IMAGES in PAEDIATRIC CARDIOLOGY

Images Paediatr Cardiol. 2000 Apr-Jun; 2(2): 17–23.

PMCID: PMC3232483

Heart disease in infants of diabetic mothers

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Abstract

Congenital anomalies occur more commonly in infants born to diabetic mothers, and cardiac defects predominate. Although respiratory problems are also frequently found in those infants, they need to be differentiated from cardiovascular problems that such patients may also have, which include cardiovascular maladaptation to extra-uterine life, congenital heart defects and hypertrophic septal cardiomyopathy. A high index of suspicion is required as the specific management may vary and digoxin, or inotropic agents which may be used in heart failure associated with structural heart defects are contraindicated if hypertrophic cardiomyopathy is present. This article reviews the epidemiology, pathophysiology, clinical presentation, prognosis and available diagnostic and therapeutic modalities. The need for antenatal fetal echocardiography in pregnant diabetic mothers is also reviewed, as well as the controversial role of maternal glycemic control in the prevention of these anomalies.

MeSH: Diabetes mellitus, Pregnancy, Newborn, Heart defects, congenital, Hypertrophic cardiomyopathy

Introduction

The risk of congenital anomalies is increased in infants of diabetic mothers (IDM), and is estimated to be between 2.5 to 12%, with an over-representation of congenital heart defects.[1,2] The incidence of malformations is the highest in the group where mothers were on insulin at the time of conception.[1] IDMs often develop respiratory problems which need to be

differentiated from the cardiovascular problems they are prone to have (structural congenital heart defect and hypertrophic cardiomyopathy) and from cardiovascular maladaptation to extra-uterine life which they may also suffer.[3,4]

1. Structural cardiac malformations

Congenital heart disease occurs in 5% of IDM. The highest relative risk for major cardiovascular defects occurs if the mother has gestational diabetes and develops insulin resistance in the 3rd trimester. It is thought that maternal diabetes, via its effects on maternal metabolism, is responsible for the increase of malformations in the offspring.[5] However, using hemoglobin A1c values as an indicator of maternal diabetic control, other studies have shown that congenital heart disease in the fetus is not significantly related to maternal diabetic control.[6] The most frequent cardiac anomalies in IDMs include ventricular septal defect, transposition of great arteries and aortic stenosis. Defects involving the great arteries, including truncus arteriosus and double outlet right ventricle, are also more prevalent in IDMs.[7,8]

The clinical presentation, diagnostic approach and therapy depend on the type of structural heart disease present, and are no different from when they occur in neonates born to non-diabetic mothers.

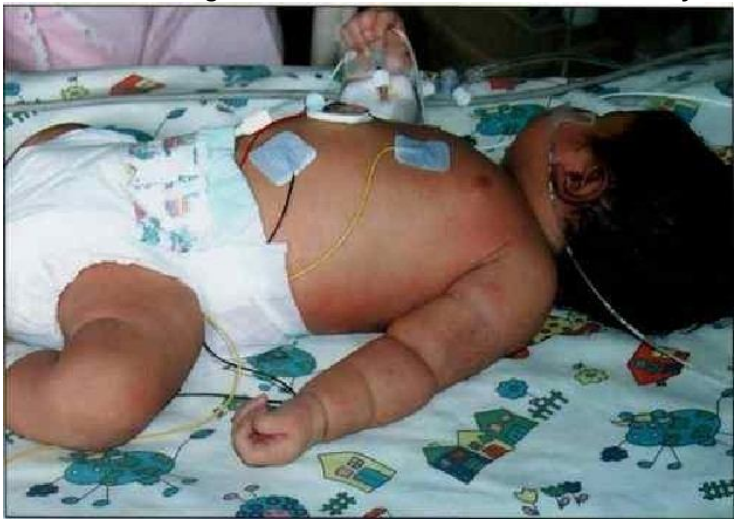
2. Cardiovascular adaptation to extrauterine life

In IDM with respiratory distress, the right ventricular pre-ejection period to ventricular ejection time ratio is elevated, suggesting an abnormality of the transitional pulmonary circulation.[3] The closure of the ductus arteriosus and postnatal decrease in pulmonary artery pressure are also delayed in these neonates.[4] This may partially explain the frequent occurrence of respiratory problems and the slowness of the recovery in such infants. Primary pulmonary hypertension may be associated with and aggravated by the polycythemia which is also frequently present in these neonates.

