International Journal of Health Sciences and Research
[Indexed, Peer-Reviewed Journal]
Volume 15; Issue: 4; April 2025
Website: www.ijhsr.org
Original Research Article *ISSN: 2249-9571*

Clinical and Genetic Profile of Down Syndrome: Insights from 10 Years of Experience at a Tertiary Care Center

Abhilasha Chaudhary[1], Komal Uppal[1], Rinmi Kasar[1], Himangi Dayal[1], Ankur Jindal[1], Sunil Kumar Polipalli[1], Seema Kapoor[1]

[1]Division of Genetics and Metabolism, Department of Medical Genetics, Maulana Azad Medical College (Delhi University), Delhi 110002.

Corresponding Author: Sunil Kumar Polipalli

DOI: https://doi.org/10.52403/ijhsr.20250401

ABSTRACT

Background & Aim: Down Syndrome (DS) is a genetic disorder characterized by distinct clinical features, predominantly caused by trisomy chromosome 21. This study aimed to conduct a retrospective analysis of clinical features, genetic profiles, and karyotype findings in Down Syndrome patients.
Materials and Methods: We performed a retrospective analysis of cases referred to the Genetic Clinic in the Department of Pediatrics at Maulana Azad Medical College (MAMC) and Lok Nayak Hospital over a ten-year period (2014-2024). Existing case proformas of patients with Down Syndrome phenotype, who underwent cytogenetic evaluation, were systematically reviewed.
Results: Analysis included 688 patients with DS, with 375 males and 313 females (M: F ratio 1.2:1). The average age at presentation was 19.4 months (range: 1 day to 26 years). Distinct craniofacial features were present in 97.8% of cases, including mongoloid slant (97.8%), flat facial profile (97%), and protruding tongue (91.7%) and epicanthic folds (62.7%). Cytogenetic findings revealed free trisomy in 95.93%, translocations in 3.05%, mosaics in 0.72%, and rare findings in 0.29%. Among the Robertsonian translocations, 52.4% were t (14;21), 9.5% t (15;21), and 38.1% t (21;21).
Conclusion: The findings emphasize the importance of early detection and comprehensive evaluation of Down Syndrome. Understanding the mechanisms of nondisjunction and its implications is vital for genetic counseling and assessing recurrence risks in families.

Keywords: Down Syndrome, Nondisjunction, translocation, Robertsonian, Mosaic syndrome.

INTRODUCTION

Down syndrome (DS) is one of the most common chromosomal aberrations associated with an additional number of Homo sapiens Chromosome 21 (HSA21) [(1,2)] which was named after a British Physician John Langdon Down. Individuals with DS manifest certain health complications, particularly neurological, musculoskeletal, and cardiovascular system resulting in a collection of clinical features with an incidence of 1:700 – 16:10000 in live births [(3,4)] wherein India's prevalence rate of 23000 - 29000 per year live births [(2,5)]. In 95% of the cases, trisomy 21 is caused by abnormal segregation of

chromosomes or meiotic nondisjunction (NDJ) [6,7] due to a decrease in the number of chiasmata between the homologous pairs and failure to resolve them during anaphase 1[8,9], which particularly occurs at meiosis 1 during maternal oogenesis in most cases [10–12]. While 4 % are caused by parental translocation between chromosomes 13, 14, 15, and 21 called Robertsonian translocations, a condition when a metacentric chromosome is formed when the long arms of two acrocentric chromosomes fuse [13]. The remaining 1% is caused by postzygotic mitotic NDJ and mosaicism, a condition when not all the cells have trisomy 21 [11,13,14].

The important risk factors of DS include advanced maternal age, as the quality and quantity of oocytes decrease in late motherhood the chance of aneuploidy increases during pregnancy[9] which may alter recombination during fetal development, accumulate damaged DNA, cohesin degradation inducing premature loss of sister chromatids [15], alterations of spindle assembly checkpoint(SAC)[16] contribute to premature onset of anaphase further delaying cell division and resulting in abnormal chromosome segregation [17]. Paternal age also influences trisomy 21 as the risk of spermatozoa breakage increases with aging [18,19]. Epigenetics is also a key risk factor through alterations in the DNA methylation process, non-coding RNA, and Histone modifications [14].

