INCIDENCE OF CONGENITAL HEART DISEASE AMONG INFANTS OF DIABETIC MOTHERS IN SULAIMANI

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ABSTRACT

Background

Infant of diabetic mother (IDM) is those infants born to mothers who suffered diabetes mellitus. There are two types of IDM, Gestational diabetes and Pregestaional diabetes. Both have the effects on morphogenesis of infants' cardiovascular system and increase the risk of congenital heart disease.

Objectives

To find out the incidence of congenital heart disease among infants of pregestational diabetic mothers.

Patients and Methods

In a prospective study that included 32 infants of pregestational diabetic mother (PGDM) age less than 7 days at the neonatal intensive care unit NICU of Sulaimani-Shar hospital and NICU of Sulaimani-Maternity hospital during the period April 1st, 2018 to March 31st, 2019.Echocardiography and abdominal ultrasound were done for all babies.

Results

There were 32 infants of PGDM during the study period. Mean mothers' age was 35.43±6.49, Last hemoglobin A1C (mean±SD) 7.23±1.17. Males and females were 17(53.1%) and 15(46.9%) respectively. Gestational age; 21 (65.6%) were term and 11 (34.4%) were preterm. Birth weight (mean±SD) 3.45±0.69. Twenty-eight (87.5%) were delivered by caesarian section C/S and 4 (12.5%) by normal vaginal delivery NVD. Echocardiography finding revealed 24 (75%) infants had CH, most common CHD were hypertrophic cardiomyopathy HCMP (40.5%), PDA (28%), ASD (18.9%). Most cases of CHD are term, male, delivered by caesarian section, mothers' body mass index between 25 to 29.9, type 2 diabetic and less than 5 years diagnosed. Abdominal ultrasound showed 26 (84.4%) were normal 5 (15.6%) were abnormal.

Conclusion

According to our study, most of the newborn of PGDM had congenital heart disease. Most common CHDs were hypertrophic cardiomyopathy, PDA and septal defects.

Keywords: *Infants of diabetic mother; Congenital heart disease; Sulaimani.*

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INTRODUCTION

Diabetes mellitus relates to maternal and neonatal-perinatal morbidity and mortality [1].

There are two types of diabetic Mellitus: Type I diabetes occurs due to a lack of pancreatic islet beta cells, caused by autoimmune destruction and resulting in an absence of insulin. Type II diabetes: occurs due to insulin resistance because beta-cell dysfunction which related to interaction between genetic, environmental and immunological factors including diet, physical activity and obesity [2-4].

IDMs are infants born to mother who suffer diabetes mellitus. There are two types of IDMs: First: Gestational diabetic mother GDM: is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. Second: Pregestaional diabetic mother PGDM: A woman who is diabetic before pregnancy.

Normally maternal acclimatization to pregnancy by alterations in the carbohydrate metabolism, mostly in late second and early third trimesters of pregnancy, develop insulin resistance in response to increase human placental lactogenic, progesterone, and cortisol, which increases glucose and amino acid transfer to the fetus [5].

Metabolic and hormonal change in diabetic-pregnancy cause maternal problems and effect on organogenesis of fetus at 3-8 weeks of gestation. Mother insulin is not transported through the placenta to the fetus, fetal hyperinsulinism occurs due to too much transport of glucose from mother to fetus. The Abnormal metabolic environment is teratogenic on fetus cause increased incidence of cardiac, Musculoskeletal and CNS malformation [6].

The morbidities associated with IDMs are respiratory distress, congenital malformations, growth restriction, hypoglycemia, polycythemia, hypocalcemia, and Hypomagnesemia. However, associated macrosomia and increased prevalence of Caesarean section contribute to higher mortality [7, 8].

Pregestaional diabetes mellitus (type one or type two) in the mother increases the risk of a CHD in the child by 4-folds [9, 10]

Treatment of cardiac disorder in IDMs is the same as other newborn with the same condition. Beta-blocker such as propranolol may be used to relieve the outflow obstruction that is seen with a septal hypertrophy. [11]

This study aimed to find out the incidence of congenital heart disease among infants of pregestational diabetic mothers in Sulaimani.

