

Research Article

Study of Echocardiographic Changes in Macrosomic Neonates

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Abstract

Background: Macrosomia defined as birth-weight over 4,000 g irrespective of gestational age or greater than the 90th percentile for gestational age. Macrosomia affect 3-15% of all pregnancies. Macrosomia is associated with numerous perinatal and maternal complications.

Objectives: To assess the echocardiographic changes of macrosomic Infants of Diabetic Mothers (IDMs), macrosomic Infants of Non Diabetic Mothers (INDMs), and Average for Gestational Age infants (AGA).

Patients and methods: A cohort prospective case control clinical study includes 78 newborns admitted and attended the outpatient clinic of Neonatal Intensive Care Unit (NICU), Pediatric department, Qena University Hospital.

Results: Our study showed highly statistical significant difference in the mean of Interventricular Septum (IVS) in macrosomic IDMs and macrosomic INDMs (5.3±1.44 mm, 5±1.5 mm respectively) in

comparison to control group (3.7±0.8 mm). Higher frequency of Asymmetrical Septal Hypertrophy (ASH) among macrosomic IDMs (51.9%) compared to other groups with statistically significant difference.

Conclusion: Asymmetrical septal hypertrophy was the commonest echocardiographic change found among IDMs, and HCM (Concentric Hypertrophy) was the commonest echocardiographic change found among INDMs. Both maternal diabetes (whatever its type) and macrosomia found to be risk factors for septal hypertrophy. Cases with asymmetrical septal hypertrophy due to maternal diabetes showed spontaneous improvement, while patients with concentric hypertrophy due to macrosomia of INDMs showed no reduction in septal or left ventricular posterior wall thickness.

Keywords: Echocardiographic measures; HA1C; Neonatal macrosomia; RBG; Risk factors

Introduction

The American College of Obstetricians and Gynecologists (ACOG) defined macrosomia as birth-weight over 4,000 g irrespective of gestational age or greater than the 90th percentile for gestational age [1]. Macrosomia affect 3-15% of all pregnancies [2]. Macrosomia is associated with numerous perinatal and maternal complications [3]. Gestational diabetes is the most important predictor of macrosomia births. The history of macrosomic births in the pregnancy period was also other predictors of such births [4]. Of course, maternal obesity, increasing age, and parity were also considered as the main risk factors for fetal macrosomia. When associated with diabetes, fetal macrosomia indicates poor maternal glucose control, and these infants are at risk of stillbirth [5].

The incidence of gestational diabetes is increasing worldwide, exposing large numbers of infants to hyperglycemia whilst in utero. This exposure may have a long-term negative impact on the cardiovascular health of the offspring. Variations exist in the reported prevalence rates of GDM within and between countries of the GCC with rates as low as 4.2% in Oman to as high as 24.9% in United Arab Emirates (UAE). Reported rates in other GCC countries are 16.3% in Qatar, 10.1% in Bahrain and 2.7% - 12.5% in Saudi Arabia [6]. The MENA region had the highest comparative prevalence of diabetes in the world in 2012, with four countries in the region among the top ten worldwide in terms of prevalence. The International Diabetes Federation (IDF) estimates that by 2030, patients with diabetes will double to current estimates of up to 59.9 million in the MENA region. Even though epidemiological studies document high diabetes prevalence in each country, there are specific regions within each country that have higher prevalence of diabetes than originally stated.

An elevated frequency of septal hypertrophy was found in IDMs. Septal hypertrophy suggests that diabetic mothers were not in good metabolic control, because it has been reported that careful glucose control during pregnancy reduces the incidence and severity of hypertrophic cardiomyopathy in the fetus but may still not prevent accelerated fetal cardiac growth [7]. Large Gestational Age (LGA) of INDMs also showed septal hypertrophy [8].

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Patients and Methods

The study included 78 newborns admitted and attended the outpatient clinic of Neonatal Intensive Care Unit (NICU), Pediatric department, Qena University Hospital. Informed consent for participation in the study was obtained from the parent or legal guardian who accompanied the infant to the hospital. The exclusion criteria were: Infants with infectious, immunological, allergic, neoplastic, dysmorphic and antenatal (irradiation or drugs except for treatment of DM) were excluded from the study [6].

