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PATAU SYNDROME [PARTIAL TRISOMY]: A CASE STUDY

RUDRAGOUDA S BULAGOUDA[1], B.M BANNUR[3], KEERTI K[2], BHEEMSHETTY S. PATIL[1] AND GURUSHANTAPPA S KADAKOL[1]*

[1]Department of Anatomy Genetics Laboratory, Shri B M Patil Medical College, Hospital & Research Center, BLDE University, Vijayapura, Karnataka, India.
[2]Department of Pediatrics, Shri B M Patil Medical College, Hospital & Research Center, BLDE University, Vijayapura, Karnataka, India.
[3]Professor & HOD department of Anatomy Shri B M Patil Medical College, Hospital & Research Center, BLDE University, Vijayapura, Karnataka, India.

ABSTRACT

We report a two newborn Childs with clinical symptoms of Patau syndrome, Karytotyping technique was used to determine chromosomal abnormalities and confirmed diagnosis. Patau syndrome is a rare and severe form of autosomal trisomics. It is coused by a chromosomal abnormality, in which some or all of the cells of the body contain extra genetic material from chromosome 13 disrupts the normal course of development, causing multiple and complex organ defects. It is related with more loss of pregnancy and survival of infants is very poor. Neonates with trisomy 13 die usually within the few hours or days of life. Eighty percent of babies affected this syndrome die within first month of life.The incidence rate of Patau Syndrome is1 in 20,000 live births. Survivors have profound mental retardation and other multiple physical abnormalities like cardio vascular defects, brain or spinal cord abnormalities,cleft palate or lip, extra fingers or toes and decreased muscle tone.

KEYWORDS: *Patau Syndrome, Cleft lip & Palate, Poly dactyly, trisomy 13, Karyotyp*

GURUSHANTAPPA S KADAKOL

Department of Anatomy Genetics Laboratory, Shri B M Patil Medical College, Hospital & Research Center, BLDE University, Vijayapura, Karnataka, India.

***Corresponding author**

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INTRODUCTION

Patau Syndrome, synonymous with trisomy 13, is a rare chromosomal abnormality which affects approximately1in20,000 live births and is associated with multisystem abnormalities[1,2] Trisomy 13 was first described in 1960 by Patau, who linked chromosomal defect with a variety of congenital malformations[3]. The frequency of newborns having abnormal chromosomes is 0.14% of Malays, 0.12% of Chinese and 0.06% of Indians [4]. The clinical features of Patau syndrome are Mental deficiency is a consistent feature. The other frequent clinical feature includes polydactyl, flexed fingers, rocker bottom feet, facial clefting, neural tube defects and heart defects. Patau syndrome is recognized at birth with the presence of structural birth defects and poor neurological performance [5]**.** Patau syndrome is caused by an extra copy of chromosome 13, a medium length acrocentric chromosome in which a person has three copies of genetic material instead of the usual two copies. So, the extra DNA from chromosome 13 appears in some or all the cells of the body. Normal development is affected by this extra material in most of the cases are not inherited, but in few cases trisomy 13 is caused by events in the sperm or egg form the fetus [5]. Spontaneous abortions, after 12 weeks of gestation, are 100 times more often caused by trisomy 13 than by any other condition. Between 12 weeks of gestation and full term, 49% (95% CI: 29-73%) of pregnancies diagnosed with trisomy 13 are estimated to end with miscarriage or stillbirth [6]. This disorder occurs advanced maternal age, additional chromosome is being origin of maternal origin. Trisomy 13 is cytogenetically classified as a full Trisomy (47XY + 13) due to the non disjunction at meiosis I or II, or mitosis (mosaicism) and partial trisomy due to translocations. Patau syndrome due to translocations can be inherited if one of the parents carries a balanced rearrangement of genetic material between chromosome 13 and another chromosome. Robertsonian translocations may involve two chromosome 13/46XX (13; 13) or chromosome 13 and another acrocentric (14, 15, 21, 22) [6]. We report two cases of Patau Syndrome confirmed by cytogenetic analysis i.e. karyotyping.

