CLINICAL PROFILE OF DOWN SYNDROME IN CHILDREN LESS THAN 14 YEARS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND

Down syndrome is the most common and most easily recognised condition causing intellectual disability. Down syndrome occurs in 1 in 700 to 1 in 1000 live births.

The aim of this study was to evaluate the incidence and clinical profile of Down syndrome in children below 14 years.

MATERIALS AND METHODS

Children below 14 years who presented with symptoms of Down syndrome from 1st December 2015 to 30th November 2017 were included in this hospital-based case series study.

RESULTS

The hospital-based incidence was found to be 0.1%. The mean age of presentation was found to be 28.6 months. The ratio of male: female was 1.57. The mean maternal age at delivery was found to be 27.6 years. About 9.5% of Down syndromes were diagnosed antenatally. The first order children were more common (42.9%) followed by second order (32.5%). Diagnosis by using Hall's criteria was done in 94.4% cases. On karyotyping 94.4% had non-disjunction and 4.6% patient had translocation.

CONCLUSION

The chromosomal non-disjunction was the most common type of chromosomal abnormality in Down syndrome. Down syndrome is associated with significant systemic abnormalities and is not infrequent among mothers younger than 25 years of age. Early diagnosis and proper screening should be undertaken among these patients.

KEY WORDS

Down Syndrome, Intellectual Disability, Karyotyping.

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BACKGROUND

Down syndrome is the most common and most easily recognised condition causing intellectual disability.^[1] Down syndrome occurs in 1 in 700 to 1 in 1000 live births.^[2] The most common type of Down syndrome accounting for 95% of cases is standard Trisomy 21 and is caused by an extra chromosome 21. The other types are translocations where only some cells will contain the extra chromosome (Mosaic Trisomy 21).^[1,3] The two sets of characteristics, most frequently associated with Down syndrome are a distinctive facial appearance and intellectual impairment. Indeed, it was the distinctive appearance and in particular the epicanthic fold that contributed to the identification of Down syndrome by Langdon Down (1866) and his association of people with Down syndrome with the 'Mongoloid race'.^[4] Down syndrome is diagnosed at birth and the facial characteristics means the syndrome is easily identifiable to anyone the child comes into contact with from an early age. The people with Down syndrome will have some degree of intellectual

impairment, though the level of impairment varies from person to person. According to Carr (1988) children and adults with Down syndrome differ from one another in term of Intelligence Quotient (IQ) to a similar magnitude to people in the non-disabled population; that is people's IQs can differ by 50 to 60 IQ points. Recent behavioural phenotype research has identified a distinct profile of behavioural strengths and weaknesses associated with Down syndrome.^[3] Behavioural phenotype research allows for a more fine grained understanding of abilities and the potential of children with genetic disorders than that provided by an IQ score.^[3,5] The greater understanding can be achieved by investigating how the phenotypes develop and change overtime.^[6] The Down syndrome behavioural phenotype includes relative strengths in areas of visual spatial processing compared with verbal processing.^[7,8] In particular, visual memory and visual motor integration appear to be areas of relative strength.^[3,9] Long term memory for words and pictures has also been found to be significantly difficult for children with Down syndrome. Social functioning has been generally considered to be an area of strength in children with Down syndrome.^[10] Children with Down syndromes are stigmatised both for having an intellectual disability and for how they look.^[5] So this study is planned to study the clinical profile of Down's syndrome.

Aims and Objectives

To evaluate the incidence and clinical profile of Down syndrome in children below 14 years.

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MATERIALS AND METHODS

After obtaining the ethical committee clearance from the Institutional Ethical Committee, the study was conducted. The children below 14 years who presented with symptoms of Down syndrome from 1st December 2015 to 30th November 2017.

It is a hospital-based case series study. Selection of cases: All the children below 14 years with clinical and laboratory evidence of Down syndrome reported/admitted to outdoor/indoor of SVP PGIP and SCB Medical College during study period fulfilling the inclusion criteria were taken as cases after taking consent from parents. 126 patients were selected for the study.

Inclusion Criteria: All the children below 14 years of age presenting with the signs and symptoms of Down syndrome or diagnosed by Karyotyping and neonate fitting to Hall's criteria were included in the study.