3. Hypertrophic cardiomyopathy

3.1 While symptomatic hypertrophic cardiomyopathy (HC) occurs in 12.1% of IDM, when routinely searched for with an echocardiographic scan it is found in 30%.[9] The left ventricular mass and contractility are increased and there is left ventricular outflow tract (LVOT) obstruction with apposition of the anterior leaflet of the mitral valve to the interventricular septum during systole. Cardiac output is significantly reduced, secondary to reduced stroke volume and is directly related to the degree of septal hypertrophy.[10] This asymmetric septal enlargement, with a disproportionally hypertrophic septum, is an anabolic result of fetal hyperinsulinemia triggered by maternal hyperglycemia during the third trimester. Cardiac septum hypertrophy correlates with maternal glycosylated haemoglobin levels and high levels of fetal insulin better than with macrosomia (fig. 1).

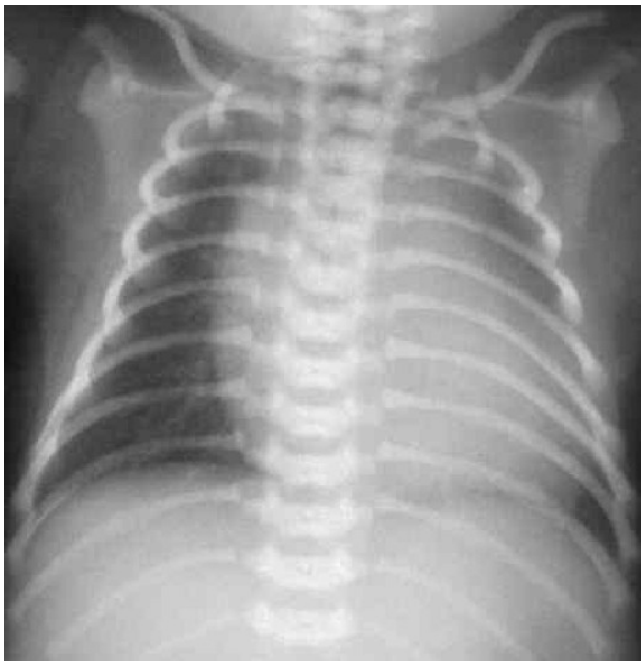
Figure 1 Large hypotonic infant of diabetic mother, lying in a frog-like position, with some bruising of the left arm due to shoulder dystocia



3.2 The severity of IDM cardiomyopathy can vary from an incidental finding on echocardiography (30% of cases) to an infant with severe symptoms of congestive heart failure (12% of cases).[11] HC is usually benign and consists of systolic murmur and transitory cardiomegaly. All symptoms usually spontaneously regress within a few weeks. Sometimes, overt congestive heart failure develops, with tachypnea, tachycardia, gallop rhythm and hepatomegaly.

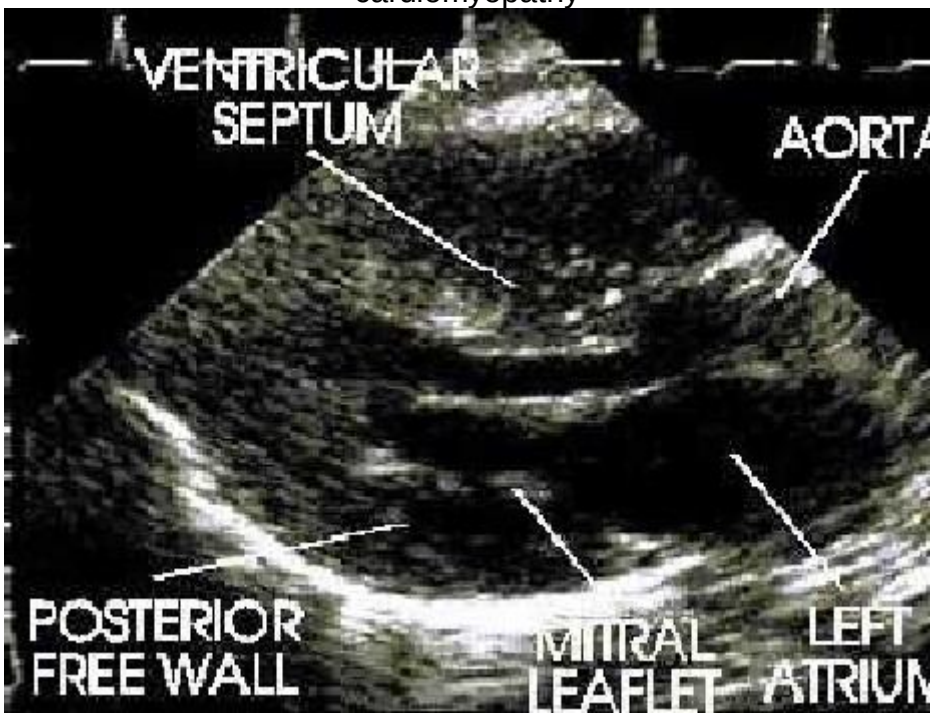
3.3 Cardiomegaly is invariably present radiologically when HC is symptomatic, with pulmonary congestion (fig. 2). The electrocardiographic findings are not usually helpful.