PATIENTS AND METHODS

This is a prospective study carried out on newborn babies admitted to the NICU of Sulaimani Maternity hospital and NICU Sulaimani Shar hospital, for diabetic mother who are known cases of diabetes mellitus diagnosed before their conception; during the period Apr.2018 to Mar. 2019.

Inclusion criteria

- Infants born to previously diagnosed mother with type 1, and type 2 diabetes mellitus before her pregnancy(PGDM) whether they are receiving treatment, diet control or none.
- Newborn whether preterm, term and post-term.

Exclusion criteria

- Age more than 7 days excluded because those infants who have HCMP by increasing their age increase their chance to resolve and make it not seen by echocardiography.
- Gestational diabetic mother

The parents consented before the interview about their participation in the study. For each case data collected about the age of mother, gravida, Para, abortion, death, and previous history of big babe. How many years she is diabetic, types of her diabetic, controlling of her blood sugar, high weight and BMI of the mother, her last HBA1c, mother smoked or not, paternal diabetes present or not and mode of delivery cesarean section C/S or NVD.

The babies were also examined for gestational age, birth weight, and sex. Examination also carried out for gross congenital anomaly, sings of birth trauma, sings of hypoglycemia, Polycythemia, signs of RDS, cyanosis present or not. Chest and precordial examination for presence of murmur.

Also, echocardiography and abdominal ultrasound done for all cases

Data analysis was performed using Statistical Package for the Social sciences (SPSS)- 24 (IBM Corp, Armonk, NY). Numerical variables were compared by Chi-

square test and continuous data were analyzed using the students' test. P-value ≤ 0.05 considered a significant

RESULTS

During the study period data from 32 babies of PGDM were recorded and analyzed. All of them in first week of their life. The mean mothers' age is 35.43±6.49 years. The body mass index BMI is like following: 7 cases between 18.5-24.9, 12 cases between25-29.9, and 13 cases more than 30.

None of the mothers were primigravida. Obstetric history were taken. 53.1% gravida G2 to G4 and 46.9% > G5. 81.2% were type 2 DM. 96.9% has no History of previous delivery of a child with congenital anomaly. 37.5% on Oral hypoglycemic agent OHA + Diet and 18.7% on Insulin + Diet.

All mother of pregestational diabetic has no smoker. All of them has no history of parental diabetes except one. Table 1 summarizes all baseline demographic characteristics of mothers.

Table 2 summarized details about the newborn babies' gestational age, birth weight, gender and mode of delivery. Most common CHDs present between BMI 18.5 to 24.9. CHD between G2-G4 and G > 5 were equal each one 12 cases, 4.1% of CHDs has history of child death.

All cases of CHD has no History of previous delivery of a child with congenital anomaly, 11(45.8%) has Previous history of a big baby, 76.9% of CHD mostly seen in those mothers has type 2 diabetic mellitus and 54.1% less than 5 years diagnosed.

Male: female 13:11 54.1% of CHD are male p value 0.026 this result is significant.

All babies of CHD has no history of mother smoking p vale 0.0001 this result significant.

According to cardiac murmur 29.2 % of CHD has cardiac murmur.

Out of 32 Babies of IDMs 24 (75%) had abnormal echocardiography. Among abnormal echo study 18.7% had hypertrophic cardio myopathy HCMP, 12.4% patent ducts arteriosus PDA+ HCMP, 9.3% has just PDA

Abdominal ultrasound result, Abdominal ultrasound done to all of them 27(84.4%) normal, 1(3.1%) single kidney, 2(6.3%) Mild abdominal free fluid, 1(3.1%) Remnant of ophthalomesentric duct with intestinal perforation, 1(3.1%) Mild left kidney pelvic dilatation with PUJO. All these 5 cases of abnormal abdominal ultrasound result has also abnormal echo study.

About the visible anomaly, just 2 cases have visible anomaly, one of them has erb'spalsy +club foot echocardiography has PDA+HCMP. The other one has both ear anotia + right hand syndactly echocardiography result is PDA+ASD+HCMP. Their mothers were on oral hypoglycemic agent for controlling of their glucose.

