The Incidence of Cardiac Lesions among Children with Down's Syndrome in Jamaica – A Prospective Study

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ABSTRACT

Objectives: *This study aimed to define the incidence of Down's syndrome and to describe the epidemiology of cardiac lesions in Jamaican children with Down's syndrome.*
Methods: *A prospective study was conducted on 53 infants during the period January 1, 2007 to December 31, 2007, at the Bustamante Hospital for Children, Kingston, Jamaica. A medical history, physical examination and echo Doppler was performed on each child.*
Results: *Forty-six thousand babies were born in Jamaica in 2007, of which 53 infants were diagnosed with Down's syndrome, giving an incidence of 1:868. Forty-two (79.2%) infants had congenital heart lesions. Of the 42 patients with cardiac lesions, 50% had an isolated cardiac lesion while 50% had multiple defects. The most common single defect was the atrioventricular septal defect found in 10 (24%) patients. The most frequent concomitant malformation was a patent ductus arteriosus, found in 16 (38.1%) of the patients. The median age of diagnosis with Down's syndrome was 0.14 weeks (interquartile range (IQR) 0 to 68 weeks). The median age of diagnosis with the cardiac lesion was 15.1 weeks (IQR 0 to 40.0 weeks).*
Conclusions: *The incidence of Down's syndrome in Jamaica is similar to the reported international experience. The distribution of cardiac malformations is similar to that in other countries; however, the main difference is the higher incidence of congenital heart disease and a higher incidence of combined lesions.*

Keywords: African descent, atrioventricular septal defect, congenital heart defect

La Incidencia de Lesiones Cardíacas entre los Niños con Síndrome de Down en Jamaica – Un Estudio Prospectivo

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RESUMEN

Objetivos: *Este estudio tuvo por objeto definir la incidencia del síndrome de Down, y describir la epidemiología de las lesiones cardíacas en niños jamaicanos con síndrome de Down.*
Métodos: *Se realizó un estudio prospectivo de 53 niños durante el período comprendido del 1^{ero} de enero de 2007 al 31 de diciembre de 2007, en el Hospital Pediátrico Bustamante de Kingston, Jamaica. A cada niño se le realizó una historia clínica, un examen físico, y una ecografía Doppler.*
Resultados: *Cuarenta y seis mil bebés nacieron en Jamaica en 2007, de los cuales 53 fueron diagnosticados con síndrome de Down, para una incidencia de 1:868. Cuarenta y dos (79,2%) infantes tenían lesiones congénitas del corazón. De los 42 pacientes con lesiones cardíacas, el 50% tenía una lesión cardíaca aislada, mientras que el 50% tuvo múltiples defectos. El defecto singular más común fue el defecto septal atrioventricular en 10 pacientes (24%). La malformación concomitante más frecuente fue el conducto arterioso permeable, encontrado en 16 (38.1%) de los pacientes. La edad promedio en el diagnóstico del síndrome de Down fue 0.14 semanas (rango intercuartil (IQR) 0 a 68 semanas). La edad promedio en el diagnóstico de la lesión cardíaca fue 15.1 semanas (IQR 0 a 40.0 semanas).*

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Conclusiones: *La incidencia del síndrome de Down en Jamaica es similar a la reportada por la experiencia internacional. La distribución de las malformaciones cardíacas es similar a la de otros países. No obstante, la principal diferencia radica en una mayor incidencia de la enfermedad cardíaca congénita, así como una mayor incidencia de lesiones combinadas.*

Palabras claves: Ascendencia africana, defecto septal auriculoventricular, defecto congénito del corazón

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INTRODUCTION

Jamaica is a developing Caribbean island with a population of approximately 2.8 million people, of which 98% are of African descent (1). A cumulative experience of the international data reports the incidence of congenital heart disease (CHD) in a population to be 8−10/1000 live births (2). It could be estimated that in Jamaica, based on a birth rate of 46 000 live births for 2007 (1), approximately 460 children were born with congenital heart defects. Ten per cent of all babies born with congenital heart defects have a chromosomal abnormality of which Down's syndrome (DS) is the commonest (2).

