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ORIGINAL ARTICLE

Paternal Age and its Relation with Congenital Cardiac Defects in Down's Syndrome at Children Hospital & ICH, Lahore

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ABSTRACT

Aim: To determine the frequency of Subtypes of Down's syndrome and congenital cardiac defects in Down's syndrome population and its association with parental age at Children Hospital, Lahore.
Study Design: Cross sectional study
Duration of Study: June 2016 to June 2017 at Genetics Deptt. Children Hospital, Lahore
Methodology: A total of 160 patients were included after taking an informed consent. A detailed history and physical examination for Down's syndrome was done. All the cases underwent karyotypic analysis for determination of the subtype of DS and echocardiography of all cases was done for CHD. Data was analyzed by SPSS 21.
Results: Mostly mothers i.e. 56(35%) were in the age of 26–30 years and fathers 99 (69.1%) in age of 31–40 years when they conceived a Down's syndrome baby. On karyotyping, the frequency of Trisomy 21 was highest in mothers in age group 02 and fathers in age group 03. PDA and VSD were common cardiac defects in Down's syndrome cases. In mothers, mostly PDA and VSD was present in age group 02 and fathers in age group 03.
Conclusion: Common type of Down's syndrome was Trisomy 21. Most common CHD were PDA and VSD. Most of the Down's syndrome babies were born to mothers in age group 25 to 30 years and fathers in age group 31 to 40 years.
Keywords: Down's syndrome, congenital cardiac defects, Trisomy 21

INTRODUCTION

Down's syndrome (DS), the most prevalent aneuploidy, is due to the extra copy of chromosome 21[1]. DS is the third congenital anomaly according to WHO. Its incidence is 1 to 2 in 1000 to 1 in 1100 live births worldwide.[2] Prevalence of DS increased from 50,000 in 1950 (3.3 per 10,000 individuals) to 212,000 in 2013 (6.7 per 10,000 individuals) in USA[3]. With DS, about 417,000 people are living in Europe[4]. Incidence of DS is more in aged 40-55 years in developed countries.[5]

The objective of the study was to determine the frequency of Subtypes of Down's syndrome and congenital cardiac defects in Down's syndrome population and its association with parental age at Children Hospital, Lahore.

METHODOLOGY

After getting permission from Institutional Ethical Review Board, a cross sectional study on 160 cases of Down's syndrome for duration of one year from June 2016 to June 2017 was conducted. An informed consent was taken from the guardians or the Down's syndrome individuals registered in Genetic Department and Cardiac Surgery Department, Children Hospital, who had 9 out of 14 selected phenotypic features characteristic of down's syndrome. Personal information and physical examination was done in the presence of either guardian or parent. Karyotyping of all cases was done in order to confirm Down's syndrome. Those whose karyotypic analysis came normal were excluded from the study. For karyotyping, a blood sample of 2ml was drawn through a syringe and immediately transferred to sterile heparin tube. After half an hour, the blood sample was transferred to a labeled culture flask and later on moved in an incubator for 72 hours at 37^0C for harvesting. By the end of 72 hours, 100 µl Colcemid was added to arrest the cells in metaphase of cell division. Repeated cycles of adding fixative, centrifugation and discarding supernatant were performed several times till fluid became milky due to cell pellet formation. Slides were stained by Giemsa stain for g-banding. After the confirmation of aneuploidy, ECG of all cases of Down's syndrome was done for the detection of cardiac defect.

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RESULTS

Detail of results is given in tables 1,2,3,4.

Table 1: Down's syndrome WRT maternal age

Maternal age(yrs)	n	%age
<20	5	3.1
21-25	23	14.4
26-30	56	35.0
31-35	43	26.9
>35	33	20.6
Total	160	100

Table 2: Down's syndrome WRT paternal age

Paternal age(yrs)	Down's syndrome	%age
≤ 30	31	19.4
31 – 40	99	61.9
41 – 50	29	18.1
51+	01	0.6
Total	160	100.0

On karyotypic analysis of 160 cases, the frequency of Trisomy 21 was 154 (96.2%), Translocation 05(3.1%) and Mosaicism 01(0.6%). Of the 05(3.1%) cases who were karyotyped positive for translocation, 04 showed 46,XX/XY, t(14q;21q), whereas only 01 was 46,XY,t(22q,21q). Out of 154 cases of trisomy 21, 55 cases (35.7%) were present in maternal age group 03 and 53 cases of trisomy 21 (34.4%) were seen in paternal age group 02.

Table 3: PDA and VSD in Down's syndrome WRT maternal age

Maternal ge(yrs)	DS cases with PDA	DS cases with VSD
≤ 30	12 (46.1%)	12 (50%)
31 – 40	13 (50%)	10 (41.7%)
41 – 50	00 (0%)	02 (8.3%)
51+	00	00
Total	25	24

Table 4: PDA and VSD in Down's syndrome WRT paternal age

Paternal age (yrs)	DS cases with PDA	DS cases with VSD
≤ 30	03 (11.5%)	06(25%)
31 – 40	19 (73%)	14(58.3%)
41 – 50	03 (15.3%)	03(12.5%)
51+	00 (0 %)	01(4.1%)
Total	25	24

DISCUSSION

In this study, maternal age is from 17 to 54 years, with a mean of 31 years. The high incidence of DS cases i.e. 35% were present in the maternal age of 26-30 years. 36.55% Down's syndrome with CHD were born to mothers in age of 26-30 years whereas 30.2% of Down's syndrome with CHD belonged to mothers in 31-35 year. Cases with CHD were seen in 12.7% in women >35 years of age. These results are in favor of Bergstrom et al who did a study on 2588 DS infants in Sweden and reported that CHD risk was 01% lower per maternal year of age[15]. This is contrary to the cases of non-syndromic CHD where maternal age >35 years has been found by Miller et al in 5289 infants in 2011. He showed that increase in maternal age increases the risk of cardiac defect by 20%[6].

In paternal age, it was found that 61.9% population of Down's syndrome was born to fathers age between 31-40 years. Fisch et al[7] in 2003 studied 3419 cases at New York and reported no paternal age influence on DS until age 35 years and more. This study was consistent with our finding as far as paternal age is concerned. A paternal age effect was seen in association with a maternal age of 35 years and older which is also comparable with our findings as the maximum number of Down's syndrome cases existed in the age group of 31-40 years for both fathers and mothers.

When we compared father's age with the occurrence of congenital cardiac defects in Down's syndrome, we found that 54% of Down's syndrome with congenital cardiac defects belonged to fathers of age 31-40 years. It was followed by 28.6% of DS with congenital cardiac defects in fathers of age <30 years. This finding was statistically significant and was not reported by any study in Pakistan before.

In our study, we compared maternal and paternal age with the incidence of PDA and VSD. In mothers the high incidence of PDA and VSD was present in age ≤ 30 years i.e. 46.1% PDA and 50% VSD. In age group 31-40 years, PDA of 50% and VSD of 41.7%. More of PDA along with VSD were present in the paternal age of 31-40 years i.e. 73% PDA and 58.3% VSD. This finding agrees with Xiu et al[8].

CONCLUSION

Common type of Down's syndrome was Trisomy 21. Most common CHD were PDA and VSD. Most of the Down's syndrome babies were born to mothers in age group 25 to 30 years and fathers in age group 31 to 40 years.

Conflict of interest: Nil

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