21	15.2	16	19.3	.7
Macrosomia		12	9.8	15	16	.08
Skeletal(Limb deformity)		11	8.3	10	11.4	.5
Haematological	Bleeding disorder Polycythemia	963	6.15.2.9	1064	12.55.27.3	.5.5.3
Neurological	Convulsions Meningocele	350	2.33.80	824	9.12.34.6	.02.5.008
Death		2	1.5	4	4.5	.2

TTN: Transient tachypnia of neoborn, RDS: Respiratory distress syndrome, CHD: Congenital heart diseases, VSD: ventricular septal defect, ASD: Atrailseptal defect, TGA: Transposition of great arteries, Associated other CHD with primary lesions, tricuspid regurge(TR), aortic regurge(AR), mitral regurge(MR), patent ductusaretriouses(PDA), Pulmonary hypertention(PHT)

Respiratory complications have significance difference in gestational DM than in pre-gestational DM. Also there is high significance difference in cardiac complications in pre-gestational than in gestationalDM . Neurological complications have a significance difference in pre-gestational than gestational DM. No significance difference in metabolic, macrosomia, jaundice and haematological complications between gestational and pre-gestational diabetes mellitus.

Discussion

All the types of diabetes mellitus(DM) in pregnancy pre-gestational diabetes mellitus and gestational diabetes mellitus are associated with a significantly increased risk of short and long-term maternal, fetal and neonatal adverse outcomes(**Wahlberg et al., 2016).**

The risk of developing pregnancy complications is associated with increased maternal blood glucose levels and it is 2 to 5 times higher in women with type 1 diabetes mellitus compared to the general population. Furthermore, there is evidence that type 2 diabetes mellitus in pregnancy has a similar impact on infants as T1DM. Additionally PGDM has a greater negative impact on pregnancy outcomes compared to pregnancies complicated with GDM**(Wasimet al., 2015).**

As regard respiratory complications, it was found in(54.5%) of the studied cases ,this was in agreement with **Rayani et al., 2009**, who reported that IDMs characteristically have worse respiratory distress for gestational age than non IDMs. They added that, the risk of surfactant deficiency with respiratory distress syndrome and hyaline membrane disease developing in these infants is six times that of normal infants until gestational week 38 and is more common in IDMs whose mothers had unstable type 1 diabetes.

About (39.5%)were suffering from metabolic complications, and 80(36.4%) of these infants were hypoglycemic this was in agreement with **Alamet al., 2009,** who reported that approximately 15-25% of neonates delivered from women with diabetes during gestation develop hypoglycemia during the immediate newborn period.

As regard hypocalcemic complications, it was detected in (3.1%) of the studied cases and this was in disagreement with**Banerjee et al.,2003,** who reported that hypocalcemia in a high percentage of IDMs, at rates up to 50% .

The percentage of CHD of the studied cases was (16.8%)infants and this was agreement with **Rolo et al., 2010,** who reported that 30% of infants born to mothers with GDM and pre-existing diabetes present with cardiac malformations.

About(16.8%) of infants were suffering from jaundice and this was agreement with **Metzger et al., 2008**, who reported hyperbilirubinemia more frequently in infants born to diabetic mothers. It is not a serious complication if non-toxic levels are diagnosed and treated.

Macrosomia was detected in (12.3%) of the studied cases and this was in agreement with **Son et al., 2010,** who reported that the risk for macrosomia increases in later gestation in those fetuses whose mothers' diabetes is poorly controlled.

The percentage of skeletal complications was (9.5%) and this was in agreement with **Mitanchez et al., 2015,**who reported that skeletal malformations were around 15% in birth of diabetic mother. The risk of skeletal malformations in neonates of mothers with GDM was lower than the neonates of mothers with PGDM.

As regard the hematological complications percentage was 19(8.6%) and this was in agreement with **Modanlou et al., 2012,** who reported that, polycythemia (a haematocrit that is > 65%) occur in 13- 33% of cases is more commonly determined in neonates from mothers with DM. Relative cell hypoxia determines an increased fetal erythropoietin secretion, which in return increases fetal erythrocyte production.

The percentage of neurological complications was(5%) and this was in agreement with **Anoon et al., 2003,** who reported that infants of diabetic mothers are prone to neurologic impairments, mainly due to perinatal asphyxia, birth traumas and metabolic disorders.

The mortality rate was (2.7%) and this was in agreement with**Nergato et al.,2012**, who reported that the perinatal mortality rate was around 8%, and maternal mortality rate was up to 10% in infants born to diabetic mothers.

As regard, pre-maturity,it was detected in (18.9%) and this was in agreement with **Hawdon et al., 2011,** who reported, preterm birth, in about 10% of the pregnancies, in 50% of women with DM and is 4.8 times higher in pregnant women with DM than in the general population.

There is a significance difference in CS delivery in the studied cases and this was in agreement with **Durockovaet al., 2017**, who reportedthat, women with DM generally have higher caesarean section rates. The frequency of this procedure in pregnant women with DM worldwide is about 42.7-78%, compared to a much lower rate in the general population (20%).