Infants were divided into three groups: group (A): compromised 28 macrosomic Infants of Diabetic Mother (IDMs), group (B): 25 macrosomic Infants of Non Diabetic Mothers (INDM), and group (C): 25 Average for Gestational Age infants (AGA). The mothers of group A: 14 had (type I) diabetes, 4 had (type II) and 10 had gestational diabetes mellitus. Of group A, 28 infants were macrosomic according to their gestational ages [9]. We used birth weight greater than 4000 gm to define macrosomia in full term babies, as this is the most commonly proposed definition [1].

Data collection

A standardized questionnaire will be completed for all the infants including the following:

Maternal history includes:

- Maternal age and Parity
- Type of diabetes mellitus (type I, type II or gestational)
- Therapeutic history during pregnancy
- History of delivery of previous macrosomic babies
- Type of delivery
- History of obstructed labor

Fetal history includes:

- Birth weight
- Gestational age
- History of respiratory distress or cyanosis
- History of pallor, plethora, petechiae
- History of congenital malformation

Laboratory methods

Random blood glucose: Random blood glucose was done for newborns for assessment of fetal hypoglycemia [Serum or whole blood glucose levels of less than 40 mg/dL within the first 24 hours after birth].

HbA1c: HbA1c was done for diabetic mothers for assessment of diabetic control at late pregnancy, sub optimally controlled diabetic mothers (HbA1c \geq 7 mg/dL) [10].

Echocardiogram:

- Echocardiogram was performed by general electronics Vivid S5, 6 MHz phased array probe
- Cardiac measurements were determined by cross-sectional M-mode echocardiography performed in the first three days after birth. Appropriate transducers of 6 MHz were used to define cardiac structures. The echocardiograms were obtained in the standard precordial positions, The echocardiograms were obtained in the

standard precordial positions, echocardiographic measurements including LVESd/LVEDd (LVESd: Left Ventricular End-Systolic Diameter, LVEDd: Left Ventricular End-Diastolic Diameter, IVS: Interventricular Septum thickness, PW: Posterior Wall thickness, IVS/PW: Interventricular Septum thickness to Posterior Wall thickness ratio, Ao: Aorta diameter, LA: Left Atrium diameter, FS%: Shortening Fraction, EF%: Ejection Fraction. All measurements were made at end-diastole in cm) for control group & macrosomic infants of nondiabetic mothers & infants of diabetic mothers

- 2D for assessment of heart anatomy
- Pulsed and continuous waves dopplar for assessment of flow across the valves
- Color flow mapping was used for assessment of presence of shunt and its direction. All measurements were compared to measurement of Mung Park, 2008

Statistical analysis

Data will be analyzed using Statistical Package for Social Sciences (SPSS) software program (version 20). Qualitative variable will be recorded as frequencies and percentages and will be compared by chi-square test. Quantitative measure will be presented as mean \pm Standard Deviation (SD) and will be compared by student t-test. Regression analysis and correlation between different variable will be performed as indicated. p value $<$ 0.05 will be significant.

Results

The results of the study on macrosomic neonates are shown in tables 1-8 and Figures 1,2.

	Control (n=25)		Group A IDM (n=28)		Group B INDM (n=25)	
	No.	%	No.	%	No.	%
Maternal age (years) (mean \pm SD)	23.6 \pm 3.3		28.94 \pm 4.1		27.6 \pm 4.3	
Type of DM						
Type I	0	0.0	14	50.0	0	0.0
Type II	0	0.0	4	15.0	0	0.0
GD	0	0.0	10	35.0	0	0.0
Type of Drug						
Insulin	0	0.0	25	89.0	0	0.0
Type of delivery						
Cs	13	52.0	27	96.0	23	92.0
NVD	12	48.0	1	4.0	2	8.0
Parity (n) (mean \pm SD)	1.6 \pm 1		2.4 \pm 2		2 \pm 1.5	
Similar condition of previous macrosomic babies	0	0.0	15	53.0	12	48.0

Table 1: Maternal demographic data of the included mother in the study.