It has been estimated that approximately 50% of patients with Down's syndrome have cardiac malformations (3). These cardiac malformations contribute to increased mortality and morbidity due to complications which include congestive cardiac failure, recurrent bronchopneumonia and pulmonary vascular disease. Pulmonary vascular disease occurs at an earlier age in infants with DS (4). Infants should be treated preferably by six months of age before pulmonary vascular disease becomes irreversible which would make surgery a very high-risk procedure (5−7).

In Jamaica, the availability of surgery for children with heart disease is *via* three channels: (i) local surgeons, (ii) visiting surgery teams from developed countries and (iii) transfer of patient to developed countries. In Jamaica, 48% of children with DS and cardiac lesions are referred for cardiac care after six months of age, at which time advanced pulmonary vascular disease is already present (8). Due to the inadequate resources available for cardiac surgery, most cases that are referred do not receive cardiac surgery in a timely manner.

This study aims to define the incidence of Down's syndrome and to describe the epidemiology of cardiac lesions in children with Down's syndrome. Once this is known, programmes could be established to address these children with special needs.

SUBJECTS AND METHOD

This was a prospective study which identified all infants suspected to have DS born between January 1, 2007 and December 31, 2007. All doctors at major institutions where infants were delivered or seen in the neonatal period were informed of the study. The physicians were requested to refer any infant suspected to have DS to a special clinic conducted by CS (a consultant paediatric cardiologist) who would review all referrals.

The diagnosis of DS was confirmed by the presence of at least six out of ten criteria for DS as documented by Smith's Recognizable Patterns of Human Malformation (9). The diagnosis of DS was the only inclusion criteria. Once confirmed, the parents of these infants were invited to participate in the study and written informed consent was obtained.

A full medical history which included information on the sociodemographics of the family was obtained and a physical examination was performed. All of the patients had echo Doppler studies done by a single operator (CS) using a General Electric Logic 500 machine manufactured in Japan.

A repeat echo Doppler was performed at one month on infants who were diagnosed with a small patent ductus arteriosus (PDA) or a patent foramen ovale (PFO) in the first few days of life. This was performed as these findings could have been a part of the normal neonatal transitional circulation. The parents were counselled and educated about the infants's condition. All studies were recorded and stored on VHS videotapes. All information was confidentially stored and descriptive analyses were performed. Chi-squared test and binomial test of proportions were conducted using SPSS version 11.0/Stata. Findings were considered significant for p-values < 0.05. Approval was obtained from the ethics committees of the University Hospital of the West Indies/University of the West Indies/Faculty of Medical Science and the Ministry of Health.

RESULTS

Fifty-three children born between January 1, 2007 and December 31, 2007, fulfilled the criteria for inclusion in the study. The number of females in the study was 35 (66%). In looking at the gender distribution, there was no statistical difference between males (n = 14) and females (n = 28) with cardiac lesions in our study (77.8% males; 82.9% females; $p = 0.65$). Most of the children, 22 (41.5%), were born in St Catherine, Kingston and St Andrew, the most densely populated area of the island. There was an even distribution of cases throughout the year, with an average 4.4 infants born per month. There were 46 000 births in Jamaica in 2007 (1), giving the incidence of one in 868 infants born with DS in this population.

None of the mothers received amniocentesis for congenital abnormalities and none of the infants clinically diag-

nosed with DS received chromosomal studies. The majority of mothers, 44 (83.0%), were informed that their infants had DS at birth; two were informed during pregnancy *via* fetal ultrasound.

The median age of diagnosis with DS was at 0.14 weeks (interquartile range (IQR) 0 to 68.4 weeks). The maternal age ranged from 15.0 to 44.2 years in 51 mothers with a median age of 36.0 years. Paternal age ranged from 21.0 to 60.7 years in 50 fathers with a median age of 34.6 years (Table 1). In 51 cases, the historian was the mother. The median age of first contact with the cardiologist was 15.1 weeks (range birth to 40 weeks).