Exclusion Criteria: The children with other syndromic associations, suspected with single gene disorders, inborn error of metabolism and multifactorial genetic diseases or other anomalies which are not diagnosed as Down syndrome were excluded from the study.

Hall's Criteria: Hypotonia, poor Moro's reflex, flat face, upward slanted palpebral fissure, small dysplastic ears, joint hyperflexibility, short neck, short fifth-digit clinodactyly, single transverse palmar crease and pelvic dysplasia.

Investigation

The following investigations were carried out in each case to determine the associated conditions. A. Blood: Complete blood count, comment on peripheral smear, thyroid function test, B. Bone marrow study, C. Radiological study: X-ray, Ultrasound of brain, abdomen, CT scan/ MRI, Barium meal follow-through, D. ECG, E. Echocardiography, F. EEG, G. Karyotyping, H. Ophthalmological examination: Slit lamp biomicroscopy, visual acuity testing, ophthalmoscopy; I. Audiological investigation: OAE, BERA.

Statistical Analysis

For statistical analyses, the data were done by chi-square test. The calculated p-value is below the threshold chosen for statistical significance.

P-value ≤ 0.05 was considered for statistical significance.

RESULTS

Incidence: 126/112949		Male	Female	Frequency	%
Total Patients		77	49	126	100
Age Group	< 1 year	46	26	72	57.1
	1 to 5 years	20	12	32	25.4
	>5 years	11	11	22	17.5
				126	0.1

Table 1. Distribution of Incidence

The hospital-based incidence was found to be 0.1%. Male: Female ratio being 1.57.

Maternal Age at Delivery in Years	Frequency	%
< 20	13	10.3
20-25	37	29.4
26-30	27	21.4

31-34	31	24.6
>35	18	14.3
Total	126	100

Table 2. Distribution of Maternal Age at Delivery

The mean maternal age at delivery was found to be 27.6 years.

Antenatal Diagnosis	Frequency	Percentage
No	114	90.5
Yes	12	9.5
Total	126	100

Table 3. Distribution of Antenatal Diagnosis

About 9.5% of Down syndrome were diagnosed antenatally.

Order	Frequency	Percentage
1 st	54	42.9
2 nd	41	32.5
3 rd	24	19
4 th	6	4.8
5 th	1	0.8
Total	126	100

Table 4. Distribution of Order of Births

The first order children were found to be more common (42.9%) followed by second order (32.5%).

Diagnosis using Hall's Criteria	Frequency	%
No	7	5.6
Yes	119	94.4
Total	126	100

Table 5. Distribution of diagnosis using Hall's Criteria

The diagnosis by using Hall's criteria was 94.4%.

Karyotyping	Frequency	Percentage
Non-disjunction	94	74.6
Translocation	5	4
Not done	27	21.4
Total	126	100

Table 6. Distribution of Karyotyping

On karyotyping, 94.4% had non-disjunction and 4.6% patient had translocation.

Features		Frequency	
		Present	%
Craniofacial dysmorphism	Epicanthic fold	115	91.3
	Flat facial facies	99	78.6
	Mongoloid slant	117	92.9
	Small dysplastic ear	58	46
	Brachycephaly	28	22.2
	Cleft lip	9	7.1
	Cleft palate	2	1.6
	Protruding tongue	37	29.4
	Low set ear	56	44.4
	Hypotonia	81	64.3
CNS Feature	Poor Moro reflex	39	31
	Motor develop delay	65	51.6
	Speech impairment	38	30.2
	Cognitive impairment	26	20.6
	Hearing impairment	77	61.1