The Mean values of maternal ages in the study group were (mean \pm SD of 28.94 \pm 4.1 years, mean \pm SD of 27.6 \pm 4.3 years and mean \pm SD of 23.6 \pm 3.3 years) for macrosomic IDMs group, macrosomic INDMs and control group respectively. As regard type of delivery it was found that caesarian section shows high percentage frequency among macrosomic IDMs and macrosomic INDMs (96%, 92% respectively) in comparison to control group (52%). In group A (macrosomic IDMs) it was found that 14 infants were born to type I diabetic mothers (50%), 4 infants were born to type II diabetic mothers (15%) and 10 infants were born to gestational diabetic mothers (35%). As sequence 25 diabetic mothers treated by insulin therapy (89%). the percentage frequency of similar condition of previous macrosomic babies in control, IDMs and INDMs (0%-53%-48%) respectively.

	Control (n=25)		Group A IDM (n=28)		Group B INDM (n=25)		p value
	No.	%	No.	%	No.	%	
Resuscitation							
Yes	2	8.0	15	53.0	12	48.0	<0.05*
NICU admission							
Yes	2	8.0	12	43.0	9	36.0	<0.05*

Table 2: Neonatal data of the studied infants versus control group.

Infant need for resuscitation was significantly high among macrosomic babies in comparison to control group (p<0.05). As a sequence a significantly high percentage of macrosomic babies were admitted to NICU.

Showed neonatal data of the studied infants versus control group.

	Group A IDM (N=28)	Group B INDM (n=25)	Control (n=25)	p value
	Mean+SD	Mean+SD	Mean+SD	
Birth weight (Kg)	4.18+0.28	4.11+0.28	2.95+0.3	<0.001**
HR (beat/min)	141.11+10.85	135+11.28	134.52+11.4	<0.05*
RR (cycle/min)	61.44+11.02	60.64+11.79	51.28+8.15	<0.001**
SBP (mm Hg)	72+5.36	67.4+6.23	54.4+6.4	<0.001**
DBP (mm Hg)	43.4 +1+3.6	39.96 + 3.82	32.6+4.57	<0.001**
Temp (c)	36.77+0.4	37.1 + 0.35	36.79+0.54	<0.05*
Length (cm)	48.15+2.03	49 + 1.96	45.76+2.37	<0.001**
HC (cm)	34.78+0.8	34.76+0.97	33.4+1.38	<0.001**

Table 3: Anthropometric measurements and vital data of the studied infants versus control group.

There was a significantly high mean values of each of birth weight, head circumference, respiratory rate, heart rate, systolic and diastolic blood pressure in macrosomic IDM in comparison to control group (p<0.001, p<0.001, p<0.001, p<0.05 and p<0.001 respectively). Also a significantly high mean values of each of length and body temperature in macrosomic infants of nondiabetic mothers in comparison to control group (p<0.001 and p<0.05 respectively).

Symptom	Group A IDMs (n=28)		Group B INDM (n=25)		Control		p value
	No.	%	No.	%	No.	%	
Macrosomia	28	100.0	25	100	0.0	0.0	NS
Hypoglycemia	21	75.0	0	0.0	0	0.0	-
RDS	8	28.0	3	12.0	4	16.0	NS
TTN	11	39.0	14	56.0	1	4.0	<0.05*
Jaundice	6	21.0	2	8.0	3	12	NS
Plethoric	8	28.0	0	0.0	0	0.0	<0.001**
Cyanosis	11	39.0	4	16.0	2	8.0	<0.05*
Apnea	2	7.0	0	0.0	0	0.0	NS
Convulsion	0	0.0	0	0.0	0	0.0	-

Table 4: Clinical data of the studied infants versus control group.

