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Research Article

PHENOTYPIC AND CLINICAL COMPLICACY ASSESSMENT IN DOWN SYNDROME REFERRALS FROM J&K

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ABSTRACT

For the present investigation a study group of total 90 subjects consisting of 40 confirmed subjects and 50 controls were undertaken to assess the frequency of different phenotypic features and congenital/ clinical complication of Down syndrome referrals. Cytogenetic profile, for confirmation, is studied and compared in both the group and these results were significantly different from control on comparison, as Karyotype was normal in healthy controls but not in confirmed group. Clinical features like mongoloid face, flat facial profile, epicanthic fold, simian crease in palm, saddle gap, open mouth, protruding tongue and other complications were more pronounced in Down syndrome group than control group. Present study laid stress upon importance of thorough clinical examination of referrals, for their confirmation at chromosomal level.

INTRODUCTION

Down syndrome, Trisomy 21, is a condition in which extra genetic material causes development delay, both at mental and physical level. Children with Down syndrome have multiple malformations, medical conditions, and cognitive impairment because of the presence of extra genetic material from chromosome 21(1, 2). Down syndrome is usually diagnosed clinically at birth by its clinical feature. It is often associated with presence of chest infection, anemia, anal malformation, jaundice and congenital heart diseases (CHD). Cardiac malformation is the principal cause of mortality in the first two years of life (3, 4). Among the more common physical findings are moon like face, hypotonia, saddle gap, epicanthal folds, flat nasal bridge, open mouth, protruding tongue, low set ears, single palmar crease, facial dysmorphism, lethargic, weak at birth. The aim of present study is to evaluate Karyotype, frequency of phenotypic features and clinical complications in Down syndrome referral cases.

MATERIAL AND METHOD

Sample: A total of 90 Cases were referred to Major research lab of institute of Human genetics, University of Jammu, by Govt. Medical College (GMC) & Acharaya Shri Chander College of Medical Sciences (ASCOM), Jammu. The study plan & questionnaire was duly approved by the Animal and Human Experimentation Ethical committee (AHEEC), university of Jammu.

Physical examination: Clinical suspected sample present numerous clinical manifestation in any part of body system. Clinical examination of patients face, mouth, eyes, nose, hands, feet was observed and regarded as normal or abnormal (5). Such features like facial dysmorphism, flat facial profile, moon like face, protruded tongue, Simian crease, saddle gap and epicanthic fold are clinical established abnormal features (5, 6). Individuals are also referred for examination if they posses any clinical complication like heart hole, jaundice etc.

Short term lymphocyte culture: Blood samples were collected by informed and written consent. Collected samples were subjected to Short term lymphocyte culture, set up with slight

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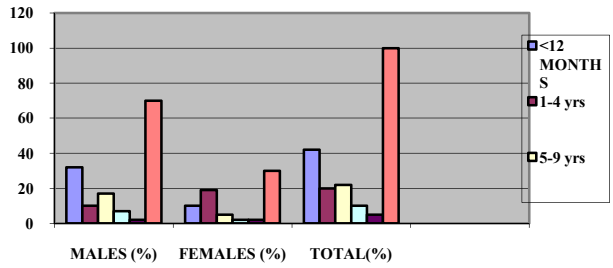
modification in the protocol given by Moorhead *et.al*., (1960) and slide preparation by GTG banding (Seabright M, 1971) to analyse metaphase chromosome prepared by Automated Karyotype Workstation (cytovision).

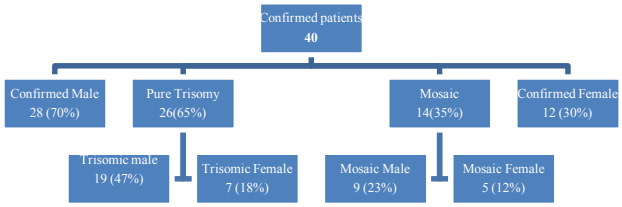
RESULTS

Cytogenetic study was conducted on 90 suspected patients, it was confirmed that 40 patients were having trisomy 21. The age of patients range between 4 months to 18 years age group, consisting 28(70%) males and 12(30%) females. Total 17(42%) patients below 12 months age group, 23(57%) were between 1 year to 18 years age. Cytogenetic testing of patients revealed that 26(65%) confirmed had pure trisomy and 14(35%) had mosaic pattern, containing 19(47%) trisomic male, 9(17%) mosaic male, 7(22%) trisomic female and mosaic female 5(12%).

Category of Down syndrome referrals (n=40) as per age groups and gender



Chromosomal result of confirmed patients



Remaining enrolled cases n=50 had normal Karyotype. Their age fall between 8 months to 16 years, among them 32 were male and 18 were female. From now onwards the cases with normal Karyotype would be considered as controls, for study data comparison with respect to confirmed cases.

