How to Cite:
Joseph, K., Teja, G. R., & Srinivas, M. (2022). Study of the clinical features of Downs's syndrome and relation between dermatoglyphics and congenital heart disease if any. *International Journal of Health Sciences*, *6*(S5), 10922–10941. https://doi.org/10.53730/ijhs.v6nS5.10965

Study of the clinical features of Downs's syndrome and relation between dermatoglyphics and congenital heart disease if any

Dr. Keziah Joseph, MD,*
Associate Professor, Department of Pediatrics, Mamatha Academy of Medical Sciences, Hyderabad.
*Corresponding author

Dr. G. Rahul Teja
Senior Resident, Department of Pediatrics, Mamatha Academy of Medical Sciences, Hyderabad.

Dr. M. Srinivas
Consultant, Yashoda Hospital, Malakpet, Hyderabad.

***Abstract*---**Introduction: Down syndrome is one of the most common cause of congenital malformation with mental retardation seen with an estimated prevalence of 1/600 – 1/800 births. A wide range of abnormalities are seen, some of which are characteristic of Downs syndrome. Objectives and Aim: The present study was aimed at studying the various clinical features including dermatologlyphic patterns in Down syndrome and to find any correlation with congenital heart disease. Materials and Methods: 34 children £18 years with features of down syndromes were assessed for various clinical presentation and dermatoglyphic patterns analyzed. Those with congenial heart disease were also noted to check for any correlation with dermatoglyphic patterns in Downs syndrome.3 ml blood was drawn and thyroid function were recorded. Results: The majority of clinical features observed include slanted palpebral fissure, icrocephaly, epicanthal fold, macroglossia, hypotonia, flat facies, brachycephaly, high arched palate. Dermatoglyphic patterns show increased prevalence of simian crease clinodactly ulnal loops on the finger tips and atd angle >45 in the children. Statistically significant correlation was found when clinodactly of the left hand, left third inter digital space pattern, open field defect and sandal gap of the toes was compared with down syndrome children with CHD. Thyroid function studies in the present group revealed only 2 children (5%) with hypothyroidism. Interpretation and Conclusion: The present

study showed a higher incidence of slanted palpebral fissure, microcephaly, epicanthic fold, macroglossia, hypotonia, flat facies, brachycephaly, high arched palate. Gastrointestinal abnormalities were seen in 34% of the cases. 34% of the cases had CHD, 45% of the mothers were less than 25 years old when these children were conceived. Thyroid functions studies were abnormal only in 5% of the cases 2 out of 34. Both of them had hypothyroidism. There exists significant correlation between dermatoglyphics seen in Downs's syndrome to Congenital Heart Disease.

***Keywords*---**Down syndrome, dermatoglyphics, congenital heart disease.

Introduction

Down syndrome is one of the most common and best known of all malformation Syndromes, with an estimated prevalence of 1/600-1/800[1]. The first person to recognize Downs's syndrome is English physician John Lansdon Down as a distinct form of mental retardation in 1862. He published his first work on this group of children, whom he referred as mongoloids, in 1866 entitled "observation on an ethnic classification ofidiots". Until the middle of 20th century, the cause of Down syndrome remained unknown, although the presence in all races, the association with older maternal age had been noticed. In 1959, Professor Jerome lejeune and Jacob et al independently discovered that Down syndrome resulted from an extra chromosome 21.

The most apparent manifestation of Down syndrome are the minor dysmorphic features which collectively constitute its distinctive physical phenotype. Although any single individual will have many of the characteristic features, and easily recognized as having Down syndrome, not all these features need be present in all cases with Down syndrome. By making use of specific phenotypic findings of Down syndrome one can develop an effective index, making the diagnosis on majority of suspects before karyotyping is complete. A list of these features were compiled by Pueschel et al.[2] Hall developed a similar criteria for neonates where four out of ten characters gives a probability of 48% D S. 6 out of 10 increasing the probability to 89%.[3]

Chromosomal analysis is time consuming and the delay leads to anxiety amongst parents whilst diagnosis is unsure. Undue worry is caused to parents of karyotypically normal children being investigated for the Down syndrome on the basis of a few clinical features. Earlier clinical diagnosis allows the parents to accept the diagnosis at an earlier stage, and in some instances, make medical decisions about the life threatening events.[4]

Down syndrome hasn't spared any race. Both the sexes are affected early. Characteristic morphological features are recognized immediately after birth. Except for mongoloid facies, no single feature is always present or pathognomic. Mental retardation is constant but nonspecific finding that becomes apparent in later infancy. Newborns with Down syndrome are slightly smaller than the normal

counter parts. The short stature persist throughout life becoming more prominent as the child grows up. Hence growth in Down children cannot be assessed by the same growth charts used for normal children. Special growth charts meant for down syndrome are available which have formulated with data from 4,650 observations of 730 children with Down Syndrome from different groups followed at the developmental evaluation clinic of Boston children's hospital, the child development center at Rhode Island hospital ,the clinical genetic service of the children's hospital of Philadelphia.[5] Charts with 5^{th} 25^{th} 50^{th} 95^{th} centile for stature and weight of children with Down Syndrome for ages 1-36months and 2-18 yrs. are used. All centiles for stature of children with Down syndrome are less than analogous centiles for the N C H S data. This has been attributed to both environmental and genetic factors.[5]

Muscle Hypotonia

One of the most characteristic features of Down syndrome in new born and infants is hypotonia. Several investigators regard this as a universal finding. The basis for the decreased muscle tone is unknown. But it was thought to be due to decrease in the concentration of 5-hydroxyl tryptamine (serotonin) in the peripheral blood. However attempts at therapy with serotonin and pyridoxine is controversial.[6] Although the histological findings have been inconsistent the brain weight is in the low normal range and the size of the cerebellum and the brainstem may be reduced to an even greater extent. A among the other findings in Down Syndrome brain are nerve cell heterotropias in the white layers of the cerebellum and vermis, which are found in 16% of infantile and fetal Down Syndrome brains.