Figure 2 Chest X-ray showing significant cardiomegaly and pulmonary venous congestion as a result of hypertrophic cardiomyopathy in an infant of diabetic mother



Echocardiography is essential for the diagnosis of HC, it will also assess the left ventricular function, the degree of LVOT obstruction and it will also rule out structural cardiac malformations. The echocardiographic features of hypertrophic subaortic stenosis are well described (fig. 3).[3,12,13] The left ventricular mass is significantly greater, with the interventricular septum being significantly thicker (mean (SD) 4.77 (1.4) mm) when compared with those born to non-diabetic mothers (2.5 (0.7) mm).[14]

Figure 3 Two-dimensional echocardiogram showing septal hypertrophy which partially obstructs the left ventricular outflow tract in hypertrophic cardiomyopathy



3.4 The natural history of HC is that of spontaneous regression of symptoms and septal hypertrophy.[15] Most of the infants need only supportive care, with fluid restriction, diuretics and oxygen. Digoxin and inotropes are contraindicated as they increase LVOT obstruction. If pharmacologic intervention is deemed necessary, beta adrenergic blocking agents such as propranolol, are the drugs of choice, as they reduces heart rate, left ventricular contractility and wall stress, with total relief of symptoms obtained with standard doses of propranolol in 30% of affected infants.[15,16]

3.5 The natural history of HC is benign, with resolution of symptoms within two to four weeks and resolution of septal hypertrophy during the first 2 to 12 months of life, irrespective of therapy.[14,15] Early or progressive hypertrophy of the LV posterior wall is a predictor of poor outcome, regardless of associated disease.[17]

Antenatal diagnosis

With congenital heart disease occuring in up to 5% of fetuses of diabetic mothers, and with 90% of the cardiac lesions identifiable prenatally, it has been suggested that detailed fetal echocardiography is offered to all diabetic

women during pregnancy.[18–22] However, when studied in relation to maternal initial HbA1c, the overall sensitivity for identifying congenital heart disease was 50% and specificity 54% and no critical level of HbA1c that provided optimal predictive power for congenital heart disease screening was identified.[23] It has also been suggested that the fetal cardiac septum thickness should be measured in utero by sonocardiography in all diabetic pregnancies.[24]

Prevention

Careful management of diabetes in pregnancy may reduce the severity of hypertrophic cardiomyopathy.[11,25] However, other studies found no relationships between the echocardiographic results and the metabolic control of pregnancy or fetal characteristics, suggesting that strict maternal diabetes control may not prevent accelerated fetal cardiac growth and abnormal development of cardiac function.[26,27]