All Relationship between CHD and demographic characteristic of mother and birth of babies summarized in Table 3 .

Echocardiographic, abdominal ultrasound result, cardiac murmur and visible congenital anomaly are summarized in Table 4.

Hypertrophic cardiomyopathy mostly found in mother BMI between 25 to 29.9 but PDA more in mother's BMI more than 30, other details relationships between echocardiography and mother's age and BMI shown in Table 5.

Hypertrophic cardiomyopathy was mostly present in term, female, product of C/S and with no cardiac murmur. But PDA was mostly present in preterm, male, product of C/S and no cardiac murmur. All other dials of relationships Echocardiography findings to baby's neonatal history are shown in Table 6.

Eighteen point seven percent have hypertrophic cardiomyopathy and 12.4% have PDA with HCMP, all details of echocardiography finding showed in Figure 1.

The abdominal ultrasound in 84.4% of the cases was normal, 15.6% was abnormal and the abnormalities are shown in Figure 2.

Table 1. Socio-demographic and clinical characteristics of the mothers

Variables	N (%)
Mothers age (mean±SD)	35.43±6.49
BMI	
Less than 18.5	0(0)
18.5-24.9	7(21.9)
25-29.9	12(37.5)
More than 30	13(40.6)
Gravida	
2-4	17(53.1)
>5	15(46.9)
Para	
1-2	11(34.4)
3-5	21(65.6)
Abortion	
0	11(34.4)
1	14(43.8)
2	7(21.9)
Death	
0	30(93.8)
1	1(3.1)
2	1(3.1)
History of previous delivery of a child with congenital anomaly	
No	31(96.9)
Yes	1(3.1)
Previous history of a big baby	
No	17(53.1)
Yes	15(46.9)
How many years she has diabetes	
Less than 5	19(59.4)
More than 5	13(40.6)
Types of diabetic	
Type 1	6(18.8)
Type 2	26(81.2)
Controlling of her blood sugar	
Oral hypoglycemic agent + Diet	12(37.5)
Insulin + Diet	6(18.7)
Diet	2(6.3)
All	12(37.5)
Last HbA1C (mean±SD)	7.23±1.17
Smoking	
No	32(100)
Yes	0(0)
Parental diabetes	
No	31(96.9)
Yes	1(3.1)

Table 2. Birth characters of the babies.

Variables	N (%)
Gestational age	
Term	21(65.6)
Pre-term	11(34.4)
Post-term	0(0)
Sex	
Male	17(53.1)
Female	15(46.9)
Birth weight (mean±SD)	3.45±0.69
Mode of delivery	
C/S	28(87.5)
NVD	4(12.5)

Table 3. Relationship between variables and CHD.