	Seizures	4	3.2
	Autistic disorder	1	0.8
	Behavioural disorder	0	0
CVS Finding	ASD	5	4
	ECD	10	7.9
	Eisenmenger complex	2	1.6
	Normal	95	75.4
	TOF	4	3.2
	VSD	10	7.9
Ophthalmological feature	Brushfield spot	3	2.4
	Cataract	4	3.2
	Hypertelorism	40	31.7
	Normal	72	57.1
	Nystagmus	4	3.2
	Strabismus	3	2.4
Limb Anomaly	Sandal gap	53	42.1
	Kennedy crease	67	53.2
	Brachydactyly	47	37.3
	Clinodactyly	46	36.5
	Polydactyly	5	4
	Simian crease	42	33.3
	Sydney line	31	24.6
	Increased ATD angle	51	40.5
	Mostly ulnar loops in finger prints	126	100
Haematological disorder	ALL	5	4
	AML	2	1.6
	Normal	108	85.7
	Transient myeloproliferative disorder	11	8.7
Thyroid disorder	Normal	115	91.3
	Hypothyroid	11	8.7
G I Malformation	Annular pancreas	4	3.2
	Celiac disease	2	1.6
	Duodenal atresia	8	6.3
	Hirschsprung disease	4	3.2
	Imperforate anus	3	2.4
	Tracheo-oesophageal fistula	5	4
	Normal	100	79.4
Musculoskeletal defect	Atlantoaxial instability	23	18.3
	Hip dysplasia	9	7.1
	Scoliosis	4	3.2
	Normal	90	71.4
Other features	Recurrent RTI	47	37.3
	Seborrhoeic dermatitis	30	23.8
	Obstructive sleep apnoea	15	11.9
	Delayed tooth eruption	25	19.8

Table 7. Distribution of Different Malformation

The table shows the frequency of different presentation of clinical signs and symptoms of Down syndrome.

Sl. No.	Disease Associated	Maternal Age at Delivery	Disease (%)	Normal	Total	P-value
1	GI Malformation	Less than 20 years	1	12	13	0.1516
		20-25 years	5	32	37	
		26-30 years	5	22	27	

		31-34 years	8	23	31	0.1239
		≥ 35 years	7	11	18	
		Less than 20 years	4	9	13	
		20-25 years	6	31	37	
		26-30 years	1	26	27	
2	Haematological Disorder	31-34 years	6	25	31	0.4679
		≥ 35 years	1	17	18	
		Less than 20 years	3	10	13	
		20-25 years	13	24	37	
		26-30 years	6	21	27	
3	CVS Disorder	31-34 years	5	26	31	0.6407
		≥ 35 years	4	14	18	
		Less than 20 years	2	11	13	
		20-25 years	4	33	37	
		26-30 years	3	24	27	
4	Hypothyroidism	31-34 years	1	30	31	0.6407
		≥ 35 years	1	17	18	

Table 8. Disease/Deformity associated with Maternal Age

There is no statistical significance seen as far as maternal age and disease is concerned.

Sl. No.	Disease	Order of Birth	Present	Normal	Total	P-value
1	GI Malformation	1 st	10	44	54	0.4279
		2 nd	9	32	41	
		3 rd	4	20	24	
		4 th	3	3	6	
		5 th	0	1	1	
2	Haematological Disorder	1 st	9	45	54	0.6678
		2 nd	7	34	41	
		3 rd	2	22	24	
		4 th	0	6	6	
		5 th	0	1	1	
3	CVS Disorder	1 st	10	44	54	0.2775
		2 nd	12	29	41	
		3 rd	7	17	24	
		4 th	1	5	6	
		5 th	1	0	1	
4	Hypothyroidism	1 st	4	50	54	0.8749
		2 nd	3	38	41	
		3 rd	3	21	24	
		4 th	1	5	6	
		5 th	0	1	1	

Table 9. Diseases/ Deformity associated with birth order

There is no statistical significance seen as far as birth order and disease is concerned.

DISCUSSION

Out of total number of 112949 reported cases in OPD and IPD, Department of Paediatrics in the expected age group during the study period, 126 cases fulfilling the inclusion criteria were included in the present study.

The incidence of Down syndrome in our study was found to be 0.1%. Jaruratanasirikul S et al found a prevalence of Down syndrome to be 1.21 per 1000 births in a population-based study in Southern Thailand. Ram Lakhan^[10] et al found the prevalence of Down syndrome to be 1.45 in tribal population, which is greater than our study. It might be due to environmental and genetic factors. Hospital based

incidence could not be compared with large population-based study, as the incidence or prevalence were calculated in a large scale population and in community based manner.

The ratio of male-to-female being 1.57 in our study. Kava MP and Tullu MS, Muranjan MM and Girisha KM (2005)^[11] found this ratio of 1.37 in their study, which was just lower to our study. This might be due to lesser sample size of our study. KR Lahiri and Satish observed that this ratio of 1.47, which is almost similar to our study. The excess of male appears to be universal and was reported in all studies in different countries and ranged from 1.1: 1 to 2.3: 1. Kovaleva NV^[12] study concluded that the sex ratio was skewed towards excess of males in majority.