CASE I

A $G_3P_2L_2$, 37 week's period of gestation male with a birth weight of 1.75kg, delivered by caesarean(LSCS) was admitted in the NICU, department of Pediatrics, Shri B M Patil Medical College Hospital & Research centre, BLDE University, Vijayapur, Karnataka, India. Prior Consent was obtained. The newborn presented with multiple congenital anomalies. The clinical features includes cleft lip & Palate with right side (fig.1, A), Microcephaly with positive sign, low set of ears in right side (fig.1, B Polydactyl with right hand (fig.2, A). Rocker bottom feet were observed in left lower limb (fig.3, D). Cardiovascular system (CVS) is positive with no sign of murmur. Central Nervous system (CNS) is C/A/T good. Baby presenting a depressed Nasal Bridge, Mild pulmonary arterial hypertension and Patent Ductus Arteriosus (PDA) were detected on Echocardiography and morphometry of head circumference shows enlarged. We also noticed that there is a wide spaced nipples. During antenatal period, the pregnancy was monitored regularly & there were no maternal problems during antenatal period. There was no history of any drug intake during pregnancy except for iron-folic acid supplementation. There was no history of neonatal death in the family. The baby was born of a non consanguineous marriage, the mother being a 28 year old 3rd gravida. The first female baby was normal& second female baby were normal delivered by few years back by normal vaginal delivery at full term.

BIOCHEMICAL & PATHOLOGICAL ASSESSMENT

Cell Reactive Protein test was performed to see the functions of protein changes but there was no significant change in the functions of protein level Table 1.Complete Haemogram report shows significance change in predominantly macrocytic cells seen, Mild anisocytosis, Many polychromatophils seen in RBCs. Nrbc-4/100WBCs.No Parasites. Total count is within normal limits with relative increase in neutrophil count.B:N ratio-0.08 were observed in WBCs. Platelets were adequate on smear and Macrocytic blood smears with relative neutrophilia Table 2.

ABDOMINAL ULTRASONOGRAPHY OF CHILD (USG)

The ultra sonography (Siemens Ac.no 700) report impression of Liver, Gall bladder, Spleen and Kidney were in normal condition. The echo texture of Pelvic organs-urinary bladder is moderately distended & is normal. No calculi. No USG Abnormality detected in the Abdomen & Pelvis (fig 4).

ECHOCARDIOGRAPHY REPORT

Echocardiography (My Lab,25 gold) was done for child this gives Cyanotic CHD, Large Ostium, Secondary ASD (6.1mm) with Left to Right Shunt .RA/PV dilated, Good Biventricular function, Left aoctin arch normal, closing PDA with left to right shunt (2.2mm) (fig.5).Morphology of child is length is 40cm & HC is 31cm (fig.6).