Though time-consuming, cytogenetic analysis of metaphase karyotypes remains the standard method for detecting trisomy 21, as well as other aneuploidies and balanced chromosomal abnormalities. Over the past decades, various methods have been developed for the rapid detection of trisomy 21, both during pregnancy and after birth, including fluorescent in situ hybridization (FISH), quantitative fluorescence PCR (QF-PCR), multiplex probe ligation assay (MLPA), paralogous sequence quantification (PSQ), and comparative genomic hybridization (CGH). Karyotyping is generally more cost-effective than techniques like MLPA, FISH, CGH, or QF-PCR for diagnosing Down syndrome. Additionally, karyotyping can identify other chromosomal abnormalities, such as large deletions, duplications, or rearrangements, that may coexist, making it a more comprehensive tool, especially in low- and middle-income countries (LMICs). Phenotypic variability is a key characteristic of the human population, and it is particularly pronounced in individuals with Down syndrome.

Our study aims to investigate the trends and distributions of DS, Robertsonian translocation, and Mosaic syndrome from 2014-2024, study the pattern of cytogenetic abnormalities, and enhance a deeper understanding of these conditions.

MATERIALS & METHODS

The study was conducted from 2014 to 2024 at the genetic lab Maulana Azad Medical College (MAMC) and Lok Nayak Hospital, New Delhi. Ethical clearance was obtained from the institute. A retrospective analysis was conducted on case proformas completed during clinical examinations of patients with DS phenotypes. Written and oral consent was obtained from the participants or the guardians/parents along with a few demographic details like age and gender.

Inclusion criteria: Patients with DS phenotype and confirmed karyotype diagnosis were included.

Exclusion criteria: included patients who were not confirmed by Karyotype and whose parents did not give consent.

To confirm trisomy21, karyotyping was done by collecting 5ml peripheral blood samples in heparinized vials. Lymphocytes were cultivated in a culture medium for 72 hours in an incubator at 37°C. Metaphase harvesting was done by administering Colchicine for 5 minutes following exposure to hypotonic fluid KCl solution for 1 hour and later fixed using a 3:1 methanol-acetic acid mix. The metaphase

chromosomes were then treated with Trypsin and stained with Geimsa for G banding and examined for numerical and structural anomalies. Following the test, genetic counseling was provided. The data were analyzed using the standard descriptive statistic method.

RESULT

A total of 688 individuals with DS, 375(54.5%) males and 313(45.5%) females were referred to the genetics lab for cytogenetic evaluation from 2014 to 2024, as shown in Table 1. Different age groups ranging from day 1 – 26 years participated in the study, of which maximum numbers of cases 257 (37%) were in 1-5 years, 68 (10%) cases in 0-30days, 149 (22%) cases in 1-6 months, 114 (16%) cases in 6-12 months, 60 (9%) cases in 5-10 years, 32 (5%) cases in 10 -15 years and 8 (1%) cases in 15 years and above, as shown in table 2, fig 1. The descriptive analysis of clinical parameters shows that the majority of 97.8 % were reported mongoloid slant, followed by 97% flat facies, the protruding tongue 91.7%, excessive skin fold on the neck 74.5%, epicantic fold 62.7%, hypotonia 53.4%, ear abnormalities 31.8%, sandal gap 31.5%, and simian crease 30.1%, shown in table 3.

NDJ free trisomy was the most common cytogenetic anomaly accounting for 95.7% with 658 cases. 21 (0.8%) cases have Robertsonian translocation – Eleven cases (52.4%) were t(14;21), Eight cases (38.1%) were t(21;21), and two cases (9.5%) were t(15;21). 5(0.8%) cases have mosaicism and 2 (0.3%) rare cases, double aneuploidy 48, XXX+21 and tetrasomy 48, XY+21+21 as per the cytogenetic report, shown in tables 4 and 5.

Table 1. Gender Distribution

Gender	no. of cases	percentage (%)
Male	375	54.5
Female	313	45.5

Table 2. Gender Distribution

Age Distribution	no. of cases	percentage (%)
0-30 D	68	10
1-6 M	149	22
6-12 M	114	16
1-5 Y	257	37
5-10 Y	60	9
10- 15 Y	32	5
15+ Y	8	1

Table 3. Common physical abnormalities

Parameters	No. of Cases	%
Mangoloid slant	673	97.8
flat facies	668	97
protruding tongue	631	91.7
Excessive skin fold on neck	513	74.5
Epicantic Fold	432	62.7
Hypotonia	368	53.4
Ear abnormalities	219	31.8
sandal Gap	217	31.5
simian crease	207	30.1

Table 4. Karyotype analysis of Down syndrome (N=688)

karyotype report	no. of cases	percentage (%)
Free trisomy	660	95.93
Robertsonain	21	3.05

Mosaicism	5	0.72
Rare	2	0.29

Table 5. Robertsonian translocation types reported (N=21)		
Types	**no. of cases**	**percentage (%)**
14;21	11	52.4
15;21	2	9.5
21;21	8	38.1