Gastrointestinal Abnormalities

Gastrointestinal defects is about 20 times more common in patients with DS than in patients without DS.[7] Gastrointestinal defects were found in 4.8% of DS live births, stillbirths and abortions.[8] Gastrointestinal defects in 6.6% of live birth patients with DS have been observed.[9] The most frequent malformations of gastrointestinal tract are duodenal atresia and Hirshprung's disease. Duodenal stenosis is seen in 4–7% of individuals with DS, but this accounts for 30–50% of all congenital duodenal stenosis.[10] About 1–2% of live birth children with DS have Hirshprung's disease and 10–15% of patients with Hirshprung's disease have Trisomy 21.[11] The other findings that may occur more frequently were omphalocele, tracheoesophageal fistula, pyloric stenosis, ileal and jejunal atresia, imperforated anus.[7,12,13,14]

Celiac Disease

Celiac disease (CD), also known as gluten-sensitive enteropathy, affects individuals of all ages, both during childhood and adolescence, and is characterized by permanent gluten intolerance. It is an autoimmune disorder, which results from a reaction to gluten, the protein present in cereals. The mean prevalence of CD is 0.3–1.5% in children between 2 and 15 years in general population.[15, 16, 17]

Congenital Heart Disease

Congenital Heart Disease refers to structural/functional heart disease present at the time of birth, but might be recognized much later. The most common cardiac defect in DS is endocardial cushion defects; the risk for this anomaly is increased 1000-fold among DS births. Although in DS the endocardial cushion defects are found in 50% of all CHD, 70% of individuals with endocardial cushion defects also have DS. 44% of the foetuses with DS bear a CHD detectable with foetal echocardiography or conversely, [18] 43% of fetuses with atrio-ventricular septal defect (AVSD) have DS. Molecular studies in individuals with Congenital Heart Disease and partial duplication of chromosome number 21q with features of Downs Syndrome led to the concept that a candidate region responsible for cardiac defects characteristic of Downs Syndrome might be in the region of 21q22.2–22.3.[19,20]

The frequency of CHD differs in different studies from 26% up to 61%. The highest frequency of CHD (60%-61.3%) was found in Oman's population in which consanguinity is widely prevalent[21] and in Saudi-Arabia. Various studies have shown that there is a increase in the frequency of CHD among children with DS. This is probably due to better diagnostic possibilities. Echocardiography performed early in life could detect CHD that might otherwise be missed.[22] Another study showed that 13% of patients with normal cardiac physical examination had an abnormal echocardiogram and in 27%, the physical examination findings did not correctly predict the echocardiographic findings. So it is important to do all neonates with DS echocardiographic investigation.[23] This is recommended by American Academy of Paediatrics.

Maternal age and its implications

It has long been recognized that the risk of having a child with Down syndrome increases with maternal age and the distribution of maternal age in the population of women having children is the primary determinant of the overall incidence of Down syndrome.[24]

Prenatal diagnosis

Three methods for screening pregnancies for Down syndrome are now being employed. The first two, amniocentesis and chorionic villus sampling (CVS), are used for a limited segment of the childbearing population. The third, maternal serum alpha- fetoprotein (AFP) screening, can be carried out on all pregnant women. The principal indications for amniocentesis and CVS carried out to detect chromosomally abnormal fetuses are the birth of a previous child trisomy 21 or other chromosome disorder, a carrier state for a Robesonian or other translocation in one of the parents, advanced maternal age, and a low value of maternal serum AFP.

Maternal serum alpha-fetoprotein screening

It was noted that pregnancies with Down syndrome were associated with lower than normal levels of MS-AFP.[25] These findings were soon extended to amniotic

fluid AFP values, and in both instances the median value of AFP concentration was 0.64 to 0.72 thatfound in normal pregnancies.[25,26]

Life expectancy of Downs Syndrome

The trend of improved life expectancy for people with all kinds of disabilities and also for persons with Downs Syndrome is global. Increased survival is not only associated with a longer period of care, but is also related to a longer period of more specialized needs. The information of life expectancy of Downs syndrome is needed in order to facilitate the development of plans for their medical care, education, employment, and integration into the community. The calculated the life expectancy in Downs Syndrome up to 68 years and found that 85% of infants survive to one year of age, 80% survive to age 10 years and 60% of DS can expect to live longer than 50 years. Although survival beyond 60 Years was markedly better than was reported earlier, it was still significantly poorer than survival for the general population. Survival of infants born with Down syndrome showed a clear improvement in the probability of survival over time; up to 92% for one year and up to 85% for ten years.[27] The mean age at death was around 25 years in the 1980s but increased to 49 years by 1997.[28]

Cognitive impairment

When the Down syndrome child reaches school age the delays start to cause problems serious enough, to require very intensive and specialized training. The major problem in a school age Down's child is the lack of ability to handle more advanced cognitive strategies and processes.[29]

Dermatoglyphics

Dermatoglyphics are the dermal ridge configurations on the digits, palms and soles.[30, 31, 32] The scientific study of papillary ridges of the hands and feet was first begun in 1823 by Evangelista Purkinje – a Czech physiologist and biologist. He was the pioneer who did a systematic categorization of fingerprint patterns. In 1892, Sir Francies Galton published his classic treatise on fingerprints. He studied the hereditary aspects of fingerprints, compared siblings, twins and genetically unrelated individuals and was the first who reported, concordance of papillary ridge patterns among relatives.[33, 35, 36]

Since then, many studies have been emerged which has increasingly shown how dermatoglyphics can predict a range of conditions and disease. The dermatoglyphics analysis is now a valuable comparison to other methods used for diagnosis of some genetic diseases (e.g., phenylketonuria) and syndromes genetically determined (e.g., Down, Turner or Klinefelter syndromes). Dermatoglyphics polymorphism results from the interplay of genetic and environmental factors during the early stages of ontogenesis. Dermal ridge configurations begin to develop about the 13th week of gestation as the fetal mounds on the digit tips, an interdigital, thenar and hypothenar areas of the hand. The pattern of formation is mostly complete by the 19th week intra uterine.

The three basic fingerprint patterns are: arches, loops and whorls or combinations' of them. The loops might be either ulnar or radial. (Figure 1)

A confluences of three-ridge systems is a triradii. Arches have no triradii; a loop pattern has one and the whorl pattern has two or more triradii. A triradius is commonly seen at the base of the palm-the axial triradius. This pattern might be displaced in a distal direction in certain conditions. The palmar creases are usually made up of proximal and distal transverse creases and a thenar creases. A single transverse (crosswise) flexion crease in the hand is called "simian crease" which is most often associated with chromosomal abnormalities such as trisomy 21, trisomy 18, trisomy 13, etc. Dermal and palmar ridges are considered to be very useful tools in medical studies especially autosomal and sex chromosomal anomalies. Their notably variable characteristics are not duplicated in other people, even in monozygotic twins.

Thyroid dysfunction and autoimmunity

Numerous reports have been published concerning thyroid dysfunction in individuals with down syndrome.