Fig 1. A. Cleft lip & Palate with right side
B. Low set of Ears in Right Side

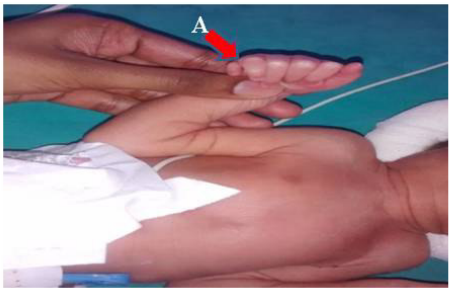


Fig 2. A. Polydactyl in right Hand

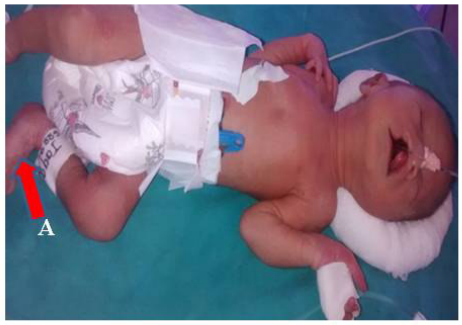


Fig. 3. A. Rocker Bottom Feet with left lower limb

Case 1 Figure 1, 2 & 3
Clinical features of Patau syndrome

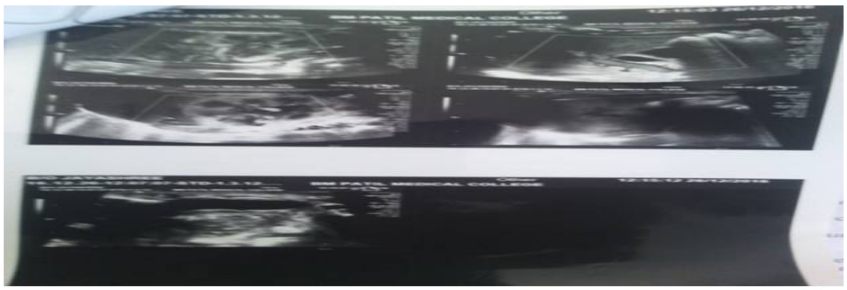


Fig. 4. Abdominal Ultrasonography

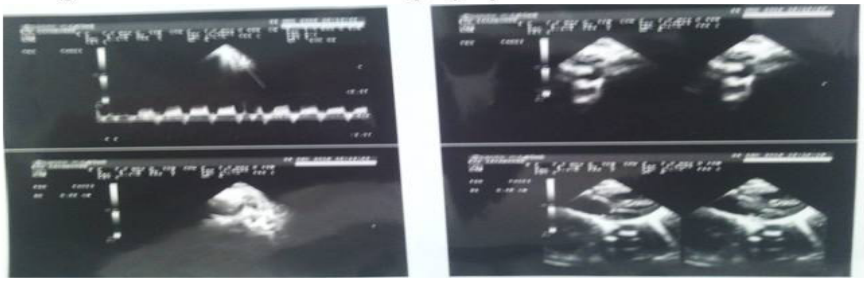


Fig. 5. Echocardiography

Case 1 Figure 4 & 5
Ultrasonography and Echocardiography

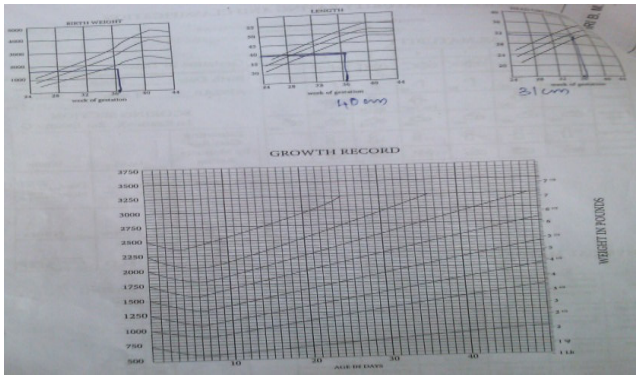


Figure 6
Morphometry of Child

Table 1
Biochemical Test

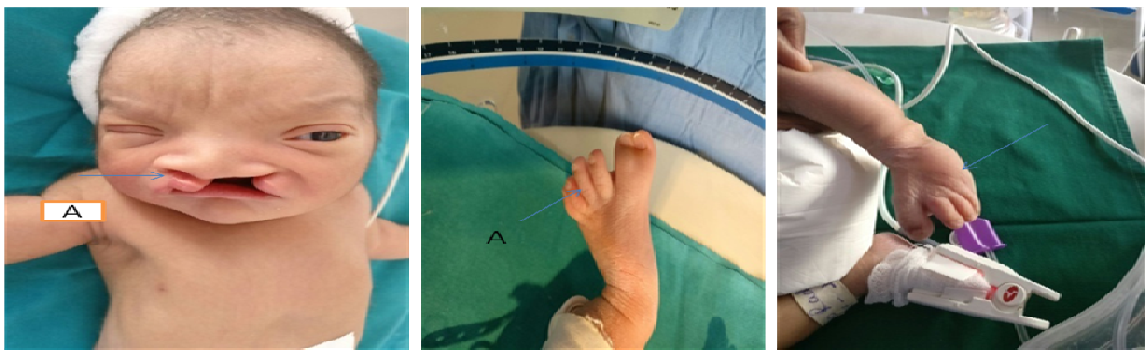
Test	Test values	Units	Reference
Serum Calcium	10.0	mg/dL	8.5-11.0mg/dL
Cell Reactive Protein	0.1	Mg/dL	0.0-0.6 mg/dL