Table 1: Maternal and childhood demographics

Variables	n	Median	Range
Maternal age at delivery (years)	51	36.0	15.0, 44.2
Paternal age at delivery (years)	50	34.6	21.0, 60.7
Child's age at diagnosis of Down's syndrome (weeks)	53	0.14	0.0, 68.4
Age at first contact with cardiologist (weeks)	53	15.1	0.0, 40.0

Eight children (15.1%) were born to parents who were married, 28 (52.8%) were born to single women and 17 (32.1%) were born to parents who were cohabiting in common-law unions. None of the cases had siblings with DS, but seven (13.2%) patients had a relative with DS. One case was the survivor of a monozygotic twin pregnancy. The other fetus that demised at 23 weeks gestation was also thought to have DS based on fetal ultrasound.

Data were available for 51 (96.2%) mothers regarding their educational status. Three (5.7%) received tertiary education, 28 (52.8%) received high school education, nine (17.0%) received junior secondary or had incomplete high school education and 11 (20.8%) received only primary education. Data on the fathers' educational status were available for 37 (69.8%) fathers, of which two (3.8%) had tertiary education, 17 (32.1%) had high school education, seven (13.2%) had junior secondary or incomplete high school education and 11 (20.8%) had primary level education alone.

The employment status of 52 mothers and 49 fathers was obtained. There were no mothers in the category of higher professionals (*ie* physicians, accountants and lawyers) and only one (2.0%) father was in the higher professional group (Table 2). Twenty-five (47.2%) of the children had at least one admission during the study period (Table 3). The reason for admission was varied and the patients might have had more than one diagnosis at admission. Pneumonia and cardiac failure were the two most common reasons for admission.

Eleven children (20.8%) had a normal heart in this study. Fifty per cent of the infants with congenital heart defects were born to mothers who were 35 years and older. Table 4 shows the breakdown of the cardiac lesions. Of the infants with cardiac defects, 21 infants (50%) had isolated defects and 21 (50%) had multiple defects.

Table 2: Parental occupation

	Maternal		Paternal	
	n	percentage (%)	n	percentage (%)
Higher professional	–	–	1.0	2.0
Skilled	12.0	23.1	31	63.3
Semi-skilled	3.0	5.8	6.0	12.2
Unskilled	13.0	25	9.0	18.4
Housewife	7.0	13.5	–	–
Students	6.0	11.5	–	–
Unemployed	11.0	21.2	2.0	4.1
Total	**52**	**100**	**49**	**100**

Table 3: Number of patient admissions during the study period

Number of admission	Number of patients	Percentage (%)
0	28	52.8
1	18	34.0
2	4	7.5
3	1	1.9
4	1	1.9
Total	**52**	**98**

One patient interview was incomplete

Table 4: Cardiac lesion diagnosed by echocardiogram in patients with Down's syndrome

Type of lesion	Number of patients	%
Isolated defect		
Atrioventricular septal defect (AVSD)	10	23.8
Patent ductus arteriosus (PDA)	6	14.2
Ventricular septal defect (VSD)	2	4.8
Atrial septal defect (ASD)	2	4.8
Tetralogy of Fallot (TOF)	1	2.4
Multiple defects		
AVSD and PDA	5	11.8
AVSD and ASD	3	7.1
VSD and PDA	3	7.1
PDA and VSD and cleft atrioventricular valve	2	4.8
AVSD and PDA and ASD	1	2.4
AVSD and TOF	2	4.8
AVSD and PDA and TOF	1	2.4
AVSD and PDA and TOF and ASD	1	2.4
PDA and coarctation of the aorta	1	2.4
PDA and right pulmonary artery stenosis	1	2.4
PDA and TOF	1	2.4
Total	**42**	**100**

The atrioventricular septal defect (AVSD) was the commonest lesion and was found in 10 (24%) patients as an isolated lesion and in 13 (31%) infants in combination with other defects. Patent ductus arteriosus was the next commonest lesion and was found in six (14.3%) infants as an isolated lesion and 16 (38.1%) in combination with other

defects. Of the six patients diagnosed with an isolated PDA, only one had a significant lesion requiring intervention.