Methodology

All children with clinical features suggestive of Down syndrome 18 years attending Kamineni Academy of Medical Sciences and Research, Hyderabad over a span of 18 months were included in the study between May 2015 and October 2016. Clearance was obtained from the ethical committee of the institute. Parents were explained the need for the study, and written consent taken. 34 cases were included in the study. A detailed proforma was used to register history, clinical features and laboratory data based on medical records of the patients. It consisted of general questions about the pregnancy, specific problems seen in Down syndrome. 3 ml of blood was drawn for the estimation of T3, T4, TSH using C.L.I.A method. All cases were carefully evaluated for clinical features including dermatoglyphics and any congenital heart disease.

For taking the dermatoglyphics prints palms and soles of the children were washed and dried, black printing ink was smeared evenly using a sponge. This was carefully copied on to a white sheet using a roller drum that was firmly rolled over the palms proximally from the wrist to distal digits. Ink was applied on the subject's finger balls gently. The inking extended from near the end of the finger to a level slightly proximal top the flexion creases of the distal interphalangeal joint. After inking paper is placed on the table top in such a manner that the distal edge of the paper coincided with the frontal edge of the table top. Then finger is first placed edge down on the paper with radial side touching it and then rolled until the opposite margin i.e. ulnar side is in contact. Thumb and finger 1, 2 and 3 are rolled from radial to ulnar, fingers 4 and 5 rolled from ulnar to radial to facilitate movement. Indicate the right and left sides as well as finger numbers on the paper. Imprints of the soles were taken in similar manner to that of the palm. They were assessed for characteristic dermatoglyphic pattern of Down syndrome. The feature included fingertip pattern, third interdigital pattern, transverse palmar flexion crease pattern, atd angle, hallucal pattern.

Each of the dermatoglyphic patterns were analyzed separately on each hand. Fingerprint patterns were labelled as radial loops, ulnar loops, whorls, and arches. No subpattterns of whorls and arches were classified for this study. Lines drawn from point 'a' to point't' and to point'd' outlined the angle 'atd'. In the third interdigital area presence or absence of pattern was indicated. Presence or absence of Simian crease, Sydney line were also considered. Hallucal patterns on each foot were considered as part of this study.

Statistical Analysis

Frequency distribution of the clinical variables was derived and presented. For studying the association of dermatoglyphics with congenital heart disease in Down syndrome, a two way contingency table was prepared and significance was evaluated adapting the chi square test.
Significance was assessed at 95% level.

Results

In this study there were 34 cases which satisfied the eligibility criteria. Of them 24 were male and 10 female. (Table 1). The ages ranged from 3 months to 18 years. Out of the 34 mothers, only 5 mothers gave history of abortion. All of them were first trimester abortions. (Table 2) Out of the 34 cases 3 fathers (8.8 %) were more than 40 years old when the babies were conceived. (Table 3)
Maximum number of mothers were seen in the <25 years age group. This amounted to 47% of the total. Mean age of the mother was 26.3. (Table 4)
The majority of the cases had Epicanthic fold, macroglossia, high arched palate, brachycephalic flat facies, Hypotonia, Mongoloid slant. (Table 5)
Out of 34 children, 12 (34%) had CHD which was confirmed by echocardiography. (Table 6)
Clinodactyly is the curvature of the little finger that resembles a hook. It is caused by bone growing in an abnormal position. Clinodactyly was seen in 68.57% of the total. (Table 7)
Majority of the Dermatoglyphics pattern on the finger tips showed ulnar loop pattern which is the characteristic feature of Down syndrome. (Table 8,9)
25 out of 34 children had presence of loop pattern on the right 3rd digital space 71.4%. The association of this finding in Down syndrome children with congenital heart disease showed a statistical significant correlation $p < 0.5$.
16 of the 34 children had loop pattern on the 3rd interdigital space of the left hand which accounted for 45.7% of the total. (Table 11)
15 out of 35 children had simian crease (42.85%). Prominent Simian crease is one of the significant finding of Downs syndrome.
14 children had open field pattern of the sole which amounted to 41% of the Total cases. (Table 13)
31 out of 34 (91.2%) children had sandal gap between the toes. (Table 14)

Chi square <.005 significant
Statistically significant correlation was found between CHD and Sandal gap $p < 0.05$. (Graph 1)

Chi square less than0.008 is statistically significant
Open field pattern of sole and CHD was found to have a statistically significant correlation with $p < 0.05$. (Table 16, Graph1)
Statistically significant correlation was found between clinodactyly and CHD. $p < 0.05$. (Table 17, Graph 3) Only two children were found to have abnormal thyroid function test. Both ofthem had hypothyroidism (5.9%). (Table 18)

Discussion

Out of 34 children 24 were male and 11 were female. Male to female ratio was 2.1:1. In a similar study of clinical features in Down Syndrome done by Kava MP et al.[37] the incidence was 1.37:1. The higher ratio of males in the present study may be due to the discrimination shown by the guardians in bringing the female children for medical check up. 5 (14.3%) mothers gave history of abortions. All of them were first trimester abortions. 32 mothers were less than 35 years at the time of conception of the babies suggesting that the affected children were due to translocation. 3 of the mothers (7.4%) were more than 35 years suggesting the affected child could be due to non-disjunction or mosaicism. The present study though having higher number of mothers <35 years old had higher incidence of trisomy. Out of 34 children karyotyping was done in 24, 22 out of these children had trisomy 21 and the other 2 were mosaic pattern.

Inheritance of DS is still not completely understood. However earlier workers strongly advocated that the advanced maternal age is the major risk factor for trisomy 21. The likelihood that a woman under the age of 25 years and 30 years who become pregnant will have a baby with down syndrome is less than 1 in 1,400 and 1 in 1,000 respectively. This increases to 1 in 350 when 35 years, 1 in 60 by 40 years and 1 in 12 by 49 years.[38] There are also contrary reports that 80% of DS babies are born to mothers lessthan 30 years.[39,40]

In a study done by Suttur S. Malini et al. in South India 75% of DS children were born to young mothers whose age ranged from 18-29 years. One of the reasons for this may be that Indian women get married and produce children earlier when compared to their western parts. Another possibility is that in India, younger women giving birth to sex chromosomal aneuploidy children are completely neglected during prenatal diagnosis, as most of attending doctors are of the established concept that only advanced maternal age is the risk factor for non-disjunction. Hence their study was of the opinion that both maternal age and paternal age have no decisive influence on the manifestation of DS.[41] In the present study 85.7% of the mothers were less than 30 years old. The average maternal age at the time of conception of the affected child was 26.4 years which is comparable to study done by Kava et al. Where the average age was 26.8 years. Similar studies have reported that the mean maternal age of Down syndrome children in various parts of India was around 30 years in Hyderabad, Mumbai, Punjab.[42,43,44,45,46]