Variables	N (%)	CHD absence N (%)	CHDpresence N (%)	P-value
Total case	32(100%)	8(25%)	24(%75)	
BMI				
Less than 18.5	0(0)	0	0(0)	
18.5-24.9	7(21.9)	2(25%)	5(20)	0.728
25-29.9	12(37.5)	2(25%)	10(41.6)	
More than 30	13(40.6)	4(50%)	9(37.4)	
Gravida				
2-4	17(53.1)	5(62.5)	12(50)	0.539
>5	15(46.9)	3(37.5)	12(50)	
Para				
1-2	11(34.4)	3(37.5)	8(33.3)	0.829
3-5	21(65.6)	5(62.5)	16(66.6)	
Abortion				
0	11(34.4)	3(37.5)	8(33.3)	
1	14(43.8)	5(62.5)	9(37.5)	0.500
2	7(21.9)	0(0)	7(29.1)	
Death				
0	30(93.8)	7(87.5)	23(95.8)	
1	1(3.1)	0(0)	1(4.1)	0.582
2	1(3.1)	1(12.5)	0(0)	
Hx. of previous delivery of a child with congenital anomaly				
No	31(96.9)	7(87.5)	24(100)	0.380
Yes	1(3.1)	1(12.5)	0(0)	
Hx. of a big baby				
No	17(53.1)	4(50)	13(54.1)	0.837
Yes	15(46.9)	4(50)	11(45.8)	
How many years she has diabetes				
Less than 5	19(59.4)	4(50)	13(54.1)	0.838
More than 5	13(40.6)	4(50)	11(45.8)	
Types of diabetes				
Type 1	6(18.8)	2(25)	4(16.6)	0.600
Type 2	26(81.2)	6(75)	20(83.4)	
Controlling of her blood sugar				
Oral hypoglycemic agent + Diet	12(37.5)	3(37.5)	9(37.5)	
Insulin + Diet	6(18.7)	2(25)	4(16.6)	0.895
Diet	2(6.3)	1(12.5)	2(8.3)	
All	12(37.5)	2(25)	9(37.5)	
Last HbA1C (mean±SD)	7.23±1.17			
Smoking				
No	32(100)	0(0)	24(100)	0.0001
Yes	0(0)	0(0)	0(0)	
Parental diabetes				
No	31(96.9)	0(0)	23(95.8)	0.054
Yes	1(3.1)	8(100)	1(4.2)	
Gestational age				
Term	21(65.6)	6(75)	15(62.5)	
Pre-term	11(34.4)	2(25)	9(37.5)	0.605
Post-term	0(0)	0(0)	0(0)	
Sex				
Male	17(53.1)	4(50)	13(54.1)	0.026
Female	15(46.9)	4(50)	11(45.8)	
Mode of delivery				
C/S	28(87.5)	7(87.5)	21(87.5)	1.00
NVD	4(12.5)	1(12.5)	3(12.5)	
Cardiac murmur				
No	24(75)	7(87.5)	17(70.8)	0.345
Yes	8(25)	1(12.5)	7(29.2)	
Visible congenital anomaly				
No	30(93.8)	8(100)	22(91.6)	0.726
Yes	2(6.2)	0(0)	2(8.4)	

Table 4 . Clinical findings of the babies.

Variables	N (%)
Cardiac murmur	
No	24(75)
Yes	8(25)
Visible congenital anomaly	
No	30(93.8)
Yes	2(6.2)
Abdominal ultrasound	
Normal	27(84.4)
Single kidney	1(3.1)
Mild abdominal free fluid	2(6.3)
Remnant of omphalomesenteric duct with intestinal perforation	1(3.1)
Mild left kidney pelvic dilatation with PUJO	1(3.1)
Echocardiography	
Normal	8(25)
HCMP	6(18.7)
PDA	3(9.3)
ASD	2(6.3)
VSD	1(3.1)
PS	1(3.1)
TR,AR,HCMP	1(3.1)
PDA,HCMP	4(12.4)
ASD,HCMP	2(6.3)
PDA, ASD, HCMP	2(6.3)
PFO	2(6.3)

Table 5. Relationship of the Echocardiography findings with mothers' age and BMI.

	Echocardiography N (%)											
Variables	**Normal**	**HCMP**	**PDA**	**ASD**	**VSD**	**PS**	**TR AR HCMP**	**PDA HCMP**	**ASD HCMP**	**PDA ASD HCMP**	**PFO**	**p.value**
BMI Less than 18.5	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0.793
18.5-24.9	2(25)	2(33.3)	1(33.3)	1(50)	0(0)	0(0)	0(0)	1(25)	0(0)	0(0)	0(0)	
25-29.9	2(25)	3(50)	2(66.7)	0(0)	0(0)	1(100)	1(100)	1(25)	1(100)	0(0)	1(100)	
More than 30	4(50)	1(16.7)	0(0)	1(50)	1(100)	0(0)	0(0)	2(50)	1(100)	2(100)	1(100)	
Mothers age (mean±SD)	34.87±6.99	34.16±2.78	32.66±9.07	36.5±7,77	33±0	33±0	48±0	33.25±10.93	33.5±0.70	38±1.41	42.5±0.70	0.684

Table 9. Relationship of the Echocardiography findings with babies' neonatal history.