The percentage frequency of each of hypoglycemia, TTN, plethora, cyanosis were significantly high among macrosomic infants of diabetic mothers (75%-28%-39% respectively) in comparison to other groups (p<0.001, p<0.05, p<0.001, p<0.05 respectively).

CHD	Control (n=25)		Group A IDM (n=28)		Group B INDM (n=25)		p value
	No.	%	No.	%	No.	%	
ASD secundum	1	4.0	2	6.0	7	28.0	NS
VSD	2	8.0	1	4.0	1	4.0	
PDA	0	0.0	4	14.0	2	8.0	

Table 5: Relative frequency of the Congenital Heart Disease (CHD) of the studied infants.

No statistically significant difference regarding the frequency of occurrence or the type of the defect among the three groups.

Echocardiographic Measures	Group A IDM (n=28)	Control (n=25)	p value
IVS (mm)	5.3±1.44	3.7±0.8	<0.001**
LVEDd (mm)	17±3.95	16.8±2.1	NS
LVESd (mm)	10.3±3.06	10.1±1.8	NS
LVPWd (mm)	3.78±1.01	3±0.5	<0.05*
RV (mm)	9.84±3.79	10.12±2.8	NS
FS%	39.78±5.34	40.2±4.8	NS
PA (mm)	10.26±2.9	9.28±2.28	NS
LA (mm)	13±3.27	13.12±2.83	NS
AAO (mm)	10.33±1.82	9.48±1.05	<0.05*
AAO flow (cm.sec)	88.26±15.46	91.48±23.01	NS

Table 6: Echocardiographic changes in macrosomic Infants of Diabetic Mothers (IDMs) (group A) versus control group.

There were significantly high mean values of each of IVS, LVEWd, and AAO of macrosomic IDM in comparison to control group.

Ratio (IVS/LVPWd)	Group A IDM (n=28)		Group B INDM (n=25)		Control (n=25)		p value
	No.	%	No.	%	No.	%	
<1.4	13	48.1	16	64.0	20	83.3	<0.05*
≥1.4	15	51.9	9	36.0	4	16.7	

Table 7: Relative frequency of the Asymmetrical Septal Hypertrophy (ASH) of the studied infants.

IVS/LVPW (RATIO) ≥ 1.4

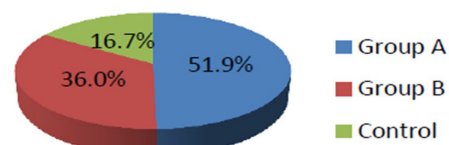


Figure 1: Relative frequency of the (ASH) of infants study.

Relative frequency of the (ASH) of infants study: The percentage frequency of the Asymmetrical Septal Hypertrophy (ASH) among macrosomic IDM was significantly high in comparison to other groups (p<0.05).

Echocardiographic Measures	Control (n=25)	Group B INDM (n=25)	p value
IVS (mm)	3.7±0.8	5±1.5	<0.001**
LVEDd (mm)	16.8±2.1	17.8±1.7	NS
LVESd (mm)	10.2±1.8	11.1±1.4	NS
LVPWd (mm)	3±0.5	3.4±0.9	NS
RV (mm)	10.1±2.8	10.4±2.8	NS
FS%	40.2±4.8	38.2±4.5	NS
PA (mm)	9.3±2.3	10±1.2	NS
LA (mm)	13.1±2.8	13.7±2.2	NS
AAO (mm)	9.5±1	10.9±1.4	<0.001**
AAO flow (cm.sec)	91.5±23	91.9±14.3	NS

Table 8: Echocardiographic changes in macrosomic infants of non diabetic mother (group B) versus control group.

A significantly high mean values of each of IVS, and AAO of macrosomic INDM in comparison to control group ($p < 0.001$).