The fathers belonging to 26-40 years age group are more compared to those above 40. In the Indian family, the age difference between the husband and the wife vary between 1-12 years. In the present study 82.8% of the father's age was between the 26-40years age group. During a 15 years study period, Harry Fisch

et al. concluded that there was no paternal age group influence on Down syndrome until the age of 35 years. A paternal age effect was seen only when it was associated with maternal age of 35 years and above. It was most pronounced when maternal age was 40 years and above. [41] Slanted palpable fissure was seen in 33 of the total number of children this accounted for 97%. One of the Down syndrome child in this group had mosaic pattern. It has been documented that the clinical features of mosaic pattern ranged from normal physical to that typical of Down syndrome phenotype.[47] Epicanthic fold was seen in 80% of the cases. Similar studies by Kava et al. showed a prevalence of 57% while Gorlin et al had 48% of incidence and Ahmed et al. had reported 63%. Hypotonia is a regular feature of all children with Down syndrome. Various studies have reported their prevalence varying between 56-80% in the present study 33 out of 35 children had hypotonia. More than 80% of them were on irregular physiotherapy. The other common clinical features noted were flat facial profile, Brachycephaly, high arched palate and macroglossia.

Less common features noticed were gastrointestinal problems, congenital heart disease, ear problems. Out of 35 children, 11 children had gastrointestinal problems, out of which 4 had symptom suggestive of gastroesophageal reflux disease which slowly resolved as the child grew up. 2 children had umbilical hernia, another 2 had constipation, and one child was operated for intestinal obstruction, anal atresia, undescended testis each.

34% of the children had congenital heart disease detected clinically and echo cardiographically confirmed. 7 (58.3%) children had VSD alone and 2 had VSD with pulmonary hypertension. Only one child had VSD and ASD combined. Kava et al. in their study reported 18.3% of CHD of which majority were VSD (25.8%). Other studies have shown prevalence CHD between 35-40%.[37, 48, 49, 50]
Ear abnormalities reported by Kava et al. was 67% where as others studies have reported incidences varying between 46-70%.[37]The present study had 12 children with ear abnormalities which accounted to 34% of the total.

Dermatoglyphics

Clinodactyly in the normal population has a 6% incidence. In the present study 68% of the children had clinodactyly. Similar studies have shown variation between 36- 57%.[37, 48, 49, 50] Dermatoglyphics on the finger tips mostly showed ulnar loop patterns (81%) instead of the normal 63%. Radial loop patterns were seen more commonly on the 4th and 5th finger tips as reported by other studies.[51,52] Different studies vary in their reporting of radial loops, such discrepancy can be explained by ethno historic and geographic variation between populations.[53,54]

The occurrence of loop pattern in the 3rd interdigital space was found to be 71.4% on the right hand and 45.7% on the left hand. Open field pattern on the soles of the foot was seen in 14 of the 35 children which accounted for 41.2% of the cases. Sandal gap between the toes was seen in 91% of the children. Other studies have reported between 46-50%. Simian crease was seen in 42.8% of the children while different studies have shown it to vary between 33-52%.[37, 48, 49, 50]

When different dermatoglyphic pattern were compared with down syndrome children having CHD, statistically significant correlation was found with right 3rd interdigital space pattern of the palms, open field pattern of the soles, left hand clinodactyly and sandal gap between the toes. In a similar study done by George et al.[55] Sydney line, 3rd right interdigital palmar pattern showed significant correlation with CHD.

Thyroid function studies

T_3, T_4, TSH values assessed in 35 children showed abnormal values only in 2 (5%). Prevalence rate between 3-54% among Down syndrome patients have been reported. The variation in the prevalence in these studies might be related to age variation among the study subjects and / or difference in the diagnosis criteria. Thyroid function studies are hence recommended at 6 months and 12 months of age followed by annual testing in all children with down syndrome.[56] Hyperthyroidism was not reported in any ofthe children.

Conclusion

- Contrary to the belief that Down syndrome is commonly seen with elderly mothers, our study showed a higher incidence in young mothers < 30 years of age.
- We found a statistically significant correlation between CHD in Down Syndrome and the presence of loop pattern on the third inter digital space on the palm, left clinodactly of the left hand, open field pattern of the hullucal area of the sole and sandal gap of between thetoes.
- Incidence of hypothyroidism in Down syndrome though significant is low (5%).
- Need a larger institutional study to check for correlation.

Conflict of Interest: No Funding: No funding received.

References

1) Adams MM, Erickson JD, Layde PM, Oakley GP. Down's syndrome. Recent trends inthe United States. JAMA. 1981 Aug 14;246(7):758-60.
2) Ahmed I, Ghafoor T, Samore NA, Chattha MN. Down syndrome: clinical and cytogenetic analysis. J Coll Physicians Surg Pak. 2005 Jul;15(7):426-9.
3) Antonarakis SE. 10 years of Genomics, chromosome 21, and Down syndrome.Genomics. 1998 Jul 1;51(1):1-16.
4) Arrieta MI, Criado B, Martinez B, Lobato MN, Gil A, Lostao CM. Fluctuating dermatoglyphic asymmetry: genetic and prenatal influences. Ann Hum Biol. 1993 Nov- Dec;20(6):557-63.
5) Arrieta MI, Martinez B, Simon A, et al. quantitative and qualitative finger dermatoglyphics in the Basque Valley of Urola, Spain. Anthropol Anz 1990; 48: 65-84.
6) Barlow GM, Chen XN, Shi ZY, Lyons GE, Kurnit DM, Celle L, Spinner NB, Zackai E, Pettenati MJ, Van Riper AJ, Vekemans MJ, Mjaatvedt CH, Korenberg JR. Down syndrome congenital heart disease: a narrowed region and a candidate gene. Genet Med. 2001 Mar-Apr;3(2):91-101.