In our study, 9.5% of patients of Down syndrome were diagnosed in antenatal period. Gilany et al^[13] in a study on Down syndrome in Mansoura, Egypt found all Down syndrome cases diagnosed after birth. About 42.9% were first child of their mother, which could be compared to the study of Gilany et al.^[13] About 94.4% of children were diagnosed by Hall's criteria in our study.

Out of 99 patients in whom karyotyping was done, 94.4% showed non-disjunction and 4.6% had translocation. 21.4% patients did not get it done in our study. Kava et al^[11] found free trisomy (non-disjunction in 95%), translocation in 3.2% and mosaicism in 1.8%. Gilany et al found non-disjunction was most common (96.1%) followed by translocation (3.1%) than mosaic (0.8%). DS Wang YF et al^[14] found that 93.02% had non-disjunction and translocation in 3.4% patients. All the studies done were found to have almost similar proportion in karyotyping.

In our study physical finding that were most prominent were epicanthic folds, flat facial facies, mongoloid slant, small dysplastic ear, brachycephaly, cleft lip and cleft palate which corresponds to 78.6%, 91.3%, 92.9%, 46%, 22.2%, 7.1% and 1.6% respectively. Low set ear were found in 44.4% of cases. Kava et al noted mongoloid slant in 83.9%, epicanthal fold in 56.9%, ear abnormality in 66.9% and flat facial facies in 50.9% cases. Källén B et al^[15] studied that there was elevated risk ratio of cleft lip and cleft palate around 3 - 5 in cases of Down syndrome in their 5581 collected samples. Irfan Ahmed et al^[16] showed that brachycephaly was seen in 40% of cases in their study. This might be due to geographical variation.

Around 64.3% children had hypotonia, 31% children showed poor Moro reflex, all of them were below 8 months age. 51.6% patients were found to have features of delayed motor development. 30.2% children showed features of delay in speech and articulation problems which could be compared with the study by Abbeduto L, Warren SF and Conners FA.^[17] Stuttering was found to be present in 10-45% of Down syndrome studied by Ray D Kent and Hourri K Vorperian.^[18] Pueschel SM^[19] showed that epilepsy occurs in 1% to 13% of children with Down syndrome. Capone G, Goyal P, Ares W and Lannigan E^[20] showed that neurobehavioural and psychiatric comorbidity in children with Down syndrome range from 18% to 38% which was higher than our study. Kava et al found that 76.3% cases had hypotonia in their study, which is similar to our study. Arya et al^[21] and Lujic et al^[22] estimated that 5 - 13% children with Down syndrome had seizures. It was slightly higher than our study. Irfan Ahmed et al^[16] found that delayed developmental delay was seen in 68.5%, which was lower than our study. Neerja