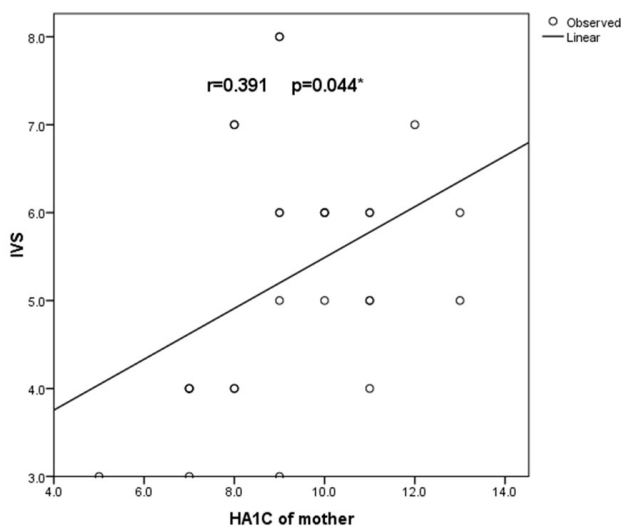


Figure 2: Correlation between Interventricular Septum thickness (IVS) and HA1c in macrosomic INDM (group A).

There was statistically significant positive correlation with ($r = 0.391$) ($p < 0.05$) between IVS and HA1c in macrosomic infants of diabetic mother (group A).

Discussion

The present study (Table 1), showed increased mean maternal age in macrosomic (IDMs) group and in macrosomic of (INDMs) group 28.94 ± 4.1 years old and 27.6 ± 4.3 years old respectively than control group (AGA) 23.6 ± 3.3 years, this was in agreement with Bloomington, (2012) who reported that old women are more likely to have a baby diagnosed with fetal macrosomia [11]. As regard type of delivery it was found that the frequency of caesarian section in macrosomic IDMs and macrosomic INDMs is higher than control group (AGA), this was in agreement with Mathew et al., who reported that

macrosomic births increased the section deliveries [4]. Also it was found that history of similar condition of previous macrosomic births increase risk of having another baby who has macrosomia, this was in agreement with Mathew et al., who reported that history of macrosomic births were determined as the main predictor of macrosomia following gestational diabetes [4]. As regard type of drug it was found 89% of the diabetic mothers were treated by insulin, this was in agreement with Vela-Huerta et al., who reported that 90.9% of diabetic mothers were treated by insulin [12].

In present study (Table 2), it was found that high frequency of Infants of Diabetic Mothers (IDMs) that needed resuscitation 15 infants (53%), and the frequency of macrosomic of INDMs were found 12 infants (48%), this was in agreement with Ikeda et al., who reported that Infants of Diabetic Mothers (IDMs) are at an increased risk of respiratory distress, and operative delivery due to macrosomia also increases the risk for Transient Tachypnoea of the Newborn (TTN) [13].

Our study showed that macrosomic Infants of Diabetic Mothers (IDMs) exhibits higher NICU admissions (Table 2), this was in agreement with Vela-Huerta et al., who reported that Infants of Diabetic Mothers (IDMs) mainly having congenital anomalies, heart disease, significant respiratory illness, or hypoglycemia need for NICU for continued care and access to subspecialists [14].

In the present study (Table 3), it was found that macrosomic Infants of Diabetic Mothers (IDMs) and (INDMs) group showed significant difference regarding weight, length, and head circumference, this was in agreement with Ng SK et al., who reported that there was a significant difference between macrosomic and normal newborns regarding weight, height, and head size, and in disagreement with Krishnaveni et al., who reported that a basic anthropometric indexes did not differ between the LGA and AGA groups with the exception of head circumference [1,15]. Regarding blood pressure macrosomic infants of diabetic mother exhibited higher systolic and diastolic blood pressure, this was in agreement with Patel et al., who reported that offspring of diabetic women have been shown to have higher systolic and diastolic blood pressure than those born to non diabetic women [16]. Respiratory rate and heart rate were found to be higher in Infants of Diabetic Mothers (IDMs), this was in agreement with Vela-Huerta et al., who reported that Infants of Diabetic Mothers (IDMs) mainly having congenital anomalies, heart disease and significant respiratory illness [14].