7) Bell R, Rankin J, Donaldson LJ; Northern Congenital Abnormality Survey Steering Group. Down's syndrome: occurrence and outcome in the north of England, 1985-99. Paediatr Perinat Epidemiol. 2003 Jan;17(1):33-9.
8) Bentley D (1975) A case of Down's syndrome complicated by retinoblastoma and celiac disease. Pediatrics 56:131–133
9) Book L, Hart A, Black J, Feolo M, Zone JJ, et al. Prevalence and clinical characteristics of celiac disease in Downs syndrome in a U.S. study. Am J Med Gen 2001; 98: 70–74.
10) Bosco JI, Rajangam S, Shankar J, Thomas IM. Dermatoglyphics in 46, XY females. J Indian Med Assoc. 2001 Aug;99(8):418-20.
11) Cooley WC, Graham JM Jr. Down syndrome--an update and review for the primary pediatrician. Clin Pediatr (Phila). 1991 Apr;30(4):233-53.
12) Cronk C, Crocker AC, Pueschel SM, Shea AM, Zackai E, Pickens G, Reed RB. Growth charts for children with Down syndrome: 1 month to 18 years of age. Pediatrics. 1988 Jan;81(1):102-10.
13) Cuckle HS, Wald NJ, Lindenbaum RH, Jonasson J. Amniotic fluid AFP levels and Downsyndrome. Lancet. 1985 Feb 2;1(8423):290-1.
14) Cuckle HS, Wald NJ, Lindenbaum RH. Maternal serum alpha-fetoprotein measurement: a screening test for Down syndrome. Lancet. 1984 Apr 28;1(8383):926-9.
15) Cummins H, Talley C, Platou RV. Palmar dermatoglyphics in mongolism. Pediatrics 1950;5:241-8.
16) Devlin L, Morrison PJ. Accuracy of the clinical diagnosis of Down syndrome. *Ulster Med J.* 2004;73(1):4-12.
17) Fisch H, Hyun G, Golden R, Hensle TW, Olsson CA, Liberson GL. The influence of paternal age on down syndrome. J Urol. 2003 Jun;169(6):2275-8.
18) Gemini, S., Lolo, L. L., Sumiati, S., Ezdha, A. U. A., & Susanti, N. Y. (2022). Correlation of fiber intakes with incidence of constipation in the elderly. International Journal of Social Sciences and Humanities, 6(1), 58–65. https://doi.org/10.53730/ijssh.v6n1.3528
19) George D, Sayee R, Thomas IM. Dermatoglyphics in down syndrome patients with congenital heart defects. Journal of the Anatomical Society India 1995; 44(2):144-8.
20) Gorlin RJ, Cohen MM, Hennekam RCM. Chromosomal syndromes: common and/or well-known syndromes. Trisomy 21 syndrome (Down syndrome). In Syndromes of head and neck. 4th ed Oxford Press 2001; pp. 35–42.
21) Hall B. Mongolism in newborn infants. An examination of the criteria for recognition and some speculations on the pathogenic activity of the chromosomal abnormality. Clin Pediatr (Phila). 1966 Jan;5(1):4-12.
22) Hartley XY A summary of recent research into the development of children with Down syndrome . J Ment Defic Res 1986; 30:1-14.
23) Hilhorst, M.I., Brink, M., Wauters, E.A.K. *et al.* Down syndrome and coeliac disease: five new cases with a review of the literature. *Eur J Pediatr* **152,** 884–887 (1993).
24) Hill ID, Dirks MH, Liptak GS, Colletti RB, Fasano A, Guandalini S, Hoffenberg EJ, Horvath K, Murray JA, Pivor M, Seidman EG; J Pediatr Gastroenterol Nutr. 2005Jan;40(1):1-19.
25) Hook EB. Estimates of maternal age-specific risks of Down-syndrome birth in women aged 34-41. Lancet. 1976 Jul 3;2(7975):33-4.

26) James SJ, Pogribna M, Pogribny IP, Melnyk S, Hine RJ, Gibson JB, Yi P, Tafoya DL, Swenson DH, Wilson VL, Gaylor DW. Abnormal folate metabolism and mutation in the methylenetetrahydrofolate reductase gene may be maternal risk factors for Down syndrome. Am J Clin Nutr. 1999 Oct;70(4):495-501.
27) Jones KL. Chromosomal abnormality syndromes. Down syndrome. In: Smith's
28) Jyothy A, Kumar KS, Mallikarjuna GN, Babu Rao V, Uma Devi B, Sujatha M, Reddy PP. Parental age and the origin of extra chromosome 21 in Down syndrome. J Hum Genet. 2001;46(6):347-50.
29) Jyothy A, Kumar KS, Rao GN, Rao VB, Swarna M, Devi BU, Sujatha M, Kumari CK, Reddy PP. Cytogenetic studies of 1001 Down syndrome cases from Andhra Pradesh, India. Indian J Med Res. 2000 Apr;111:133-7.
30) Källén B, Mastroiacovo P, Robert E. Major congenital malformations in Downsyndrome. Am J Med Genet. 1996 Oct 16;65(2):160-6.
31) Karlsson B, Gustafsson J, Hedov G, Ivarsson SA, AnnerenG. Thyroid dysfunction in Down's syndrome: relation to age and thyroid autoimmunity. Arch Dis Child 1998; 79: 242-245.
32) Kaur A, Mahajan S, Singh JR: Cytogenetic profile of individual with mental retardation. Int J Hum Genetics 2003, 3(1): 13-16.
33) Kava MP, Tullu MS, Muranjan MN, Girisha KM. Down syndrome: clinical profile fromIndia. Arch Med Res. 2004 Jan-Feb;35(1):31-5.
34) Korenberg JR, Bradley C, Disteche CM. Down syndrome: molecular mapping of the congenital heart disease and duodenal stenosis. Am J Hum Genet. 1992 Feb;50(2):294- 302.
35) Kothare S, Shetty N, Dave U: Maternal age and chromosomal profile in 160 DS cases-Experience of tertiary genetic center from India. Int J Hum Genetics 2002, 2(1):49-53.
36) Kurtieva, S. (2021). Adaptation capabilities of functional systems of the body of adolescents with vegetative dystonia syndrome. International Journal of Health & Medical Sciences, 4(1), 129-135. https://doi.org/10.31295/ijhms.v4n1.1622
37) Lai FM, Woo BH, Tan KH, Huang J, Lee ST, Yan TB, Tan BH, Chew SK, Yeo GS. Birth prevalence of Down syndrome in Singapore from 1993 to 1998. Singapore Med J. 2002 Feb;43(2):070-6.
38) Leonard S, Bower C, Petterson B, Leonard H. Survival of infants born with Down's syndrome: 1980-96. Paediatr Perinat Epidemiol. 2000 Apr;14(2):163-71. doi: 10.1046/j.1365-3016.2000.00252.x. PMID: 10791661.
39) Mäki M, Mustalahti K, Kokkonen J, Kulmala P, Haapalahti M, Karttunen T, Ilonen J, Laurila K, Dahlbom I, Hansson T, Höpfl P, Knip M. Prevalence of Celiac disease among children in Finland. N Engl J Med. 2003 Jun 19;348(25):2517-24.
40) Malini, S.S., Ramachandra, N.B. Influence of advanced age of maternal grandmothers on Down syndrome. *BMC Med Genet* **7,** 4 (2006). https://doi.org/10.1186/1471-2350-7-4
41) McElhinney DB, Straka M, Goldmuntz E, Zackai EH. Correlation between abnormal cardiac physical examination and echocardiographic findings in neonates with Down syndrome. Am J Med Genet. 2002 Dec 1;113(3):238-41.
42) Mutton D, Ide RG, Alberman E. Trends in prenatal screening for and diagnosis of Down's syndrome: England and Wales, 1989-97. *BMJ.*