About, (56.8%) of the studied cases their mothers were used insulin therapy and this was in agreement with **Singhet al., 2007**, who reported that insulin therapy should be used if the plasma glucose goals are not met on two or more occasions during a 1 to 2 week follow-up. They have been shown to be safe mainly in type 1 diabetic women, but they are also used in women with GDM.

As regard oralhypoglycemic drugs it was found in(15%) of cases and this was in agreement with **Tertti et al., 2008,** who reported that, oral hypoglycemic agents (glyburide and metformin) have been shown

to be a possible alternative to insulin in the medical treatment of GDM.

There is a significance difference between the CHD, neurological and macrosomic complications in pre-gestational DM and gestational DM and this was in agreement with **Mitrovic et al., 2014,** who reported that, patients with GDM had significantly less feto-maternal complications as compared to known diabetic patients. And this occur as hyperglycemia during the period of organogenesis is responsible for congenital malformations and miscarriage specially to known diabetic patients. Additionally, GDM usually develops in the second half of the pregnancy and the period of organogenesis is over so it is unlikely that patients manifest such problem.

Complications in infants of maternal use of insulin have a significance difference and this was in agreement with **Zuckerwisa et al.,2012,** who reported that poor control was mostly seen in patients taking insulin, also lack of education, noncompliance and infrequent follow-up of patients poses difficulty in better glycemic control. So glycemic control was single most important underlying factor which was related to the development of complications.

References

Alam M, Raza SJ, Sherali AR,Akhtar AS.(2006). Neonatal complications in infants born to diabetic mothers. J Coll Physicians Surg Pak, 16(3):212-5.

Anoon SS, Rizk DE, Ezimokhai M. (2003). Obstetric outcome of excessively overgrown foetuses. J Perinat Med, 31: 295-301.

Banerjee S, Mimouni FB, Mehta R. (2003). Lower whole blood ionized magnesium concentration in hypocalcemic infants of gestational diabetic mothers. Magnes Res, 16:127–30.

Duraucova L, Kristufkova A, Korbel M. (**2017**).Pregnancy and neonatal outcomes in women with type 1 diabetes mellitus,118(1)56-60.

Hawdon JM. (**2011).** Babies born after diabetes in pregnancy: what are the short- and long-term risks and how can we minimise them? BestPract Res ClinObstetGynaecol, 25:91-104 .

Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR et al.,(2008). Hyperglycemiaand adverse pregnancy outcomes, 358:1991-2002.

Mitanchez D, Yzydorczyk C, Siddeek B. (**2015**). The offspring of diabetic mother, short and long term complications. Best pract Res Chin ObstectGynacol, 29(2):256-69.

Mondanlou HD. (2012). Maternal obesity, diabetic pregnancy and infant of diabetic mother. Neonatal Today;7(3):1-9.

Mitrovic M, Stojic S, Tesic D. (2014). The impact of diabetes mellitus on the course and outcome of pregnancy.Vonjnosanit Pregl, 71(10):907-14.

Negrato C, Mattar R, Gomes M. (2012). Adverse pregnancy outcomes in women with diabetes.DiabetolMetabSyndr, 4(1):41.doi:10.1186/1758-5996-4-46.

Pearson DWM, Kernaghan D, Lee R. (2007). Scottish Diabetes in pregnancy study group. Short communication: the relationship between pre-pregnancy care and early pregnancy loss, major congenital anomaly or perinatal death in type I diabetes mellitus. BJOG 114:104-107.

Rayani HH, Gewolb IH, Floras J.(2009).Glucose decreases steady state mRNA content of hydrophobic surfactant proteins B and C in fetal rat lung explants. ExpLung Res.,25:69–79.

Rolo LC, Marcondes Machado Nardozza L, Araujo Junior E. (2011). Reference curve of the fetal ventricular septum area by the STIC method: preliminary study. Arg Bras Cardiol, 96:386–92.

Singh C, Jovanovic L. (2007). Insulin analogues in the treatment of diabetes in pregnancy.ObstetGynecolClin North Am, 34(2):275-291.

Son GH, Kwon JY, Kim YH, Trimble ER, Chaovarindr U, Coustan DR. (2010). Maternal serum triglycerides as predictive factors for large-for-gestational age newborns in women with gestational diabetes mellitus.ActaObstetGynecolScand, 89:700–4.

Tertti K, Ekblad U, Vahlberg T,Rönnemaa T. (2008). Comparison of metformin and insulin in the treatment of gestational diabetes: A retrospective, case-control study. Rev Diabet Stud. 5(2):95iabetic mother. Neonatal Today,7(3):1-9.

Wahlberg J, Ekman B, Nystrom L. (2016). Gestaional diabetes; glycemic predictor for fetalmacrosomia and maternal risk of future diabetes. Diabetes Res Clinpract, 114;99-105.

Wasim T, Wasim A, Ashraf M. (2015). Feto maternal outcome in pregnant patients with diabetes, 21(2):108-12.

Zuckerwise LC, Werner EF, Pettker CM.(2012). Pre-gestational diabetes with extreme insulin resistance: use of U-500 insulin in pregnancy. ObstectGynecol, 120:439-442.