

## Effect of Gestational Diabetes on Interventricular Septum Thickness in Newborns in the Golestan Province, Iran

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### ABSTRACT

**Background and objectives:** Despite advances in prenatal care, there is a high rate of morbidity and mortality in infants of diabetic mothers. Interventricular septal hypertrophy is a well-known congenital heart abnormality in neonates of mothers with gestational diabetes. In this study, we investigate the effect of gestational diabetes mellitus on interventricular septum thickness.

**Methods:** In this cross-sectional cohort study, 42 neonates from mothers with gestational diabetes mellitus and 42 neonates from non-diabetic mothers were selected from gynecology ward of Sayyad Shirazi Hospital in Gorgan (Iran) between April 2016 and April 2017. Ventricular septum thickness in neonates was measured by M-mode echocardiography. Comparison of septum thickness and frequency of septal hypertrophy between the two groups was performed using t-test, Mann-Whitney test and chi-square test. All statistical analyses were preformed in SPSS 16 at significance level of 0.05.

**Results:** The mean septum thickness was  $4.51 \pm 1.58$  mm in newborns of non-diabetic mothers and  $5.84 \pm 1.44$  mm in newborns of diabetic mothers ( $P < 0.001$ ). Septal hypertrophy (thickness of  $\geq 6$  mm) was significantly more common in newborns of diabetic mothers ( $P = 0.029$ ). In addition, we found no significant difference in septum thickness between newborns of diabetic mothers receiving diet or insulin therapy.

**Conclusion:** Overall, our findings suggest that there is a significant correlation between gestational diabetes and ventricular septal hypertrophy. In addition, glycemic control with diet or insulin therapy has no significant impact on septum thickness.

**Keywords:** Gestational diabetes mellitus, ventricular septum, Neonates

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## INTRODUCTION

Development of diabetes during pregnancy increases the risk of morbidity and fetal death (1). Gestational diabetes accounts for 80% of all cases of diabetes during pregnancy, followed by pre-pregnancy diabetes and glucose intolerance (2). Changes in glucose metabolism during pregnancy have short- and long-term effects on the fetus (3, 4).

Hypertrophic cardiomyopathy affects 10% to 40% of infants born to diabetic mothers. The functional impact of septal hypertrophy in infants can vary from an asymptomatic form to congestive heart failure due to left ventricular outflow tract obstruction. Cardiac hypertrophy in infants of non-diabetic mothers is rare (5, 6), while gestational diabetes causes an 18-fold increase in the relative risk of developing septal hypertrophy (7).

The exact causes of gestational diabetes-induced septal hypertrophy in fetus are not clear. Although hyperglycemia is the hallmark of diabetes, results of studies on the possible correlation of maternal glycemia with fetal septal hypertrophy have been inconsistent (6, 8-13).

Neonates born to mothers with glycemic control are also at risk of developing septal hypertrophy (14-16). Surprisingly, infants of diabetic mothers under strict glycemic control, despite having very low glycosylated fetal hemoglobin (HbF1c) levels, are also at high risk for septal hypertrophy (17).

Although the effect of gestational diabetes on interventricular septum thickness have been investigated in different populations (1, 4, 18-21), a limited number of studies have been performed on this issue in Iran (22, 23). Therefore, we aimed to study interventricular septum thickness in neonates of diabetic and non-diabetic mothers in an Iranian population.

## MATERIALS AND METHODS

In this cross-sectional cohort study, study population consisted of all pregnant women referred to the gynecology ward of Sayyad Shirazi Hospital of Gorgan (Iran) between April 2016 and April 2017. Subjects were selected via convenience sampling. Mothers were divided into a diabetic and non-diabetic group based on medical history and

interviews. The interventricular septum thickness was measured in newborns from both groups (each group contained 42 newborns). Written consent was obtained from the subjects' parents after explaining the research objectives. Inclusion criteria for mothers were no history of hyperlipidemia, preeclampsia/eclampsia, hypertension, hypothyroidism, hyperthyroidism, smoking, drug abuse, alcoholism and heart, liver and renal failure. Neonates with hypoglycemia or electrolyte imbalance, hyperbilirubinemia, preterm birth, as well as those requiring hospitalization for any reason such as phototherapy were excluded.

Interventricular septum thickness was determined by fetal two-dimensional Doppler echocardiography using M-Mode (1). A 12-lead electrocardiogram (ECG) was also performed for all newborns for 10 seconds at the heart clinic of the hospital by the same operator.

Comparison of diabetic and non-diabetic mothers in terms of demographic variables and characteristics of newborns were also performed. Neonates of diabetic mothers were divided into two groups based on their glycemic control during pregnancy and insulin therapy. Normal distribution of data for septal hypertrophy was assessed using the Kolmogorov-Smirnov test. Given the non-normal distribution of data, comparisons were made between the two groups using the Mann-Whitney test. Neonates were divided into two groups based on interventricular septum thickness of greater than 6mm and less than 6mm, and differences between the groups were assessed using chi-square test. All statistical analyses were performed using SPSS 16 at significance level of 0.05.