In present study (Table 4), it was found that 21 infants of macrosomic Infants of Diabetic Mothers (IDMs) (75%) presented with neonatal hypoglycemia in first few hours after birth (1/2 h-1 h-2 h), 12 infants were corrected by administration of glucose and oral feeding as early as possible, and 9 infants presented with severe hypoglycemia that require NICU admission for IV administration of glucose (bolus dose 2 mL/kg of glucose 10% followed by a continuous infusion of glucose 10% at an infusion rate of 6-8 mg/kg/min), this was in agreement with Vela-Huerta et al., showed that hypoglycemia was found in (72.7%) in IDMs, and in agreement with Mäkelä et al., who reported that hypoglycemia is common presentation in IDMs, caused by hyperinsulinemia due to hyperplasia of fetal pancreatic beta cells consequent to maternal-fetal hyperglycemia [12,17]. Our study showed that high frequency of plethoric babies 28% among macrosomic IDMs, this was in agreement with Cetin et al., who

reported that 34% of macrosomic IDMs presented with polycythemia caused by increased erythropoiesis triggered by chronic fetal hypoxia [18].

Regarding the frequency or type of the defect of CHD there was no significant difference among the three groups (macrosomic Infants of Diabetic Mothers (IDMs) IDMs - macrosomic infants of non diabetic mothers INDMs and control group) (Table 5). Echocardiographic evaluation of the studied macrosomic IDMs revealed that two (6%) neonates had a trial septal defect of the secundum type (ASD II), one (4%) of them had VSD, and four (14%) had PDA. These anatomic abnormalities were hemodynamically insignificant, this was disagreement with Potter et al., who reported that cardiac malformations in IDMs are five times higher than in normal pregnancies [10].

Macrosomic Infants of Diabetic Mothers (IDMs) showed significant difference regarding IVS and LVPWd compared to control group (Table 6), this was in agreement with Russell et al., who reported that myocardial hypertrophy is frequent in fetuses of diabetic mothers and it is thought to be secondary to maternal and fetal hyperglycemia [19].

In present study (Table 7 and Figure 1), it was found that 51.9% of macrosomic IDMs had asymmetrical hypertrophy of septum, this was in agreement with Sardesai et al., who reported that HCM in macrosomic IDMs is characterized by disproportionate hypertrophy of septum and ventricular walls [20]. By following up after 3 months our study showed that all cases of HCM in form of (asymmetrical septal hypertrophy) among IDMs improved and return to normal dimensions but HCM in the infants of non-diabetic mother INDM not improved, this was in agreement with Leopold et al., who reported that all cases of HCM among IDMs return gradually to a normal size in the first months after birth in contrast to the infant of a non-diabetic mother where HCM is usually progressive and associated with a very poor prognosis [21].

Macrosomic Infants of Non Diabetic Mothers (INDMs) show high significant difference regarding IVS (Interventricular Septum) compared to the control group (AGA) (Table 8), which was in agreement with Lindsay et al., who reported that LGA-INDMs showed septal hypertrophy [8].

Positive statistically significant correlation between IVS and HbA1c in infants of diabetic mothers (Figure 2), this was in agreement Ullmo et al., who reported an association between poor maternal glycemic control and HCM [22]. Also in agreement with Weber et al., reported that good maternal glycemic control during pregnancy assures a normal fetal cardiac growth. On the contrary, Rizzo et al., found an increase in the cardiac size in fetuses of diabetic mothers, in spite of a careful metabolic control [23,24].

Conclusion

Asymmetrical septal hypertrophy was the commonest echocardiographic change found among IDMs, and HCM (concentric hypertrophy) was the commonest echocardiographic change found among INDMs. Both maternal diabetes (whatever its type) and macrosomia found to be risk factors for septal hypertrophy. Cases with asymmetrical septal hypertrophy due to maternal diabetes showed spontaneous improvement, while patients with concentric hypertrophy due to macrosomia of INDMs showed no reduction in septal or left ventricular posterior wall thickness.

Conflict of interest

All authors declare that they have not received any support from any organization for the submitted work. No financial relationships with any organizations that might have an interest in the submitted work and no other relationships or activities that could appear to have influenced the submitted work.

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