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Prenatal detection of fetal anomalies and its prevalence by sonography in pregnancies complicated by pre-gestational diabetes mellitus

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Diabetes mellitus is being diagnosed in 0.3% of women at the reproductive stage of their life. Prevalence is around 10% in the urban Srilankan population.

Objectives
1. to analyze the prevalence of fetal malformations in pre-gestational diabetic pregnancies compared to uncomplicated non diabetic pregnancies.
2. to evaluate the clinical utility of a comprehensive program inclusive of clinical features, glycemic assessment and prenatal detailed ultrasound with fetal echocardiography for congenital anomalies in pregnancies complicated by diabetes mellitus.

Methodology
prospective cohort study carried out in a maternity hospital- Colombo, Sri Lanka between August 2006 to August 2008 .A 789pre-gestational diabetic women who were registered in hospital clinics during Aug 2006 to Aug 2008 and their newborns were compared with age and parity matched low risk non diabetic population of 780 antenatal mothers for the development of fetal malformations

Study Instruments
Interviewer administered questionnaire included detailed history, examination checking glycemic assessment and comprehensive fetal ultrasonography inclusive of a standard four-chamber view of the heart and detailed power Doppler fetal echocardiography according to ISUOG standards. Glycemic control was set at 90-130mg/dl at pre and postprandial values and target HbAiC was set at below 6.2%

Results
anomalies were identified in 49 of 789(6%) fetuses and neonates: 12 central nervous system, 03 abdomincal wall defects, 03 diaphragmatic hernias, 08 renal tract defects , 03 cystic hygromas, 02 isolated hydrothorax ,04 hydrops with multiple congenital abnormalities, 04 gastro intestinal malformations, 02 limb defects and 04 cardiac abnormalities were detected prenatally. 03 cardiac lesions 02 limb defect (VACTERAL) and down

syndrome fetus detected postnatally. The results were compared with age and parity matched non diabetic control group of 780 routine visits mothers and antenatal admissions having 21/780 (2.7%) with only 1 cardiac abnormality this was significant
p< 008 at (95% CI 0.77 – 5.03).

Recommendations and Conclusions
This study demonstrates and confirms the view that pre-gestational diabetic pregnancy, despite the improved metabolic control, is still a strong risk factor for alterations in fetal development leading to fetal malformations.
This study also demonstrate the advantage of a comprehensive program to detect fetal anomalies in pregnancies complicated by pre-gestational diabetes mellitus focusing further attention towards detecting fetal cardiac abnormalities.
Key words: congenital malformations, PGDM, diabetic pregnancy, prenatal ultrasound diagnosis, newborns

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INTRODUCTION

Diabetes mellitus is being diagnosed in 0.3% of women at the reproductive stage of their life. Prevalence in Srilanka around 10% in urban population (Annual Health Bulletin (2013). Metabolic disturbances related to glucose intolerance and hyperglycemias are known to affect the health and life of women planning motherhood. They can also impair the development of fetuses and newborns. Observations indicating a relationship between pre-gestational maternal diabetes and the occurrence of malformations were issued already by the end of the 19th century. Since then, numerous epidemiological studies have confirmed the assumption that a poorly controlled diabetes mellitus in pregnant women favors the development of fetal malformations (Ylinen, Aula, Stenman, Kesaniemi-Kuokkanen, and Teramo, 1984).

The frequency of fetal developmental defects in diabetic pregnancies is 2–5 times higher compared to uncomplicated gestations. In the population of infants born to diabetic mothers, malformations are found in 2.7–16.8%, while in that born to healthy mothers they were only in 2–3% infants.(Oztunc, Madazli, Yuksel, Gokalp, and Oncul, 2014).

The early period of fetal development, i.e. the period of organogenesis (up to the 12th week of gestation), is of particular vulnerability in this respect. The influence of teratogenic factors during this period cause mostly large congenital defects, mainly of the central nervous system (CNS), the cardiovascular (CVS), skeletal, and urogenital systems (Wong, Chan, Cincotta, Oats, and McIntyre, 2002).

The results of numerous studies show that the occurrence of congenital defects is much more frequent in infants born to mothers who presented with increased glycemia during the first trimester of pregnancy (Key, Giuffrida, and Moore, 1987). The etiology of malformations appearing in diabetic pregnancy is not entirely clear, but the results of many studies indicate particular metabolic states such as hyperglycemia, hypoglycemia, hyperketonemia, excessive formation of free oxygen radicals, undue production of insulin like growth factors, disturbed lipid and protein (lipoprotein) metabolism, deviation of the arachidonate metabolic pathway, divergent myoinositol metabolism, as well as a deficient supply of vitamins and microelements as the potential causal factors (Lucas, Leveno, Williams, Raskin, and Whalley, 1989). The unfavorable effect of diabetes mellitus on fetal development may also be derived from the impairment of blood vessel flow due to morphological changes in the capillary and arterial vessel walls. Among numerous effects of hyperglycemia, the teratogenic influence seems to be the best documented. Langer O (2002) The results of many studies indicate that a very strict control of maternal metabolism at the early stage of fetal development, preferably during the pre-conception period (in a planned pregnancy) results in a substantial decrease of the risk of malformation (Eriksson, Borg, Forsberg, and Styrud, 1991) .

