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Congenital Visceral Malformations in Children with Down Syndrome (DS) Followed in the Pediatric Unit of the CNHU, Cotonou, Bénin

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Abstract

Introduction: Mortality in Down syndrome (DS) remain high and often in relation with visceral malformations. The aim of this work was to describe the congenital visceral malformations associated with DS in children followed in the pediatric unit of National Health Teaching Hospital of Cotonou, in order to improve their management.

Patients and methods: It was a prospective and descriptive survey conducted on children who were treated for DS at the pediatric unit of the National Health Teaching Hospital of Cotonou from October 2015 through July 2016. All children had a diagnosis of DS based on karyotype with trisomy 21 and underwent heart, gastrointestinal and kidney ultrasonographies.

Results: A total of 36 children were included. The sex ratio was 1.25 and infants under 12 months were the most represented age group (55.56 %). The mean age at diagnosis was 18.8 months. The majority of mothers were aged than 35 years. Clinical features were dominated by up slanting palpebral fissures and hypertelorism. The visceral malformations were observed only in heart with a frequency of 55.55%. Atrio-ventricular septal defect (27.78%) and patent ductus arteriosus (16.76%) were predominant. Nondisjunction trisomy 21 was found in all children.

Conclusion: Congenital visceral malformations associated to DS in children at pediatric unit of the National Health Teaching Hospital of Cotonou were exclusively cardiac with atrioventricular septal defect as major type. Early diagnosis of DS with malformations screening are essential for better management of affected children.

Keywords: Down syndrome; Birth defect; Congenital heart disease; Gastrointestinal malformation; Kidney malformation

Introduction

Down syndrome (DS) is the most common chromosomal disease in Human. It results from the presence of three copies of chromosome 21 in the cells, and affects approximately one newborn per every 650 to 1000 live births [1-3]. Its clinical features include psychomotor delay, hypotonia, dysmorphism ± malformations [4-6]. The most important of these malformations affected heart with a frequency that ranges from 44% to 58 % [5-7]. Congenital heart diseases (CHDs) are considered to be the most important clinical phenomenon of DS contributing to morbidity and mortality in affected infants [8]. The aim of this work was to describe the congenital visceral malformations that were associated with DS in children followed in the pediatric unit of the National Health Teaching Hospital of Cotonou, in order to improve their management.

Patients and Methods

It was a prospective and descriptive survey, with sequential recruitment of under 15 children that were seen at the pediatric unit of the National Health Teaching Hospital of Cotonou from October 2015 through July 2016 for Down syndrome. The diagnosis was confirmed by cytogenetic analysis that showed trisomy 21. The cytogenetic study was performed according to the international standards in the cytogenetic laboratory of Health Sciences School of Cotonou, using the whole blood collected on heparin and cultured for 72h. The chromosomes were stained according to G banding technic [9]. The karyotyping was established using an images' analyzer (Applied Imaging®).

Data were collected on socio-demograhic and clinical characteristics completed with malformation's profile. Congenital visceral malformations screening was done using HITACHI EUB 5500 sonograph for heart, gastrointestinal and kidney. The heart scans were performed according to the American Society of Echocardiography recommendations [10]. The digestive system and kidney scans were performed by a senior operator. The data were processed and analyzed using SPSS version 21. This study was approved by local IRB. Parents signed free consent forms prior inclusion and agreed with scientific use of photographs.

Results

By the end of the survey, 36 Down syndrome children had been included.

Socio-demographic and clinical data

The mean age of the children at diagnosis was 21.4 months, ranging from 11 days to 72 months (six years). The most represented age group was the 0-12 month group, accounting for 55.56% as shown on (Table 1). These children were mostly boys giving a sex ratio of 1.25 (male/female:20/16). Down syndrome was diagnosed postnatally in 35 of the

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36 children (97.22%). Cytogenetic analysis revealed nondisjunction trisomy 21 in all 36 children. The mean mothers' age at birth was 34.2 years, ranging from 21 to 46 years as presented on (Table 2). Mothers aged than 35 years accounted for 61% of all children mothers. The clinical features of these children with DS were dominated by up slanting palpebral fissures (100%) and hypertelorism (100%) as summarized on (Table 3). Psychomotor delay was present in 77.78% of these children. Heart murmur was the most common cardiovascular sign (n=12) at clinical examination.

Congenital visceral malformations associated with Down syndrome

A congenital visceral malformation was present in 55.55% of the children with Down syndrome. All of these malformations were cardiovascular as shown in Table 4. An association of CHDs has been noted in 15 cases. The different types of congenital heart disease that have been found were atrioventricular septal defect, patent ductus arteriosus, ventricular septal defect, atrial septal defect and tetralogy of Fallot. The main CHD was atrioventricular septal defect (n=10), which was present in 27.78% of the children with Down syndrome but it accounted for 50% of CHDs in DS patients. All mothers of children presenting with CHDs were aged than 35 years.

Age (months)	No. of children	%
≤ 6	10	27.78
7-12	10	27.78
13-24	7	19.44
25-48	6	16.67
>48	3	08.33
Total	36	100

Table 1: Age of the children at the time of Down syndrome diagnosis.