1998;317(7163):922-923. doi:10.1136/bmj.317.7163.922
43) Paladini D, Tartaglione A, Agangi A, Teodoro A, Forleo F, Borghese A, Martinelli P. The association between congenital heart disease and Down syndrome in prenatal life. Ultrasound Obstet Gynecol. 2000 Feb;15(2):104-8.
44) Pétremand-Hyvärinen R. Aspects morphologiques et dermatoglyphiques du syndrome de Klinefelter 47,XXY [Morphologic and dermatoglyphic aspects of Klinefelter 47,XXY syndrome (author's transl)]. J Genet Hum. 1978 Nov;26 Suppl:1-83. French. PMID: 571455.
45) Polin A, Ditmar MF In:Paediatric secrets 1989.Philadelphia :Hanley and Berfus Inc CV Mosby 1989.
46) Pueschel SM, Sassaman EA, Scola PS, Thuline HC, Stark AM, Horrobin M. Biomedical aspects in Down syndrome. In: Pueschel SM, Rynders JE, eds. Down syndrome. Advances in biomedicine and behavioral sciences. Cambridge, MA: Ware, 1982:169.
47) Qazi QH, Mapa HC, McGann B, Woods J. Dermatoglyphics in Down's syndrome patients of different racial origins. Am J Ment Defic. 1977 Nov;82(3):229-32.
48) Rao VB. Mean maternal age of Down's syndrome in Hyderabad, India. J Indian Med Assoc. 1999 Jan;97(1):25. PMID: 10549185.
49) Reed T. Dermatoglyphics in medicine--problems and use in suspected chromosome abnormalities. Am J Med Genet. 1981;8(4):411-29.
50) Refining chromosomal region critical for Down syndrome-related heart defects with a case of cryptic 21q22.2 duplication Rika Kosaki, Kenjiro Kosaki, Kazushige Matsushima, Norimasa Mitsui, Naomichi Matsumoto, Hirofumi Ohashi
51) Rex AP, Preus M. A diagnostic index for Down syndrome. J Pediatr. 1982 Jun;100(6):903-6. doi: 10.1016/s0022-3476(82)80509-x. PMID: 6211531.
52) Schaumann B, Alter M. Dermatoglyphics in Medical Disorders. New York : Springer Verlag, 1976.
53) Schaumann BA, Opitz JM. Clinical aspects of dermatoglyphics. Birth Defects Orig Artic Ser. 1991;27(2):193-228.
54) Shiono H. Dermatoglyphics in medicine. Am J Forensic Med Pathol 1986; 7 :120-6.
55) Stoll C, Alembik Y, Dott B, Roth MP. Study of Down syndrome in 238, 942consecutive births. Ann Génét 1998; 41: 44–51.
56) Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Get vaccinated when it is your turn and follow the local guidelines. International Journal of Health Sciences, 5(3), x-xv. https://doi.org/10.53730/ijhs.v5n3.2938
57) Torfs CP, Christianson RE. Effect of maternal smoking and coffee consumption on the risk of having a recognized Down syndrome pregnancy. Am J Epidemiol. 2000 Dec 15;152(12):1185-91.
58) Tubman TR, Shields MD, Craig BG, Mulholland HC, Nevin NC. Congenital heartdisease in Down's syndrome: two year prospective early screening study. BMJ. 1991 Jun 15;302(6790):1425-7.
59) Venugopalan P, Agarwal AK. Spectrum of congenital heart defects associated with Down Syndrome in high consanguineous Omani population. Indian Pediatr. 2003 May;40(5):398-403.
60) Yang Q, Rasmussen SA, Friedman JM. Mortality associated with Down's syndrome in the USA from 1983 to 1997: a population-based study. Lancet. 2002 Mar 23;359(9311):1019-25.

Annexure:

Table – 1 : Sex Distribution

Sex	**No. of cases**	**Percentage**
Male	24	71
Female	10	29

Table – 2: Children with history of abortion in mother

Abortion in Mother	**No. of Cases**	**Percentage**
Yes	5	14.7
No	29	85.3
Total	34	100

Table – 3: Age of father at the time of conception

Age Distribution	**No. of Cases**	**Percentage**
20-25	3	8.8
26-30	9	26.5
31-35	11	32.3
36-40	8	23.6
41-45	1	2.9
>46	2	5.9
Total	**34**	**100**

Table – 4 : Age of mother at the time of conception

Age Distribution	**No. of Cases**	**Percentage**
20-25	16	45.71
26-30	13	40.00
31-35	2	5.71
36-40	1	2.86
41-45	2	5.71
Total	**34**	**100**

Table – 5: Common Clinical features seen

Clinical Features	**No. of cases**	**Percentage**
Slanted palpebral fissure	33	97
Hypotonia	33	97
Flat facies	31	91
Brachycephaly	31	91
High arch palate	30	88
Macroglossia	28	82

Epicanthic fold	29	85
G I problems	12	35
C H D	12	35
Fissured tongue	13	38
Ear problems	12	35

Table – 6 : Congenital Heart Disease

	No. of Cases	**Percentage**
Yes	12	35.3
No	22	64.7
Total	**34**	**100**

Table – 7 : Occurrence of Clinodactyly

Clinodactyly	**No. of Cases**	**Percentage**
Yes	24	68.57
No	11	31.43
Total	**34**	**100.00**

Table – 8: Dermatoglyphics - Right Hand

	Thumb	**Index**	**Middle**	**Ring**	**Little**
Ulnar loop	30	33	32	15	24
Whorl	4	0	1	6	2
Radial loop	0	1	1	11	8
Arch	0	0	0	2	0