Defects occurring in the infants of diabetic mothers are of great variety, and it is impossible to distinguish malformations which would be specific for pregnancies complicated by diabetes mellitus. Kitzmiller JL, Gavin LA, Gin GD, Jovanovic-Peterson L, Main EK, Zigrang WD (1991) The caudal regression syndrome with femoral shortening seems to be the most characteristic malformation, because it is diagnosed 200–600 times more frequently in the population of newborns born to diabetic mothers (NDM) compared to newborns of non-diabetic mothers. (Goldman JA, Dicker D, Feldberg D, Yeshaya A, Samuel N, Karp M (1986) In NDM, defects of the cardiovascular system, such as transposition of great vessels, septal defects, aortal coarctation, persisting arterial duct (PAD), single heart ventricle, ventricular hypotrophy, pulmonary stenosis, and situs inversus, constitute the most frequently observed malformations (Nazer and Ramirez, 2000).
Malformations are also found in other parts of the body, such as the skeletal system (spinal defects and limb deformation) and the urogenital system (renal agenesis, polycystic renal degeneration, hydronephrosis, hypospady, and cryptorchism) (Key et al., 1987).

Background.

The prevention of congenital malformations in the newborns of pre-gestational diabetic mothers still constitutes one of the main problems in this group of patients in Srilanka.

Objectives

1. To analyze the prevalence of fetal malformations in pre-gestational diabetic pregnancies compared to uncomplicated non diabetic pregnancies.
2. To evaluate the clinical utility of a comprehensive program inclusive of clinical features, glycemic assessment and prenatal detailed ultrasound with fetal echocardiography for congenital anomalies in pregnancies complicated by diabetes mellitus. (Nicholaides K.H, Gianluigi Pilu (2008). Diagnosis of Fetal abnormalities "18 -23 weeks Fetal anomaly ultrasound scan and Doppler 12 (2)"9-55). Glycemic control was set at 90-130mg/dl at pre and post prandial values and target HbA1C was set at below 6.2%.

METHODS

STUDY DESIGN

Hospital based prospective cohort study**.** Study setting**:** De Soyza maternity hospital- Colombo, Sri Lanka.

Study period: August 2006 to August 2008 Study population: 789 pre-gestational diabetic women who were registered in hospital clinics during Aug 2006 to Aug 2008 and their newborns. The results were compared with age and parity matched low risk non diabetic population of 780 antenatal mothers.

Study Instruments: Interviewer administered questionnaire included detailed history, examination checking glycemic assessment and comprehensive fetal ultrasonography inclusive of a standard four-chamber view of the heart and detailed power Doppler fetal echocardiography according to ISUOG standards. Data collection: The purpose of the study was explained to the pregnant women and informed written consent was taken. Data analysis: using the Statistical Package of Social Sciences (SPSS), version 17.0, did Data entry and analysis.

RESULTS

Anomalies were identified in 49 of 789 (6%) fetuses and neonates: 12 central nervous system ,03 abdomincal wall defects , 03 diaphragmatic hernias , 08 renal tract defects , 03 cystic hygromas, 02 isolated hydrothorax , 04 hydrops with multiple congenital abnormalities, 04 gastro intestinal malformations, 02 limb defects and 04 cardiac abnormalities were detected prenatally. 03 cardiac lesions 02 limb defect (VACTERAL) and down syndrome fetus detected postnatally. The results were compared with age and parity matched non diabetic control group of 680 routine visits mothers and antenatal admissions having 21/780 (2.7%) with only 1 cardiac abnormality this was significant $p < 008$ at (95% CI 0.77 – 5.03).

Central nervous system defects including hydrocephalus, holoporencephaly, encephalocele accounted for nearly 25% of total anomalies and renal tract abnormalities 15% All these anomalies in all systems except 3 cardiac and 2 limb defects were detected prenatally. Cardiac abnormalities including cardiac septum and great vessels, accounted for 15% of all fetal defects of which only 72% detected prenatally. Missed lesions were detected at neonatal 2D echo and these included a large ASD ,a ventricular septal defect and PDA. There were seven neonatal deaths and five therapeutic pregnancy terminations associated with congenital anomalies. There were three fetal interventions done on 2 Isolated renal obstructive uropathy and one hydrothorax with a success of 50%.

CONCLUSIONS

This study demonstrates confirm the view that pre-gestational diabetic pregnancy, despite the improved metabolic control, is still a strong risk factor for alterations in fetal development leading to fetal malformations.

This study also demonstrate the advantage of a comprehensive program to detect fetal anomalies in pregnancies complicated by pre-gestational diabetes mellitus focusing further attention towards detecting fetal cardiac abnormalities

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