Table 2
Complete Haemogram Test

Test	Parameters	Test Values	Units	Reference
Complete Haemogram	TC	9350	Cells/cmm	4000-11000cels/cmm
	Neutrophils	**75**	**%**	**40-75%**
	Lymphocytes	22	%	25-40%
	Eosinophils	00	%	1-6%
	Monocytes	03	%	2-8%
	Basophils	00	%	0-1%
	RBC	**5.17**	**Millions**	**3.8-4.8**
	Hb	20.3	%	11.6-14%
	PCV	63.5	%	36-46%
	P_LCR	-	%	21.50%
	MCV	122.8	fl	80-100fl
	MCH	39.3	pg	27-32pg
	MCHC	32.0	%	31.5-34.5%
	Platelet count	1.55	Lakhs/cmm	1.5-4lakhs
	ESR	QNS	mm 1st Hr	5-20 mm 1st Hr
	RDW	18.8	%	11.6-14fl
	PDW	14.9	fl	10-14fl
	MPV	11.1	fl	7.4fl-11.4fl
	CH_Others	-	-	-

CASE II

A $G_4P_3L_2D_1$ with 37 week's 5days period of gestation male with a birth weight of 1.39kg, delivered by normal vaginal, was admitted in the NICU, department of Pediatrics, BLDE University's Shri B M Patil Medical College Vijayapur and Karnataka,India. The newborn presented with multiple congenital anomalies. The baby was born of a consanguineous marriage, the mother being a 30 year old. She is having 3 childrens one female with 8years, female with 4yrs full term normal vaginal delivery (ftnvd). MC Cycle with regular 5-6 days. She is admitted with complaint of malformation, per veginal leak, bleeds, bob disturbance, came for ANC check up in vivo of hydrocephalus no excess of radiation of teretogeric, past history tells she is having fever, excess of vomiting. Fe & Calcium supplements taken. No PV leak or bleed. During antenatal period, the pregnancy was monitored regularly & there were no maternal problems during antenatal period. During pregnancy period iron-folic acid supplementation taken. There was no history of neonatal death in the family. The clinical features include Bilateral Cleft lip & Palate (fig.7, A), Polydactyl in left lower limb (fig 8, A), Low set of ears on both sides (fig 9, A), Rocker bottom feet (fig 2, D) were observed. The child with large head, HC is 36cm, length is 43cm. Ultrasonography Test (Siemens Ac.no 700) for Mother was carried out in our hospital report gives GA (gestational age) 38 weeks 5days with hydrocephaly with polyhydramniss (FIG.10). Obstetric Scan was done in the Dept of Radiology, BLDE University's Shri B M Patil Medical College & Hospital Vijayapur and Karnataka, India. Fetal cardiac activity is seen with heart rate of 179 bpm. Single Intrauterine Live fetus with GA (gestational age) age of 17 weeks 4 days. Gross hydrocephalus, Small posterior fossa (fig.11).