Table – 9 : Dermatoglyphics - Left Hand

	Thumb	**Index**	**Middle**	**Ring**	**Little**
Ulnar loop	30	30	33	23	25
Whorl	3	3	1	5	3
Radial loop	0	0	0	5	6
Arch	1	1	0	1	0

Table – 10: Dermatoglyphics: presence of loop pattern in right hand third interdigital space

Right third inter digital space	**No. of Cases**	**Percentage**
Yes	25	73.5
No	9	26.5
Total	**34**	**100**

Table – 11 : Dermatoglyphics :presence ofloop pattern in third left interdigital space

Left third inter digital space	No. of Cases	Percentage
Yes	16	47.0
No	18	53
Total	**34**	**100**

Table – 12 : Simian crease

	No. of Cases	Percentage
Simian present	15	44.2
Simian absent	17	50
Sydney ln	2	5.8
Total	**34**	**100**

Table – 13 : Open field pattern on the sole

	No. of Cases	Percentage
Yes	14	41.2
No	20	58.8
Total	**34**	**100**

Table – 14: Sandal Gap

Sandal	No. of Children	Percentage
Yes	31	91.2
No	3	8.8
Total	**34**	**100**

Table – 15 : Comparison of Sandal Gap between toes with CHD

Sandal Gap	CHD		Total
	Yes	No	
Yes	11	20	31
No	1	2	3
Total	**12**	**22**	**34**

Table – 16 : Comparison of open field pattern of the sole with CHD

Open field pattern of sole	CHD		Total
	Yes	No	
Yes	5	10	15
No	7	12	19
Total	**12**	**22**	**34**

Table – 17 : Comparison of clinodactyly left hand & CHD

Clinodactyly	CHD		Total
	Yes	No	
Yes	8	15	23
No	4	7	11
Total	**12**	**22**	**34**

Table – 18 : Thyroid Function Test

	No. of Children	Percentage
Yes	2	5.9
No	32	94.1
Total	**34**	**100**

Table – 19 : Common Clinical Features

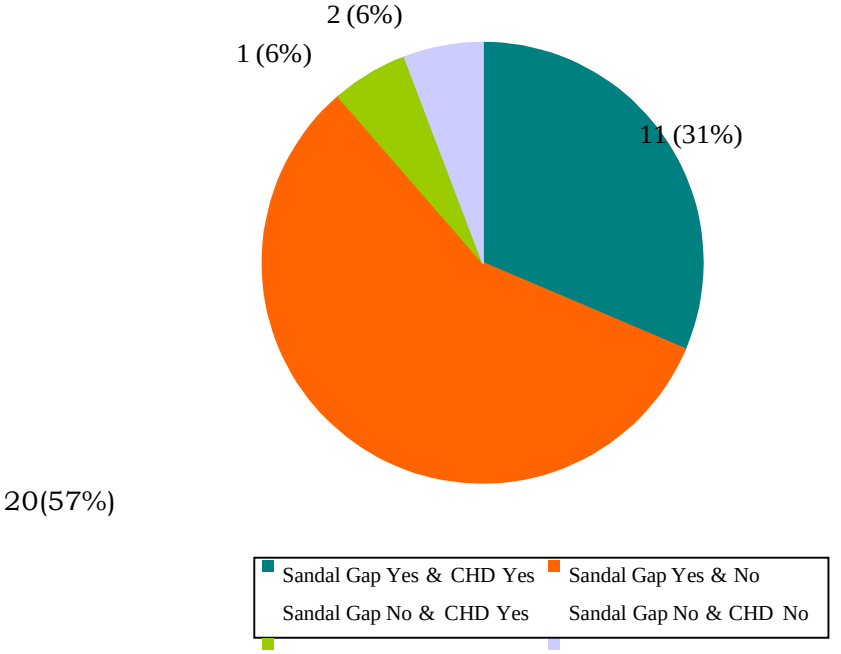
	Gorlin et al 2001[48]	Kava et al 2004[37]	Ahmed et al[49]	Smith[57]	Present study
Mongoloid slant	79%	84%	83%	80%	94%
Hypotonia	-	76%	56%	80%	94%
Flat facies	-	51%	-	90%	91%
Macroglossia	42%	30%	-	-	82%
Epicanthic fold	48%	57%	63%	-	-
G I problems	-	2%	5%	12%	31%
C H D	-	18%	35%	40%	34%
Ear problems	70%	67%	46%	60%	34%

Table - 20 : Dermatoglyphic pattern

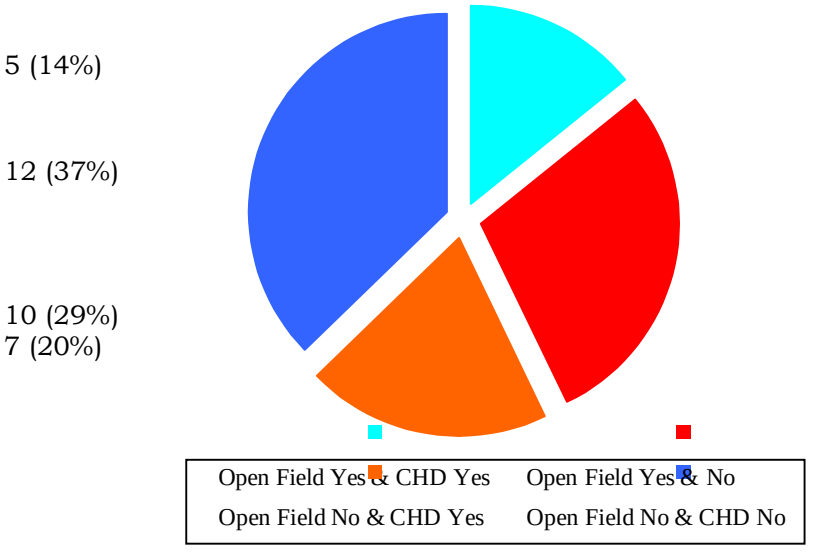
	Gorlin et al2001[48]	**Kava et al2004[37]**	**Ahmed et al[49]**	**Smith[57]**	**Present study**
Clinodactyly	59%	36%	25%	50%	68%
Simian crease	52%	33%	65%	45%	42.8%
Sandal gap	50%	46%	46%	-	91.2%