Variables	Echocardiography N (%) Normal	HCMP	PDA	ASD	VSD	PS	TR AR HCMP	PDA HCMP	ASD HCMP	PDA ASD HCMP	PFO	p.value
Gestational age												
Term	6(75)	5(83.3)	2(66.7)	1(50)	1(100)	1(100)	0(0)	0(0)	2(100)	1(50)	2(100)	
Pre-term	2(25)	1(16.7)	1(33.3)	1(50)	0(0)	0(0)	1(100)	4(100)	0(0)	1(50)	0(0)	0.161
Post-term	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
Birth weight (mean±SD)	3.46±0.58	3.43±0.72	4±0.5	3.6±1.27	4.3±0	3±0	2.8±0	3.12±1.18	3.45±0.07	3.60±0.84	3.25±0.49	0.880
Sex												
Male	4(50)	1(16.7)	2(66.7)	1(50)	1(100)	1(100)	0(0)	3(75)	1(50)	1(50)	2(100)	0.541
Female	4(50)	5(83.3)	1(33.3)	1(50)	0(0)	0(0)	1(100)	1(25)	1(50)	1(50)	0(0)	
Mode of delivery												
C/S	7(87.5)	5(83.3)	3(100)	2(100)	1(100)	1(100)	1(100)	2(50)	2(100)	2(100)	2(100)	0.703
NVD	1(12.5)	1(16.7)	0(0)	0(0)	0(0)	0(0)	0(0)	2(50)	0(0)	0(0)	0(0)	
Cardiac murmur												
No	7(87.5)	5(83.3)	2(66.7)	2(100)	1(100)	1(100)	0(0)	2(50)	1(50)	1(50)	2(100)	0.564
Yes	1(12.5)	1(16.7)	1(33.3)	0(0)	0(0)	0(0)	1(100)	2(50)	1(50)	1(50)	0(0)	

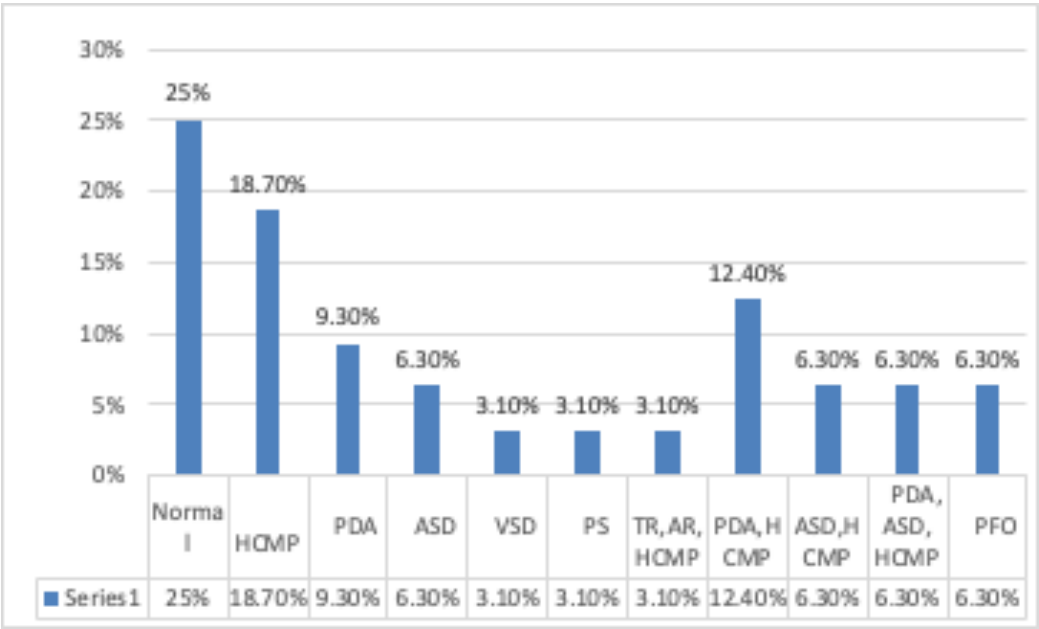

Figure 1. Distribution of the patients according to the echocardiographic findings.