Agarwal Gupta et al^[23] found that hearing loss could be conductive or sensorineural and seen in 75% of children with Down syndrome and majority of patients had serous otitis media, which was higher than our study. Raut et al^[24] in their study showed the incidence of hearing loss in first year of life which was 34.1%. Nightingale E et al^[25] in their study found that permanent hearing loss was found in 24.9% of cases. Most common cardiovascular abnormality in our study was VSD (7.9%) and endocardial cushion defect (7.9%) followed by ASD (4%). TOF was seen in 3.2% cases and Eisenmenger complex in 1.6% cases. Kava et al found VSD in 25.8% cases, TOF in 15.5% cases and ASD in 12.1% cases. Benhaourech Sanna et al in their study from 2156 patients with CHD, 128 were identified with Down syndrome where most common was Endocardial cushion defects in 29% followed by VSD in 21.5% cases comparable to our study. In the study of Gilany et al they had seen CHD in 18.9% cases of Down syndrome cases, which were 24.6% cases. In their study, most common defect was VSD in 7.9% cases, which was similar to our study. Irfan Ahmed et al found CHD in 39.4% cases which included VSD in 36.9% cases, which included VSD in 36.9% cases, ECD in 33% cases, ASD in 14.5% cases and TOF in 7.8% of children. Lahiri et al said that ECD to be the most common CHD followed by VSD in their study. The most common ophthalmological finding was Hypertelorism in 31.7% cases followed by Cataract and Nystagmus 3.2% cases separately, Brushfield spot in 2.4% patients and Strabismus in 2.4% cases. Kava MP et al^[11] found Hypertelorism (33.9%), Nystagmus (3.2%), Brushfield spot (3.2%), Strabismus (2.7%) and Cataract (1.9%) which is comparable to our study. Irfan Ahmed et al^[16] demonstrated Hypertelorism (62.4%), Nystagmus (6.1%), Brushfield spot (5.4%), Strabismus (6.4%) and Cataract (1.9%), which was slightly higher than our study. Wong V et al^[26] found strabismus in 20% and nystagmus in 11% of cases in their study. Dermatoglyphics features like sandal gap, Kennedy line, brachydactyly, clinodactyly, polydactyly, simian crease, Sydney line, increased ATD angle and Ulnar loop represents 42.1%, 53.2%, 37.3%, 36.5%, 4%, 33.3%, 24.6%, 40.5% and 100% cases respectively. Kava et al found sandal gap in 46.2%, simian crease in 33.2%, clinodactyly in 36.1% and brachydactyly in 11.1% respectively which could be comparable to our study. Irfan Ahmed et al said that in their study sandal gap was present in 46.4% cases, clinodactyly in 24.7%, simian crease in 64.7% and brachydactyly in 23.7% cases. S. Rajangam et al^[27] told that in their study, out of 235 Down syndrome cases the ATD angle deferred significantly from control, i.e. more than 80 and mostly ulnar loop pattern observed in all cases. Castilla EE et al^[28] found association between polydactyly and Down syndrome in a retrospective study.

Brink DS^[29] found that transient myeloproliferative disorder of Down syndrome occurred in approximately 10% of Down syndrome neonates and in phenotypically normal neonates with trisomy 21 mosaicism which is similar to our study. John K Choi^[30] found that up to 10% of all Down syndrome patients have transient myeloproliferative disorder, although more recent studies found lower percentage (3 to 6%). In all three studies including our study, transient myeloproliferative disorder was the most common haematological disorder.

Irfan Ahmed et al^[17] found hypothyroidism in 7.1% cases and Gilany et al found 7.9% of cases of Down syndrome which is comparable to our study. Kava et al found GI anomalies in 7 cases, Down syndrome which included 3 cases of imperforated anus, 2 cases of Hirschsprung disease, 1 case of duodenal atresia and 1 case of Morgagni hernia; whereas Irfan et al found 1.7% cases of imperforated anus, tracheo-oesophageal fistula in 1.3% cases, Hirschsprung disease in 1% and duodenal atresia in 0.7% cases which is lower than our study. Fawzi Elhami Ali et al^[31] had observed that Atlantoaxial instability affected 10 - 20% of individuals, which is comparable to our study.

G Ram et al^[32] found around 45% of 1 - 3 years old children followed by less than 1 year of age were admitted for respiratory cause, which is similar to our study. Ondarza A et al^[33] found delayed eruption of teeth in patients with Down syndrome. On contrary to this in our study, only 19.8% cases had delayed dentition.

Irfan Ahmed et al found that 56.7% with trisomy had maternal age of > 35 years, which is different from our study. Jyothy et al^[34] documented that the Down syndrome cases were born to younger mothers (< 25 years).

The statistically insignificant values were observed in almost all cases. It might be due to less number of cases, shorter duration of study period or the changing pattern of presentation of Down syndrome. Further studies are required to obtain statistical significance.