GRAPHS

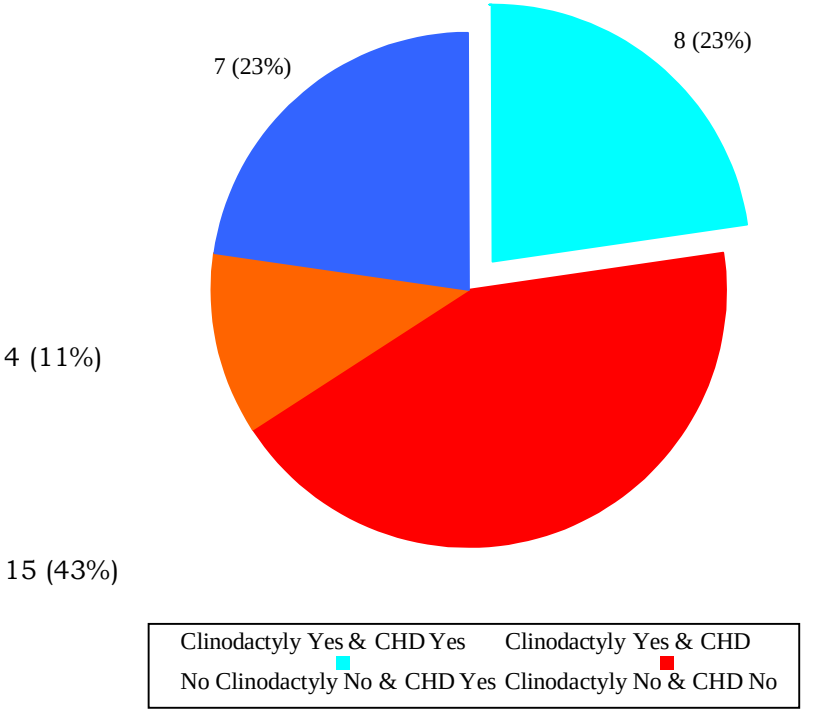
Graph – 1: Comparison of Sandal Gap between toes with CHD



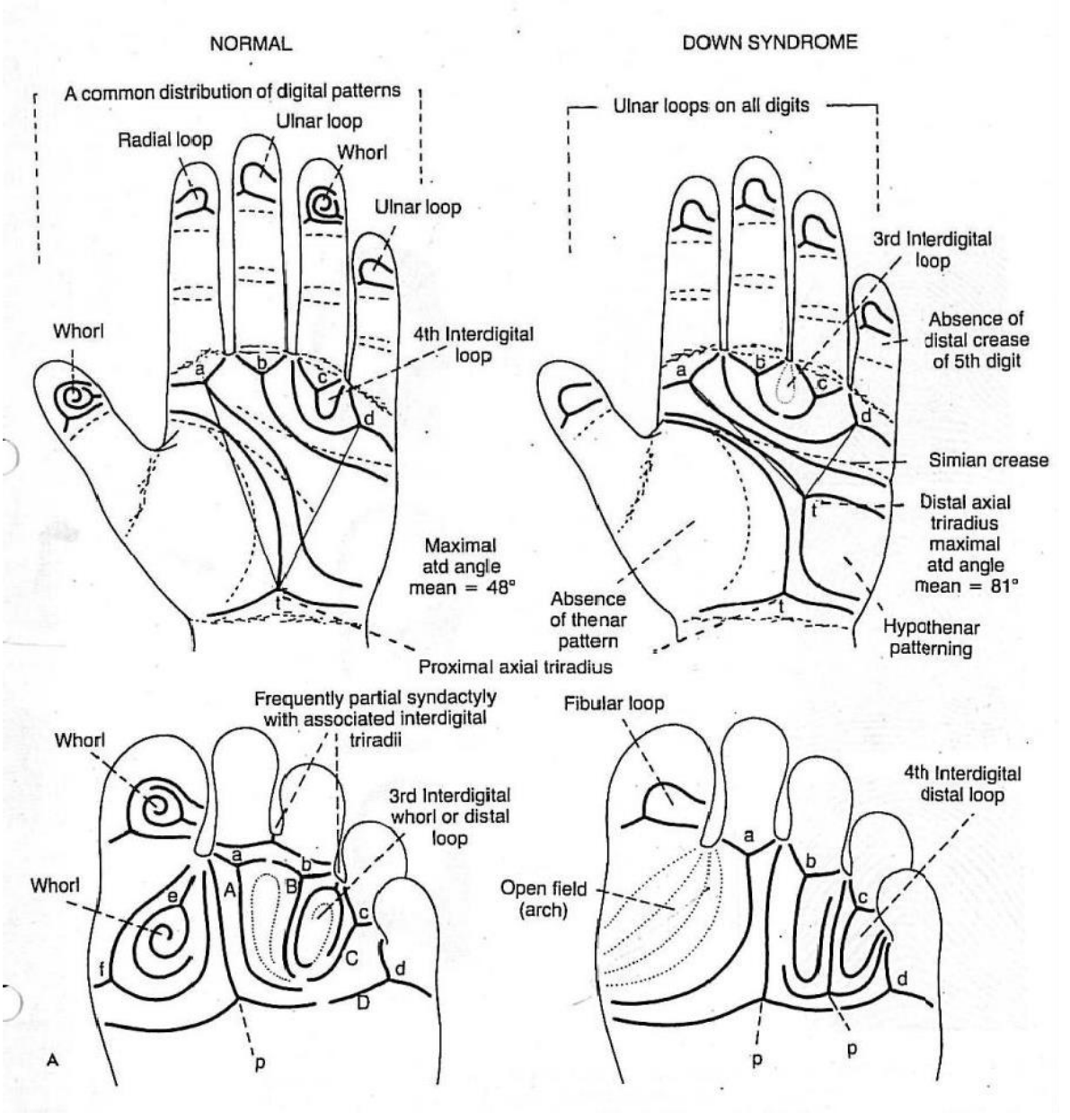
Graph – 2 : Comparison of open field pattern of the sole with CHD



Graph – 3 : Comparison of clinodactyly left hand & CHD



FIGURES


NORMAL
A common distribution of digital patterns
Radial loop
Ulnar loop
Whorl
Ulnar loop
Whorl
4th Interdigital loop
Maximal atd angle mean = 48°
Proximal axial triradius
DOWN SYNDROME
Ulnar loops on all digits
3rd Interdigital loop
Absence of distal crease of 5th digit
Simian crease
Distal axial triradius maximal atd angle mean = 81°
Absence of thenar pattern
Hypothenar patterning
Frequently partial syndactyly with associated interdigital triradii
Whorl
3rd Interdigital whorl or distal loop
Whorl
A
Fibular loop
4th Interdigital distal loop
Open field (arch)