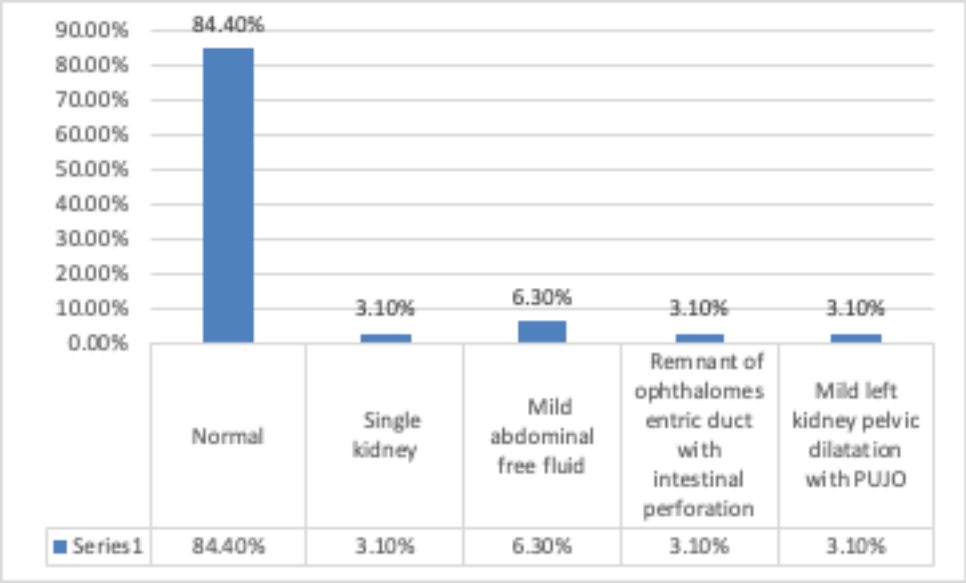

Figure 2. Distribution of the patients according to the abdominal ultrasound

DISCUSSION

In this current study among those cases of CHDs male were predominant, (53.1%) were male (46.9%) were female, In Nina Øyen et al 2016 [12] male (43.96%) and female (56.03%) female is predominant. This discrepancy may be due to different sampling methods or may be related to that CHDs is already most common among male newborns than female newborns.

According to Previous history of a big baby didn't find any study. In this study, 53.1% hadn't the history of big baby, 46.9% has a history of a big baby. This is maybe related to that 40.6% has a history of diabetic Mellitus more than 5 years and all of them multiparas gravida more than two. Poor control of their blood sugar increases their chance to have a previous history of a big baby.

All 32 cases of IDMs are multiparas and gravida ≥ G2. As mentioned in study Mohamed Akhatim Alsammani et al 2015 DM found in %9 of multiparous G1 to G4 and 12% of grand multiparous >G5. Found that there was a significant association between multiparty and adverse pregnancy outcomes like fetal macrosomia, DM and pregnancy induced hypertension. [13]According to gestational age (65.6%) are term and (34.4%) are preterm, the result of the prematurity is near the results In Sibai BM et al 2000. [14] The overall rates of preterm delivery were higher among women with pregestational diabetes mellitus (38%) whether they are spontaneous or indicated preterm delivery.

M Behjati et al 2011 [15] in their prospective study, echocardiography was done to 75 full-term newborns of IDMs. Newborns were classified into two subgroups according to the types of the mothers' diabetes: pre-gestational and gestational: 26 (35%) and 49 (65%) respectively. in these 26 cases of pregestational DM 21 (80.7%) had CHD exclusion HCMP. The most common echocardiographic findings in pregestational diabetic are shown in Table 7 with detailed comparisons between that study and the current study.

Table 7. Comparisons between M Behjat 2011 [15] and this study .

M Behjat 2011 pregestational DM No.26 cases	Our study pregestational DM No. 32 cases
Echo result: PDA:15 HCMP: 8 VSD: 3 ASD: 1 CoA: 1 TGA: 1	Echo result: Normal : 8 HCMP: 6 PDA :3 ASD:2 VSD:1 PS:1 TR,AR,HCMP: 1 PDA,HCMP : 4 ASD,HCMP : 2 PDA, ASD, HCMP: 2 PFO: 2
CHD excluding HCMP: 21 (80.7%) PDA is most common	CHD exclusion HCMP: 18 (56.25%) PDA is most common

In M Behjati et al 2011[15] study generally there is a comparison between CHD in pregestational and gestational DM, found that PDA is no significant difference between gestational and pregestational DM, but other CHD like HCMP, VSD, ASD and COA in pregestational DM is more risky than gestational DM. these results are nearly similar to the results in our study also CHD in pregestational diabetic are 75% includes HCMP, PDA, ASD, VSD and PFO. Also in M Behjati et al 2011, the incidence of congenital heart diseases was higher in macrosomic than non-macrosomic infants of diabetic mothers .in our study cases with CHD mean of their birth weight is 3.46 kg.