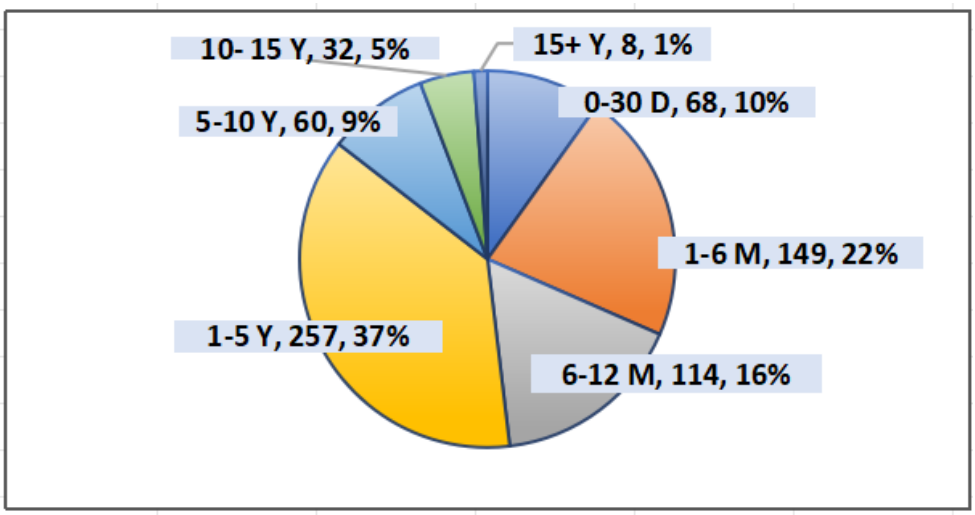

Figure 1: Age groups with Down syndrome.

Fig 1. The pie chart represents different age groups for individuals with Down syndrome. Each segment represents a specific age group and its proportion in the total dataset. Maximum individuals with down syndrome presented in the age group of 1-5 years.

DISCUSSION

A total of 688 individuals with suspected Down syndrome or Down-like phenotypes were referred to the Division of Genetics in the Department of Pediatrics for genetic confirmation. Cytogenetic analysis was performed on all patients using metaphase karyotyping. A male predominance was observed, with 375 males (54.5%) compared to 313 females (45.5%), resulting in a male-to-female ratio of approximately 1.2:1. This trend aligns with findings from several Indian and global studies, which report a male-to-female ratio ranging from 1.2 to 1.5:1 [11,20,21].

The underlying cause of this male predominance remains unclear. However, proposed genetic mechanisms include the co-segregation of chromosome 21 and the Y chromosome during spermatogenesis, as well as the nondisjunction of chromosome 21 during the second meiotic division of oogenesis, influenced by Y chromosome-bearing spermatozoa. Additionally, environmental factors and parental reproductive behaviors, such as the frequency of sexual intercourse, have been suggested to indirectly affect chromosomal segregation errors, potentially contributing to the observed male preponderance [20,22].

The age distribution of our study population revealed that the highest number of cases (37%) occurred in the 1-5 years age group at the time of karyotype analysis. Global trends indicate a significant shift over the years, with most cases now diagnosed early, often shortly after birth, based on physical features (e.g., flat facial profile, an upward slant to the eye, short neck, white spots on the iris, and a single, deep transverse crease on the palm). There is also a growing emphasis on prenatal diagnosis through various screening and diagnostic methods. In low-and middle-income countries

(LMICs) like India, Down syndrome is often diagnosed later due to a combination of factors, including limited access to antenatal care [(23)], high rates of non-institutional deliveries, and restricted availability of prenatal screening [(24)]. Prenatal screening tests are typically offered only at a few tertiary care centres within each state [(25)].

Healthcare inequality exacerbates this issue, as India's healthcare system is highly fragmented, leading to significant disparities in access to care between urban and rural populations. Consequently, many cases of DS in India are diagnosed postnatally based on physical characteristics observed after birth, resulting in delays in diagnosis, particularly when clinical features are subtle or when healthcare-seeking behavior is hindered.

Two common scenarios encountered in practice include: first, parents from rural areas presenting at tertiary centres with other health concerns—such as a poorly thriving child, developmental delays, or congenital heart disease—often unaware of DS diagnosis. Second, even individuals with a DS phenotype who are under follow-up at medical institutions as having a "Down phenotype" frequently do not receive a genetic diagnosis until late infancy or childhood, primarily due to the limited number of centres providing genetic diagnostic services. As a country with a high prevalence of genetic disorders, the only way to prevent the disease is through raising awareness about the disease among the health care providers and community, screening and genetic counseling.