Phenotypic features of studied group: In Present phenotypic study of confirmed and control showed highest frequency (54%) of incubation of baby at birth, open mouth and mongloid face (47%), hypotonia (45%), epicanthic fold (44%), depressed nasal bridge (43%), distance of eyes (42%)etc.

Table No.1 showing percentage of phenotypic features in all referral cases

Open mouth	42	47%	Low birth weight	37	41%
Epicanthic fold	40	44%	Incubation at birth	49	54%
Low set ears	15	17%	Hypotonia	41	45%
Simian crease	18	20%	Distance of eyes	38	42%
Facial dysmorphism	8	9%	Protruding abdomen	5	5%
protruding tongue	26	29%	Mongloid face	42	47%
Depress nasal bridge	39	43%	Saddle gap	31	34%

with least prominent feature protruded abdomen (5%).

Different co-existing clinical complications with Down syndrome observed in present investigation are depicted in **table No.2**

Gastrointestinal	**Constipation, jaundice, anal blockage, high arched palate, acute dysentery, blood stool, recurrent fever, seizures, decreased feeding**
Respiratory	Chest infection, sleep apnea, respiratory distress, cough, fast breathing, bronchopneumonia
Heart complication	Heart hole
Developmental delay	Mentally retarded, cerebral atrophy
Muscle deformity	Hypotonia, standing and walk problem, legs very weak, feet toward inner side
Others	Low birth weight, lethargic, incubation of baby, hospitalization at birth, irritability, up rolling eyeballs, anemia

Moon like face was commonly seen phenotypic feature (80%) as per the following data of confirmed cases, whereas others were distance of eye (67%), hypotonia (57%), epicanthic fold (55%), protruded tongue (50%), flat nasal bridge (45%), open mouth (38%), saddle gap (37%) and least one is simian crease (32%).

The age group division of data obtained expresses most of children born have caesarian route (85%) and low birth weight (80%) as major complication followed by gastric anomalies (77%), development delay and jaundice at birth (65%), chest infection (62%), heart problem and anemia (32%).

Phenotypic variation of whole sample was assessed and comparison of confirmed and control is concluded that depicted open mouth and moon like face were highly expressed phenotypic feature overall whereas protruded tongue and simian crease were less commonly expressed by studied sample that is 29% and 20% respectively. Among the control group such features are also expressed but at very low percentage like only 2 (4%) patients were found to have protruded tongue, 3 (5%) were having saddle gap and epicanthic fold likewise 4 (8%) patients were of hypotonia, 5 (10%) of simian crease with this distance of eye, mongloid face, flat nasal bridge were confirmed in 11(22%), 10 (20%) & 21(42%) normal control cases respectively.

DISCUSSION

Down syndrome is a common birth defect and phenotypic appearance aids in early diagnosis although karyotypic performance is necessary for confirmation of suspected having either pure trisomy 21, mosaicism or translocation. The Down syndrome patients have variety of congenital and non-congenital complicacy that possibly has impact on their physical and mental level development. Our cytogenetic results provided 65% of pure trisomy and 35% of mosaic cases where as study conducted by Demirhan *et al*., showed 93% free trisomy and 2.5% of mosaic cases (7), similarly in another study by kaur and kaur in 2013 represent 87.71% free trisomy and 5.26% translocation cases (8). Earlier findings from Jammu region by Balwan and Gupta reported 15.58% mosaicism which was lower in comparison to present findings (9).

In the present study 42% DS children were diagnosed early below the age of 12 months and 20% of cases between 1-4years.

Phenotypic features of the Down syndrome patients are shown in **Table No.3**

Age groups	DS patient (n= 40)	Open Mouth N(%)	Distance of eye N(%)	Protuded tongue N(%)	Moon like face N(%)	Hypotonia N(%)	Simian crease N(%)	Saddle Gap N (%)	Epicanthic fold N (%)	Flat nasal bridge N(%)
<12month	17 42%	17 42%	14 35%	11 27%	16 40%	13 32%	8 20%	6 15%	12 30%	6 15%
1-4 yr	8 20%	7 17%	5 12%	6 15%	8 20%	5 12%	3 7%	6 15%	4 10%	6 15%
5-9 yr	9 22%	6 15%	5 12%	3 7%	5 12%	3 7%	1 2%	2 5%	5 12%	4 10%
10-14 yr	4 10%	3 7%	1 2%	0 0	2 5%	2 5%	0 0	0 0	1 2%	2 5%
15-19 yr	2 5%	1 2%	2 5%	0 0	1 2%	2 5%	1 2%	1 2%	0 0	0 0
total	40	34 38%	27 67%	20 50%	32 80%	23 57%	13 32%	15 37%	22 55%	18 45%