7. A.Bilateral Cleft lip & Palate 8.A. Polydactyl with left lower limb 9.A. Rocker bottom feet in left lower limb

Case II Figure 7, 8, 9
Clinical features of Patau syndrome

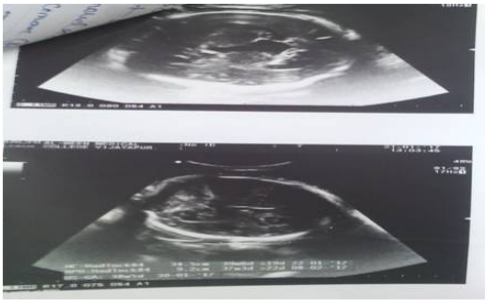


Fig.10. Ultrsonography of Mother

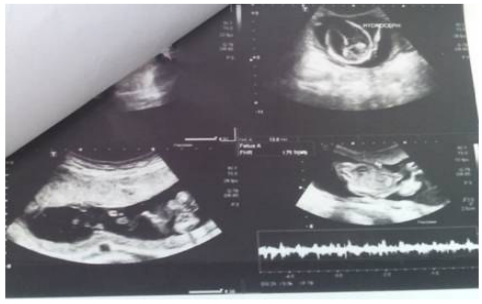


Fig.11.Obstetric Scan of Mother

Table 3.Fetal Biometry is as follows

Biparietal diameter	41.9	mm	18	weeks	5	days
Head circumference	152.5	mm	18	weeks	2	days
Abdominal circumference	108.8	mm	16	weeks	5	days
Femoral length	22.5	mm	16	weeks	5	days

CYTOLOGICAL STUDY

1 ml of peripheral blood was collected in Sodium Heparin Vacutainer (BD franklin Lakes NJ USA) from both children's and then immediately transferred to Laboratory of Genetics. Standard procedures were performed on the Patau Syndrome karyotype. In this study, the Roswell Park Memorial Institute (RPMI) 1640 medium containing 25% fetal bovine serum (FBS), antibiotics such as Pen Strip were used (products of GIBCO). Medium under the laminar air flow was prepared. For cultivation, 9 ml of cell culture medium in culture tube (50ml, product of Nunc), 100µl Phytohemagglutinin (PHA) and 1 ml peripheral blood were added and incubated for 72 h with 5% CO_2 at 37 ° C respectively. Tubes containing those medium were gently shaken daily. At the time 71.5 hrs 50µl of colcemid was added to culture tube and kept in CO_2 incubator for half an hour, harvesting steps was done. Tubes were placed for 15 minutes in the water bath for 37^0c for 35 minutes. After centrifugation, at 1200 rpm for 10 min, cells isolated from the culture medium were impressed with the hypotonic solution (KCl; 0.75 M).After centrifugation, the cells were exposed to the fixative solution (methanol and acetic acid at a ratio of 3:1) and they were centrifuged again. After several washing steps with fixative solution, a clear suspension of lymphocytes obtained. Drop shot technique was used with sterile Pasteur pipette and several slides were prepared [7].With the G- banding method, metaphase spreads were prepared on the slides. First, metaphase spreads were exposed to trypsin for 15 seconds and then placed in Giemsa solution. After 10 minutes, the slides were washed with distilled water. Pictures were taken from slides of each patient and with Geneasis karyotyping software, they were analyzed and descriptive statistics were diagnosed(fig.12).