## RESULTS

Table 1 shows demographic characteristics of diabetic and non-diabetic mothers. There was no significant difference between gender of newborns from diabetic and non-diabetic mothers. The mean age of newborns at the time of study did not differ significantly ( $P=0.43$ ). In addition, the mean birth weight of newborns did not differ significantly ( $P=0.57$ ).

**Table 1. Comparison of demographic characteristics of neonates of diabetic mothers and non-diabetic mothers in the Golestan Province, Iran**

Variable		Non-diabetic	Diabetic	P-value
Gender of newborn	Male	19 (45%)	20 (47.7%)	1
	Female	23 (54.7%)	22 (52.3%)	
Type of delivery	Caesarean section	28 (66.6%)	33 (78.5%)	0.53
	Vaginal delivery	14 (33.3%)	11 (26%)	
Birth weight (kg)		3.07±1.2	3.04±1.14	0.57
Age of newborn (days)		5.5±1.38	5.12±1.68	0.43
Length of pregnancy (weeks)		38.5±2.15	38.1±1.57	0.37

**Table 2. Mean ventricular septum thickness in neonates of mothers with gestational diabetes mellitus and in those from non-diabetic mothers in the Golestan Province, Iran**

Variable	Newborns of diabetic mothers	Newborns of non-diabetic mothers	P-value
Mean septum thickness (mm)	5.84±1.44	4.51±1.58	0.001
Frequency of septal hypertrophy	17 (38%)	6 (14.2%)	0.029

**Table 3. Comparison of mean interventricular septum thickness between newborns of mothers under diet therapy and insulin therapy**

Variable	Under insulin therapy	Under diet therapy	P-value
Mean interventricular septum thickness (mm)	6.14±1.35	5.69±1.5	0.34

As shown in table 2, the mean septum thickness was 4.51±1.58 mm in newborns of non-diabetic mothers and 5.84±1.44 mm in newborns of diabetic mothers ( $P<0.001$ ). Septal hypertrophy was significantly more common in newborns of diabetic mothers ( $P=0.029$ ).

The effect of insulin and diet therapy on incidence of septal hypertrophy was investigated in newborns of diabetic mothers. For this purpose, mothers were divided into two groups of insulin therapy ( $n = 14$ ) and diet therapy ( $n=28$ ). As shown in table 3, mean septum thickness did not differ significantly between the two groups ( $P=0.34$ ).

## DISCUSSION

The present study is one of the few to investigate the relationship between the incidence of interventricular septal hypertrophy in neonates and maternal gestational diabetes in Iran. Our findings

showed that ventricular septum was thicker in neonates of diabetic mothers than in neonates of non-diabetic mothers. On the other hand, glycemic control in diabetic mothers during pregnancy had no effect on ventricular septum.

Many studies have reported a significant relationship between gestational diabetes mellitus and septal hypertrophy (1, 4, 18, 19, 22). For example, in a study by Russell et al., ventricular septum was significantly thicker in fetus of mothers with gestational diabetes in the last trimester of pregnancy (18). Ghandi et al. also reported that septal hypertrophy was more common in neonates of diabetic mothers (22).

Although some studies reported no association between maternal glucose level and septal hypertrophy in neonates (10, 11), septal hypertrophy occurs in 35% of neonates from diabetic mothers.

In the present study, we found no significant difference in septum thickness between newborns of diabetic mothers receiving diet or insulin therapy. A high incidence of septal hypertrophy has been reported in diabetic mothers with strict glycemic control. Some studies also reported that septal hypertrophy is significantly more common in diabetic mothers with strict glycemic control and glycosylated hemoglobin levels significantly lower than fetal glucose levels (14, 16, 22).

Other factors resulting from gestational diabetes, such as nutrient transfer via altered placenta or hormonal imbalance may be related to septal hypertrophy (24). A study by Gordon et al. found that rapid and temporary exposure to hyperglycemia results in ventricular septal hypertrophy in newborns, even in those from non-diabetic mothers (24).

In the present study, we did not measure glucose levels during the pregnancy period, which can be considered a limitation of our study. In addition, the small population size limited elimination of the effect of possible confounding factors.

#### CONCLUSION

Overall, our findings suggest that there is a significant correlation between gestational diabetes and ventricular septal hypertrophy. In addition, glycemic control with diet or insulin therapy has no significant impact on septum thickness.

#### DECLARATIONS

##### *Funding*

This study was supported by a grant from the Ischemic Disorders Research Center of the Golestan University of Medical Sciences, Iran.

##### *Ethics approvals and consent to participate*

The study was approved by the ethics committee of the Golestan University of Medical Sciences, Iran. A written informed consent was taken from all subjects prior to participation.

##### *Conflict of interest*

The authors declare that there is no conflict of interest.

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