Category of Down syndrome referrals as per their most commonly observed clinical complications in **Table No.4**

Age groups	DS patients (n=40)	Chest infection (n=25)	Developme nt delay (n=26)	Low birth weight (n=32)	Cesarian route (n=34)	Heart problem (n= 13)	Jaundice at birth (n=26)	Anemia (n=13)	Gastric Anomalie (n=31)
<12month	17 42%	11 27%	15 37%	16 40%	16 40%	8 20%	14 35%	4 10%	13 32%
1-4 yrs	8 20%	6 15%	3 7%	6 15%	7 17%	3 7%	6 15%	4 10%	7 17%
5-9 yrs	9 22%	4 10%	6 15%	6 15%	7 17%	1 2%	4 10%	3 7%	7 17%
10-14 yr	4 10%	3 7%	2 5%	2 5%	2 5%	1 2%	1 2%	1 2%	2 5%
15-19 yr	2 5%	1 2%	0 0	2 5%	2 5%	0 0	1 2%	1 2%	2 5%
Total	40	25 62%	26 65%	32 80%	34 85%	13 32%	26 65%	13 32%	31 77%

Comparison of phenotypic features of the Study Cases in **table no.5**

Types	Open Mouth	Distance of eye N(%)	Protruded tongue N(%)	Mongloid face N(%)	Simian crease N(%)	Saddle gap N (%)	Epicanthic fold N (%)	Flat nasal bridge N(%)	Hypot -onia N(%)
Control (n=50)	8 9%	11 22%	2 4%	10 20%	5 10%	3 5%	3 5%	21 42%	4 8%
DS patient (n=40)	34 38%	27 67%	20 50%	32 80%	13 32%	15 37%	22 55%	18 45%	23 57%
Total (n=90)	42 47%	38 42%	26 29%	42 47%	18 20%	31 34%	40 44%	39 43%	41 45%

Thus 62% patients were diagnosed below 5years of age and rest of 37% were within 5-19years which appears that pediatrics and other clinicians are familiar with the typical features and early diagnosis is possible. Results from Lebanon are 47.3% (10) and Estonia 48% (11) were also similar regarding early patients diagnosis.

On comparison of clinical features and complicacy between control and confirmed indicated variety of differences. Around 10 cardinal features given by Hall in 1966 (12).The result of clinical examination revealed moon like face as most commonly observed about 80% of the total cases ,distance of eye (67%), hypotonia (57%), epicanthic fold (55%), protruded tongue (50%), flat nasal bridge (45%), open mouth (38%), saddle gap (37%) simian crease (32%) whereas study of Kaur and Kaur represent epicanthal folds (78.1%) as most commonly observed followed by protruding tongue (67%), developmental delay (59%), depressed nasal bridge (57.01%), chest infection (55.26%), low set and small ears (54.38%), simian crease (45.61%), palpebral fissures (39.47%), sleep apnea in 21.92% cases, respiratory distress in 9.64% cases(8). In a study done by Bertelli *et al*., Flat facial profile 98%, hypotonia 59%, simian crease 84%,epicanthic fold 79%,open mouth 48%, saddle gap 64% ,flat nasal bridge 93%(13).

Similarly, in another study by Bertelli *et al*., a higher frequency of low birth weight 12.3% reported (13). Our data had 80% low birth weight. The protruding tongue, observed in 33.9% of the evaluated children (13), Kava *et al*., described similar frequency 29.9% in a sample of DS individuals in India (14). Down syndrome, a risk factor for a number of diseases. In some studies the incidence of Down syndrome congenital heart disease is high as 58% (15). Ferencz *et al*., found it to be occurs in 40%-50% of those with DS (16).

The percentage of Congenital heart disease in the present investigation was 32% which was lower as reported for Abbag (17) and Podder *et al*., study (18). In some other study, 56.5% of the children presented congenital heart diseases (13). The study of Balwan *et al*., reported Double Trisomy 48, XXX case with typical features of Down syndrome (19) but no such case was observed in our study. In another study of Gupta *et al*., analysis of 24 cases of anorectal malformation, 4 cases showed the association with Down syndrome, such association was observed in our sample (20). Occurance of jaundice at the time of birth is usually seen in DS patients similar observations were found in present study and studies done by different researchers (8,18).

CONCLUSION

The prevalent cytogenetic cause of DS was found to be pure trisomy in comparison to mosaicism in the present investigation. Among phenotypic variations associated with DS frequency of mongloid face and open mouth was high followed by epicanthic fold and flat nasal bridge. Apart, males were more affected in judgement to females. Knowledge of the cytogenetic, clinical profile and clinical implications helps clinician/geneticist to determine the recurrence risk in subsequent pregnancies and couples in decision making. Thus, decreases the load of disease in society.

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