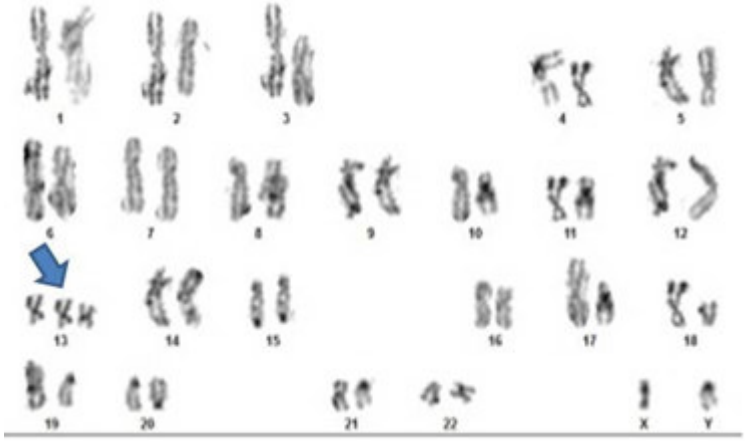
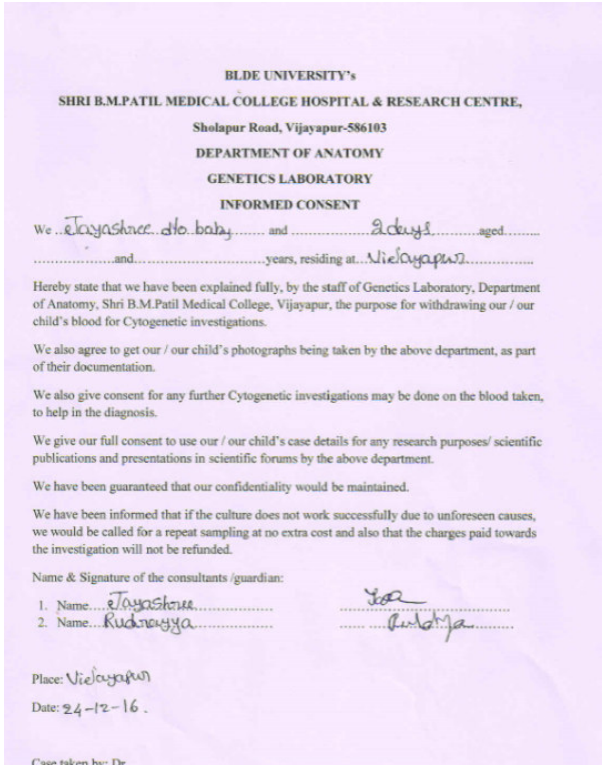


Figure 12
Karyotype showing trisomy 13 with 47XY male



BLDE UNIVERSITY's

SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE,

Sholapur Road, Vijayapur-586103

DEPARTMENT OF ANATOMY

GENETICS LABORATORY

INFORMED CONSENT

We ...Jayashree...d/o baby..... and .....2days.....aged.....

.....and.....years, residing at...Vijayapur.....

Hereby state that we have been explained fully, by the staff of Genetics Laboratory, Department of Anatomy, Shri B.M.Patil Medical College, Vijayapur, the purpose for withdrawing our / our child's blood for Cytogenetic investigations.

We also agree to get our / our child's photographs being taken by the above department, as part of their documentation.

We also give consent for any further Cytogenetic investigations may be done on the blood taken, to help in the diagnosis.

We give our full consent to use our / our child's case details for any research purposes/ scientific publications and presentations in scientific forums by the above department.

We have been guaranteed that our confidentiality would be maintained.

We have been informed that if the culture does not work successfully due to unforeseen causes, we would be called for a repeat sampling at no extra cost and also that the charges paid towards the investigation will not be refunded.

Name & Signature of the consultants /guardian:

1. Name....Jayashree.....
2. Name...Kudreyya.....

Place: Vijayapur

Date: 24-12-16.