References

1. Day RE, Insley J. Maternal diabetes mellitus and congenital malformation. Survey of 205 cases. Arch Dis Child. 1976;51:935–8. [PMCID: PMC1546153] [PubMed: 1015845]
2. Ramos-Arroyo MA, Rodriguez-Pinilla E, Cordero JF. Maternal diabetes: the risk for specific birth defects. Eur J Epidemiol. 1992;8:503–508. [PubMed: 1397216]
3. Mace S, Hirschfield SS, Riggs T, Fanaroff AA, Merkatz IR. Echocardiographic abnormalities in infants of diabetic mothers. J Pediatr. 1979;95:1013–1019. [PubMed: 159351]
4. Seppanen MP, Ojanpera OS, Kaapa PO, Kero PO. Delayed postnatal adaptation of pulmonary hemodynamics in infants of diabetic mothers. J Pediatr. 1997;131:545–548. [PubMed: 9386656]
5. Chung CS, Myrianthopoulos NC. Factors affecting risks of congenital malformations. II. Effect of maternal diabetes on congenital malformations. Birth Defects Orig Artic Ser. 1975;11:23–38. [PubMed: 769859]
6. Gladman G, McCrindle BW, Boutin C, Smallhorn JF. Fetal echocardiographic screening of diabetic pregnancies for congenital heart disease. Am J Perinatol. 1997;15:59–62. [PubMed: 9259899]
7. Adams MM, Mulinare J, Dooley K. Risk factors for conotruncal cardiac defects in Atlanta. J Am Coll Cardiol. 1989;14:432–442. [PubMed: 2787814]
8. Ferencz C, Rubin JD, McCarter RJ, Clark EB. Maternal diabetes and cardiovascular malformations: predominance of double outlet right ventricle and truncus arteriosus. Teratology. 1990;41:319–326. [PubMed: 2326756]
9. Vural M, Leke L, Mahomedaly H, et al. Should an echocardiographic scan be done routinely for infants of diabetic mothers? Turk J Pediatr. 1995;37:351–356. [PubMed: 8560603]
10. Walther FJ, Siassi B, King J, Wu PY. Cardiac output in infants of insulin-dependent diabetic mothers. J Pediatr. 1985;107:109–114. [PubMed: 4009327]
11. Reller MD, Kaplan S. Hypertrophic cardiomyopathy in infants of diabetic mothers: an update. Am J Perinatol. 1988;5:353–358. [PubMed: 2971360]
12. Gutgesell HP, Mullins CE, Gillette PC, et al. Transient hypertrophic subaortic stenosis in infants of diabetic mothers. J Pediatr. 1976;89:120–125. [PubMed: 945337]
13. Halliday HL. Hypertrophic cardiomyopathy in infants of poorly-controlled diabetic mothers. Arch Dis Child. 1981;56:258–263. [PMCID: PMC1627227] [PubMed: 7195689]
14. Deorari AK, Saxena A, Singh M, Shrivastava S. Echocardiographic assessment of infants born to diabetic mothers. Arch Dis Child. 1989;64:721–4. [PMCID: PMC1792021] [PubMed: 2730127]
15. Way GL, Wolfe RR, Eshaghpour E, et al. The natural history of hypertrophic cardiomyopathy in infants of diabetic mothers. J Pediatr. 1979;95:1020–1025. [PubMed: 159352]
16. Lusson JR, Gaulme J, Raynaud EJ, Cheynel J. Hypertrophie septale asymetrique du nouveau-né de mère diabétique. Arch Fr Pediatr. 1982;39:433–436. [PubMed: 6890794]

17. Suda K, Kohl T, Kovalchin JP, Silverman NH. Echocardiographic predictors of poor outcome in infants with hypertrophic cardiomyopathy. Am J Cardiol. 1997;80:595–600. [PubMed: 9294988]
18. Meyer-Wittkopf M, Simpson JM, Sharland GK. Incidence of congenital heart defects in fetuses of diabetic mothers: a retrospective study of 326 cases. Ultrasound Obstet Gynecol. 1996;8:8–10. [PubMed: 8843611]
19. Wheller JJ, Reiss R, Allen HD. Clinical experience with fetal echocardiography. Am J Dis Child. 1990;144:49–53. [PubMed: 2294719]
20. Zielinsky P. Role of prenatal echocardiography in the study of hypertrophic cardiomyopathy in the fetus. Echocardiography. 1991;8:661–668. [PubMed: 10149277]
21. Cooper MJ, Enderlein MA, Dyson DC, Roge CL, Tarnoff H. Fetal echocardiography: retrospective review of clinical experience and an evaluation of indications. Obstet Gynecol. 1995;86:577–582. [PubMed: 7675383]
22. Buskens E, Stewart PA, Hess J, Grobbee DE, Wladimiroff JW. Efficacy of fetal echocardiography and yield by risk category. Obstet Gynecol. 1996;87:423–428. [PubMed: 8598967]
23. Shields LE, Gan EA, Murphy HF, Sahn DJ, Moore TR. The prognostic value of hemoglobin A1c in predicting fetal heart disease in diabetic pregnancies. Obstet Gynecol. 1993;81:954–957. [PubMed: 8497362]
24. Fenichel P, Hieronimus S, Bourlon F, et al. Macrosomie du foetus de mère diabétique. Presse Med. 1990;19:255–258. [PubMed: 2138296]
25. Reller MD, Tsang RC, Meyer RA, Braun CP. Relationship of prospective diabetes control in pregnancy to neonatal cardiorespiratory function. J Pediatr. 1985;106:86–90. [PubMed: 3880822]
26. Rizzo G, Arduini D, Romanini C. Accelerated cardiac growth and abnormal cardiac flow in fetuses of type I diabetic mothers. Obstet Gynecol. 1992;80:369–376. [PubMed: 1495691]
27. Sheehan PQ, Rowland TW, Shah BL, McGravey VJ, Reiter EO. Maternal diabetic control and hypertrophic cardiomyopathy in infants of diabetic mothers. Clin Pediatr (Phila) 1986;25:266–271. [PubMed: 3698447]