In our study, we conducted a detailed comparative analysis of common physical characteristics associated with Down syndrome (DS), revealing intriguing similarities and differences with previous findings. Remarkably, 97.8% of our subjects exhibited a Mongoloid slant, a feature consistently highlighted across other studies, with Verma PK et al [(26)] reporting 83.9% and Kava et al [(27)] and Kumar et al [(28)] both at 80%. Flat facies, a hallmark of DS, were nearly universal in our cohort (97%), closely mirroring the 90% reported by both Kumar et al [(28)] and Jones KL[(29)], although Verma PK et al. recorded an even higher incidence (100%). Interestingly, the prevalence of a protruding tongue in our study (91.7%) was notably higher than the 74.4% found by Verma PK et al [(26)]. and dramatically more frequent than Kava et al.'s report of just 29.9%. Excessive skin folds on the neck were another distinctive feature in our group, present in 74.5% of cases, situating our findings between the lower rates of Verma PK et al. (53.5%) and the higher figure observed by Fryns JP [(30)] (81.45%). The epicanthic fold, observed in 62.7% of our subjects, demonstrated broad variation across studies, being significantly higher than Verma PK et al.'s 32.6%, but aligning more closely with Kava et al. (56.9%) and Kumar et al. (60%). Hypotonia, a frequent finding in DS, was observed in 53.4% of our cases, a rate notably lower than the 88.4% reported by Verma PK et al. and the 76.3% noted by Kava et al., suggesting potential population or methodological differences. Ear abnormalities, present in 31.8% of our cohort, were consistent with Verma PK et al. (34.9%) but significantly lower than the 66.9% noted by Kava et al. Meanwhile, the prevalence of the sandal gap and simian crease, at 31.5% and 30.1% respectively, showed consistency across the literature, aligning well with figures from Verma PK et al. and Kava et al, shown in Table 6. [(26,27,28,29,30)]

Table 6. Comparative Analysis of common physical abnormalities in DS in our study with previous literature

Parameters	Our study (%)	Verma PK et al.	Kava et al.	Kumar et al.	Jones KL	Fryns JP
Magnoliid slant	97.8		83.9		80	80
Flat facies	97	100	50.9		90	90

Protruding tongue	91.7	74.4	29.9			
Excessive skin fold on neck	74.5	53.5	36.8		80	81/45
Epicanthic Fold	62.7	32.6	56.9	60		40
Hypotonia	53.4	88.4	76.3	80	80	21-77
Ear abnormalities	31.8	34.9	66.9		60	50
Sandal Gap	31.5	32.6	46.2			45
Simian crease	30.1	32.6	33.2	40	45	48

The karyotype analysis in our study revealed that the majority of individuals (660, 95.93%) exhibited chromosomal nondisjunction leading to free trisomy. This condition typically arises from meiotic nondisjunction in one of the parents, most commonly during the first maternal meiotic division. Although rare, NDJ can also occur during the second maternal division or meiosis I or II in the father, with similar probabilities. Free trisomy is closely associated with advanced parental age and is a common feature of DS.

In 21 cases (3.05%), translocations were identified. Of these, 11 cases (52.4%) involve t (14;21), 8 cases (38.1%) involved t (21;21), and 2 cases (9.5%) involved t (15;21). Translocations, a type of chromosomal abnormality observed in some DS cases, often involve centric fusion, most commonly between chromosomes 14 and 21 [t (14;21)] or between both copies of chromosome 21 [t (21;21)]. Less commonly, translocations may involve other chromosomes such as 15, 13, 20, or 22. Although the total chromosome count remains normal at 46 due to centric fusion, the genome contains an extra copy of chromosome 21. Translocations may arise either through a "de novo" mutation or be inherited from a parent. When a parent is a carrier of a Robertsonian translocation, the risk of passing Down syndrome to offspring ranges from 2% to 100%, depending on the specific translocation. Notably, if a parent carries a t (21;21) translocation, the risk is 100%.

Mosaicism was observed in only 5 cases (0.7%). Mosaicism occurs post-fertilization and results in two distinct cell lines—one with free trisomy and the other with a normal karyotype. This condition is associated with significant phenotypic variability, ranging from a normal phenotype to classical trisomy 21.

Two individuals had very rare genotypes: double aneuploidy 48, XXX, +21, and 48, XY, +21+21 i.e tetrasomy 21. The precise number of cases worldwide is difficult to determine due to limited documentation and the rarity of the condition. Several case reports have documented individual instances of 48, XXX+21 across different populations [31–33] and 48, XY+21+21 i.e. tetrasomy 21. Literature indicates that these combinations of chromosomal anomalies, i.e., double trisomy, tend to occur due to nondisjunction during cell division [34].