Nina Øyen 2016 [12], congenital heart disease among PGDM s were (3.17%).in our research 32 cases of PGDM, 24 of them has CHDs (75%) . their result is too much lower than our result this is maybe related to a big sample size or good antenatal care or effectiveness of their program in prevention of diabetes in pregnancy early screening and diagnosis with rapid initiation of treatment and close follow-up surveillance could reduce the morbidity and mortality associated with pregestational and gestational diabetes . Also in Nina Øyen 2016 study CHD mostly present in those mothers has DM more than 5 years .in current study (59.4%) had DM less than 5 years and (40.6%) had DM more than 5 years and CHD present more in mothers who had DM less than 5 years. In Nina Øyen 2016 most common CHD is septal defect and second is conotruncal defect. In Than T. Hoang 2017[16] the most common CHD was also septal defect and second most common was right ventricular outflow tract anomaly RVOT mostly pulmonary stenosis. But in our study, most common CHDs was HCMP, second was PDA, third was septal defect. This discrepancy in that result is due to that in both of these studies Nina Øyen 2016 and then T. Hoang 2017 didn't include cases of HCMP and PDA so also in our study if we exclude HCMP and PDA the septal defect will be the most common CHD.

In our current study, those cases with CHD their mother's last HBA1c are between 4-9.5. In Roman Starikov et al 2013. Studied on 535 patients, 30 (5.6 %) of them delivered an infant with CHD. Among the patients with poor glycemic control, 8.3 % (n = 17) delivered an infant with CHD, whereas 3.9 % (n = 13) of those with an HbA1c level lower than 8.5 delivered an infant with CHD. Poor glycemic control in early pregnancy is associated with an increased risk of CHD in offspring. The incidence of CHD in patients with adequate glycemic control still is sufficiently high to justify routine fetal echocardiography for all gravidas with preexisting diabetes regardless of HbA1c level. [17]

In Correa et al 2008 [18] study, there is Significant associations were seen between PGDM and isolated cases of seven non cardiac defects, 1)anencephaly and craniorachischisis,2)hydrocephalus, 3) anotia or microtia, 4) cleft lip with or without cleft palate, 5) atresia of anorectal,6) bilateral renal agenesis or hypoplasia, 7) limb deficiencies. In this current study visible congenital anomaly seen in 2 cases (6.25%) one of them has both ear microtia and syndactyly of right hand the other one has club foot plus Erb's palsy.

In our current study, all 32 cases of pregestational diabetic mother abdominal ultrasound done within one week of their age, (84.4%) were normal, (15.6%) abnormal; (3.1%) Single kidney, (6.3%) mild abdominal free fluid, (3.1%) remnants of omphalomesenteric duct with intestinal perforation, (3.1%) mild left kidney pelvic dilatation with PUJO. Phillipa B. Sharpe et al 2005[19] a population-based cohort study Between 1986 and 2000, the prevalence of congenital anomalies in the infants of mothers with preexisting diabetes mellitus, gestational diabetes mellitus, or impaired glucose tolerance was significantly higher than in the total population; relative risk = 2.01 (1.66–2.43) and 1.19 (1.08–1.31), respectively.

The current study has shown that eighty-seven per cent (87.5%) of neonates were delivered by C/S. This result is higher than the result found by Cousins which was (45%). [20] This high result may be due to macrosomia, bad obstetric history, failure of induction of labour, previous history of C/S and obesity.

In conclusion, most of the newborn of pregestational diabetic mother has congenital heart disease; the most common CHDs were hypertrophic cardiomyopathy, PDA, and septal defects.

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