Age of the mothers (years)	No. of mothers	%
<25	3	8
25-29	4	11
30-34	7	20
≥ 35	22	61
Total	36	100

Table 2: Age of the mothers of the Down syndrome children at the time of birth.

	Number of children (n=36)	%
Psychomotor retardation	28	77.78
Cardiovascular signs		
Murmur	12	33.33
Dyspnea	7	19.44
Cyanosis	1	2.78
Dismorphic signs		
Obliquity of the palpebral	36	100
Fissures		
Epicanthic folds	35	97.22
Hypertelorism	36	100
Flattened nasal bridge	36	100
Open mouth		
Short	25	69.44
Brachydactylia	36	100
Single transverse crease	35	97.22
	22	61.11

Table 3: Clinical features of children with Down syndrome.

	No. of children (n=36)	%
Heart malformations	20	55.55
AVSD	10	27.78
PAD	6	16.67
VSD	4	11.11
ASD	3	8.33
ToF	1	2.78
Gastrointestinal malformations	0	0
Kidney malformations	0	0

Table 4: Congenital malformations in children with Down syndrome.

Discussion

The mean age at diagnosis of the children with Down syndrome was 18.8 months. This age at diagnosis is quite late compared to the ages that were reported from countries with advanced medical technologies. Indeed, in these countries, the diagnosis is usually done within the very first month of life [11]. In a previous survey in 2015 at the same place, the mean age of children at diagnosis of DS was 30 months. The difference between these studies conducted in the same hospital may be due to the better awareness of pediatricians and general practitioners reading pediatrics [12]. The age at diagnosis could be reduced towards 24 to 48 h after birth if all children receive appropriate and well done systematic examination at birth [13]. Early diagnosis should come from the implementation of systematic neonatal examination, familiarity with genetic services and dysmorphology. The mother age at birth of these children with Down syndrome in the study was around 34.4 years with extremes of 21 and 46 years. Advanced maternal age is the only well-established risk factor in Down syndrome. This condition incidence is moderate in the young before climbing and rising from 0.25% at 35 years to 3% at 45 years [14,15]. CHDs were observed in 55.55% of the children with Down syndrome included in this survey. Congenital heart diseases are considered to be the most important clinical phenomenon of Down syndrome to have a real impact on morbidity and mortality in affected infant [8]. The types of congenital heart diseases vary from region to region. In this survey, AVSD was the most frequent with 27.78%, followed by PDA with 16.67% and VSD with 11.11%. Divers trends have been reported. AVSD was the main congenital heart disease of the child with Down syndrome in American, Turkish and Swedish studies [16-19]. In a recent publication with the description of CHDs among Swedish live born infants with DS from 1992 to 2012, the rate of AVSD decreased from 46% to 30%, whereas the rate of ventricular septal defect had doubled from 14% to 31% [20]. In a Brazilian study conducted on 604 children with DS, atrial septal defect (ASD) was the main CHD at 42.1%, followed by AVSD at 15.1% [6]. Ventricular septal defect was the most commonly isolated lesion in a study in China, affecting 45.6% of DS patients, while patent ductus arteriosus (PDA) was the most frequent in a report from Guatemala (26.5%) [21,22]. Although the distribution of CHDs varies with geography, the limited size of our survey was not sufficient to draw any conclusion on the actual situation in Benin. Larger-scale studies are awaited to better classify the congenital heart diseases in Down syndrome in Cotonou. All mothers of children presenting with CHDs were aged than 35 years. Similar data were reported in a study from South Malaysia [23]. This finding suggests that maternal age higher than 35 years is probably a predisposing factor for the occurrence of heart malformations in DS even if the size of our study population is not sufficient to draw definitive conclusion. The reported CHDs were diagnosed after birth. Echocardiography plays nowadays a major role in detecting structural and functional cardiovascular anomalies and could identify heart malformations with precision. Its role, before and

after birth is essential for diagnosing CHDs in Down syndrome fetus but in also the general population [24]. This technique allows early diagnosis of heart defects between 10 and 12 weeks of gestation [24]. No gastrointestinal or kidney malformations were found after clinical and ultrasound examinations. The size of this population and the low incidence of digestive (4-10%) and urogenetital (3%) malformations probably played a role in this unfruitful work [7,25]. In a report on children with DS with a follow up program from 1999 to 2004, 6.7% of gastrointestinal anomalies were noticed. These anomalies included duodenal atresia/stenosis, anal atresia/stenosis, Hirschsprung's disease, esophageal atresia/tracheoesophageal fistula and pyloric stenosis [7].

Conclusion

Congenital visceral malformations in children with Down syndrome which were treated in the pediatric unit of the National Health Teaching Hospital are mainly cardiac. These malformations were present in 55.55% of affected children. Atrioventricular septal defect was the major type of congenital heart diseases with a frequency of 27.78%. Early diagnosis of Down syndrome and neonatal birth defect screening are essential for the early and better management of Down syndrome. Antenatal care should help reaching this goal.

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