During the study period, three patients died; all had complete AVSDs and severe cardiac failure. Three patients with complete AVSDs had successful surgical repair. Eleven patients developed severe pulmonary vascular disease and were inoperable.

DISCUSSION

This is the first study conducted in the English-speaking Caribbean which describes the incidence of DS and the epidemiology of congenital cardiac abnormalities in DS. Early medical reports suggested that the existence of DS among persons of African descent is rare. Up until 1955, authorities believed that DS did not occur in people of African origin (10). This belief was dismissed after the first study from Africa was published in 1982 reporting the incidence of DS (11). The incidence of one in 868 live births in our study was similar to the incidence reported in other parts of the world and identical to that reported in a study from Nigeria, one of the countries in West Africa from which most Caribbean blacks originate (11−14).

Advanced maternal age is still the only established risk factor known to be involved in the aetiology of DS (15, 16). The age range of mothers in this study was 15 to 44.2 years with a median age of 36.0 years. Other studies report a mean age of 33.5 ± 8.1 years which is similar to our findings (17−20). We were unable to perform chromosomal studies in our patients due to a lack of facility locally and the expense for overseas testing. The median maternal age identified in this study was greater than 35 years and there is a link with advanced maternal age and non-disjunction (15, 16). This therefore implies that the commonest cause of DS in our population might be due to non-disjunction. Studies have shown that there is an increased incidence of DS in younger mothers (11, 21). Anecdotally, the perception in Jamaica was that a significant number of infants with DS were born to younger mothers. Our data did not support this.

The effect of paternal age and risk of DS has not been frequently reported; however, most of the studies that examined this variable, adjusting for maternal age, found an increasing incidence of DS with advancing paternal age (19, 20, 22). This study attempted to include sociodemographic factors of the father, and father's age was not significantly different from that of the mother.

A gender difference in DS has been previously described where there tends to be a male predominance (18, 23). Our study showed a greater proportion of females, similar to findings of a previous study conducted in Jamaica which reported on a ten-year review of cardiovascular malformations in Jamaican children with DS (8) and a study from Malaysia (21) where a female preponderance was also reported.

Our study demonstrated varying educational levels among our parents with three of our mothers achieving tertiary education. Dzurova and Pikhart found that there was a lower incidence of DS in educated women in California compared to their counterparts in the Czech Republic and thought that this might reflect the selective impact of prenatal diagnosis, elective termination, and acceptance of prenatal diagnostic measures in the Californian population (24). The incidence of DS in our study is most likely unaffected by this educational confounder as the majority of women in this study achieved only up to secondary level education.

The overall incidence of CHD within our study population was 79.2%, which was not significantly different (p = 0.08) when compared with the study by McElhinney *et al* which showed that 75 of their 114 neonates (66%) had echocardiographic findings of CHD (26). However, a study similar to ours carried out in Guatemala by Vida *et al* reported that 189 of 349 patients (54.1%) had CHD, which is significantly lower than the findings in our study [p = 0.0006] (27). The reason for the higher incidence seen in our study could be that minor lesions such as transitional PDAs were included. If these lesions are excluded, the incidence would be lower, but still increased at 69.8%, when compared to the study by Vida *et al* (27). We are unable to make any statistical comparisons as the studies above did not indicate if their children with transitional PDAs were excluded. Vida *et al* also reported a high frequency of PDAs (27). In that study, PDA was the most common single defect and was also the most frequent concomitant malformation (27). Chaohab *et al* reported that mothers younger than 32 years had a higher risk for the development of CHD in infants with DS (28). This observation was in contrast to our study as we found that approximately 50% of our mothers who had infants with CHD were 35 years and older.

The distribution of cardiac malformations found in our study was similar to other countries such as Guatemala where AVSD was the most common single congenital malformation (27). There are, however, important differences, the main being the higher incidence of CHD and the higher incidence of combined congenital heart lesions where our study showed a significant difference (p = 0.0001) compared with the one from Guatemala (27).

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