Case taken by: Dr

DISCUSSION

Screening or prenatal diagnosis are mandatory in future pregnancies. Women with a previous trisomy pregnancy, especially those under 35 years, have an increased risk in future pregnancies [8].Specific ultrasound findings like nuchal translucency, cardiac defects, neural tube defects, facial clefting, renal abnormalities and omphalocele may suggest trisomy 13 and subsequent cytogenetic study will help in confirmation [9]. Our study reveals that patient is under 35 years of age, above tests are carried out for the confirmation of trisomy 13. Less associated anomalies, such aspolyhydramnios, oligohydramnios, intrauterine growth retardation, single umbilical artery, eye defects, such as congenital glaucoma [10], these clinical features were not seen in our studies. Some of the osteomuscular abnormalities reported in the literature. In our patients, including post-axial polydactyly in the hands, deep palmarcreases in the hands, rocker-bottom feet, and convex soles were present [11]. Patau syndrome (trisomy 13) occurs most commonly by disjunctional errors in meiotic or mitotic cell divisions. The non disjunction autosomal chromosome is occurs during pregnancy period. Cleft lip and palate, ear malformations, omphalocele and abnormalities of the hand as seen in the present cases have also been reported by other authors[12,13]. Approximately 50% of spontaneous abortions before 15 weeks of gestation & 50% of these due to trisomics [14]. About 2 to 3% of fetus with trisomy 13 survive up to birth. New born with trisomy 13 have median survival of 7days & 5% have 6 months of age [15]. Coco et al reported a two months old child with Patau syndrome with 46, XY, 14-, T (13q14q) + karyotype [16]. There are reports of long survival till adulthood[17-19]. In our cases there is no spontaneous abortion, children's were having multiple anomalies and survival chances are less. Genetic factors causing malformations in children with trisomy 13, unknown exogenous agents must be taken into account as possible mechanisms [20]. Different cytogenetic techniques, including normal karyotyping & Fluorescent In Situ Hybridization (FISH) can be used to diagnose Patau syndrome. Zhou et al. [21] reported a case of Patau syndrome with paternal origin of an extra chromosome 13 due to nondisjunction during the first meiotic division of the further, which was confirmed by Fluorescent In Situ Hybridization (FISH).The main differential diagnosis of trisomy 13 is pseudo- trisomy 13, Meckel-Gruber syndrome and Edward syndrome (trisomy18).Pseudo trisomy 13 shows normal karyotype with holoprosencephaly and postaxial polydactyly with microcephaly, hydrocephaly, agenesis of corpuscallosum[22]. Meckel- Gruber syndrome shows cystic renal dysplasia, posterior encephalocele, or other abnormalities in central nervous system and postaxial polydactyl[23]. Trisomy 18 and trisomy 13 may have similar features and difficult to differentiate on sonography and therefore can be confirmed by karyotyping. 90% of cases, however, the diagnosis is made at birth, with the karyotype evaluation [13]. Amniocentesis during pregnancy, to differentiate it from its main differential diagnosis Meckel Gruber syndrome [24].Our results are also confirmed by the Karyotyping. Trisomy 13 is a rare genetic disorder there is no treatment or cure for it.

CONCLUSION

Patau syndrome is the most severe & rare kind of disorder, three autosomal trisomies affecting almost all the systems presenting with very short survival. The rare survivors have profound mental retardation and seizures. Patau syndrome involves a recognizable pattern of multiple congenital anomalies with increased neonatal and infant mortality and significant intellectual disability in older children, making care challenging for the family, primary care practitioners, and specialists.

Diagnosis of congenital anomalies requires in-depth knowledge, awareness and experience in the interpretation of antenatal scan. However, the success of providing a clinical diagnosis with cytogenetic techniques could be improved using FISH and other complementary molecular studies. Certainly, the replacement of cytogenetic diagnosis by direct DNA diagnosis has great importance,Therefore, we recommend the special training of the medical personnel who is conducting and reporting Cytological testing. We recommend early referral of the patient to a maternal fetal specialist for prenatal diagnosis and further management due to the poor prognosis of this syndrome.

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CONFLICT OF INTEREST

Conflict of interest declared none.

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Reviewers of this article

Dr. B.G. Patil MBBS, MD

Profressor, Dept of Anatomy
Shri B M Patil Medical College,
Hospital and Research Centre,
Solapur Road, Bijapur, Karnataka
INDIA 586103

Mr. Anubrata Paul M.Sc. Biotech (Research)

Affiliation
Department of Biotechnology, Natural Products Research Laboratory, Centre for Drug Design Discovery & Development (C-4D) , SRM University, Delhi-NCR,Sonepat.

Prof.Dr.K.Suriaprabha

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Prof.P.Muthuprasanna

Managing Editor , International Journal of Pharma and Bio sciences.

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