SUMMARY

The hospital-based incidence was found to be 0.1%. The mean age of presentation was found to be 28.6 months. The ratio of male: female was 1.57. The mean maternal age at delivery was found to be 27.6 years. About 9.5% of Down syndrome were diagnosed antenatally. The first order children were found to be more common (42.9%) followed by second order (32.5%). The diagnosis by using Hall's criteria were 94.4%. On karyotyping, 94.4% had non-disjunction and 4.6% patients had translocation. The distribution of craniofacial dysmorphism showed flat facies in 78.6%, epicanthal fold in 91.3% cases, Mongoloid slant in 92.9% cases, small dysplastic ear in 46%, brachycephaly in 22.2% cases, cleft lip in 7.1%, cleft palate in 1.6%, patients with open mouth protruding tongue in 29.4% cases and lowest ear in 44.4% cases. In CNS features, Hypotonia was present in 64.3% of cases. Poor Moro's reflex in 31% cases, motor developmental delay in 51.6% cases, speech impairment in 30.2% cases, cognitive impairment in 20.6% cases, hearing impairment in 61.1% cases, seizures in 3.2% of cases and autism in 0.8% cases. In Echocardiography finding ECD and VSD both were present in 7.9% of cases, ASD in 4% cases, TOF in 3.2% cases and Eisenmenger complex in 1.6% cases. In ophthalmological finding hypertelorism being most common was present in 31.7% cases, nystagmus and cataract was found in 3.2% cases each, Brushfield spot and strabismus in 2.4% cases. Limb and dermatoglyphics feature showed sandal gap in 42.1% cases, Kennedy crease in 53.2% cases brachydactyly in 37.3% cases, clinodactyly in 36.5% cases, polydactyly in 4% cases, simian crease in 33.3% cases, Sydney line in 24.6% cases and increased ATD angle in 40.5% cases. We found mostly ulnar loops in fingerprints in 100% cases. Transient myeloproliferative disorder (8.7%) was found to be most common haematological disorder in our

study followed by AML (4%) and ALL (1.6%). Hypothyroidism was found to be present in 8.7% of cases in our study. Duodenal atresia was found to be most common GI malformation, i.e. 6.3% cases followed by tracheo-oesophageal fistula in 4% cases, annular pancreas in 3.2% cases, imperforated anus in 2.4% cases and coeliac disease in 1.6% cases. Atlantoaxial instability was found to be the most common (18.3%) followed by hip dysplasia (7.1%) and scoliosis in 3.2% cases in musculoskeletal defects. Around 87.3% cases were coming to hospital for recurrent respiratory tract infections. Around 23.8% cases were having seborrhoeic dermatitis and 19.8% of cases were having delayed tooth eruption. Most number of Down syndrome patients (29.4%) have delivered from mother of age group of 20 - 25 years followed by 31 - 34 years (24.6%) cases and 26 - 30 years of age in 21.4% of cases.

CONCLUSION

The chromosomal non-disjunction was the most common type of chromosomal abnormality in Down syndrome. The early presentation of Down syndrome in our setup is due to the hospital delivery and referral from the nearby community health centre. Down syndrome is associated with significant systemic abnormalities and is not infrequent among mothers younger than 25 years of age. Early diagnosis and proper screening should be undertaken among these patients. There must be a review for the recurrence risk in subsequent pregnancies and availability of prenatal diagnosis as provided in genetic counseling. The patients must be undergoing audiological evaluation annually, ophthalmologic evaluation every 2 yearly, TSH evaluation annually and other investigations must be at proper intervals. Effective early stimulation therapy, behavioural intervention, positive home environment, education, vocational training, occupational therapy, speech therapy and physiotherapy are helpful in improving the overall functioning and productivity of these children. Accurate and latest information must be provided in a supportive and empathetic manner.

Abbreviations

AAI: Atlantoaxial Instability.
 ALL: Acute Lymphoblastic Leukaemia.
 AML: Acute Myeloblastic Leukaemia.
 ARDS: Acute Respiratory Distress Syndrome.
 ASD: Atrial Septal Defect.
 ASM: Autistic Spectrum Disorder.
 ATD: Axial Triradius.
 BERA: Brainstem Evoked Response Audiometry.
 CBC: Complete Blood Count.
 CHD: Congenital Heart Disease.
 CPS: Comment on Peripheral Smear.
 CT: Computed Tomography.
 CVS: Chorionic Villus Sampling.
 ECD: Endocardial Cushion Defect.
 ECG: Electrocardiograph.
 EEG: Electroencephalograph.
 GI: Gastrointestinal.
 IQ: Intelligence Quotient.
 MDD: Motor Developmental Delay.
 MRI: Magnetic Resonance Imaging.
 OAE: Otoacoustic Emissions.
 TFT: Thyroid Function Test.
 TMD: Transient Myeloproliferative Disorder.

TOF: Tetralogy of Fallot.
 USG: Ultrasonography.
 VSD: Ventricular Septal Defect.

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