The distribution of karyotypes in our study—predominantly free trisomy, followed by translocations and mosaicism—mirrors global and national trends observed over the past few decades [35,36,37]. However, a few studies from India have reported contrasting findings, with higher frequencies of mosaicism relative to translocations. For instance [38] analyzed 1,001 DS cases in Hyderabad and found free trisomy in 87.9%, mosaicism in 7.7%, and translocations in 4.4% of cases. Similarly in a study of 1,950 cases at the Centre for Genetic Disorders in Amritsar, reported free trisomy in 90.5%, mosaicism in 3.1%, and translocations in 2.7% [39]. Some international studies have also shown variability in karyotype distributions [40]. This variability could be attributed to differences in the populations selected for these studies, influenced by factors such as parental age and family history.

Although DS has been the subject of research for more than 15 decades, it continues to be one of the least understood genetic disorders. This is largely due to the

significant variability in phenotypes among individuals with DS, a factor that still puzzles professionals. However, research efforts have shifted from a collective focus to an individual-centric approach, aiming to identify and understand the differences within the DS population across various clinical areas.

Numerous working hypotheses aim to elucidate the phenotypic variability observed in trisomy 21. The predominant molecular mechanism is the gene dosage imbalance. This hypothesis posits that individuals with Down syndrome (DS) exhibit an increased dosage or copy number of genes located on human chromosome 21 (HSA 21), which may result in heightened gene expression [41,42]. Furthermore, this hypothesis has been expanded to suggest that certain genes or specific subsets may regulate particular phenotypes associated with DS [43].

Additionally, the critical region hypothesis has been incorporated into this framework. Phenotypic analyses of individuals with partial trisomy of HSA 21one in the past have revealed that a limited number of small chromosomal regions, known as "Down syndrome critical regions" (DSCR), are implicated in the majority of DS phenotypes. However, comprehensive analyses of both human studies and DS animal models done in the last couple of decades indicate that no single critical gene region can account for the full spectrum of DS phenotypes. Instead, multiple critical regions or specific genes likely contribute to various phenotypes or groups of phenotypes associated with DS, ranging from common physical characteristics to more severe medical conditions [44].

CONCLUSION

The distinct craniofacial features associated with Down syndrome underscore the critical importance of early detection and thorough evaluation of the condition. Prompt therapeutic intervention and appropriate genetic counseling are essential for effectively addressing the challenges posed by Down syndrome. An analysis of the distribution and prevalence rates of free trisomy, Robertsonian translocations, mosaicism, and rare findings have demonstrated that nondisjunction is the most prevalent etiology of this chromosomal abnormality. Understanding these mechanisms is crucial for assessing the recurrence risk of Down syndrome in families and for providing reassurance to affected families regarding their concerns.

Declaration by Authors

Ethical Approval: Approved

Acknowledgement: Gratitude to the Division of Genetics, Lok Nayak Hospital, New Delhi & patient's family.

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Ataman AD, Vatanoglu-Lutz EE, Yildirim G. Medicine in stamps: history of Down syndrome through philately. J Turk Ger Gynecol Assoc. 2012;13(4):267-9. Available from: https://jtgga.org/articles/doi/jtgga.2012.43
2. Antonarakis SE, Skotko BG, Rafii MS, Strydom A, Pape SE, Bianchi DW, et al. Down syndrome. Nat Rev Dis Primers. 2020;6(1):9. Available from: https://www.nature.com/articles/s41572-019-0143-7
3. Weijerman ME, De Winter JP. Clinical practice: The care of children with Down syndrome. Eur J Pediatr. 2010;169(12):1445-52. Available from: http://link.springer.com/10.1007/s00431-010-1253-0
4. Oster-Granite ML, Parisi MA, Abbeduto L, Berlin DS, Bodine C, Bynum D, et al. Down syndrome: National conference on patient registries, research databases, and biobanks. Mol Genet Metab. 2011;104(1-2):13-22. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1096719211002186
5. Kaur H, Bhalla AK, Panigrahi I. Percentile charts for body mass index of Indian Down syndrome children. J Pediatr Genet. 2022;11(4):261-6. Available from: http://www.thieme-

connect.de/DOI/DOI?10.1055/s-0041-1724115
6. Antonarakis SE. Parental origin of the extra chromosome in trisomy 21 as indicated by analysis of DNA polymorphisms. N Engl J Med. 1991;324(13):872-6. Available from: http://www.nejm.org/doi/abs/10.1056/NEJM199103283241302
7. Freeman SB, Allen EG, Oxford-Wright CL, Tinker SW, Druschel C, Hobbs CA, et al. The National Down Syndrome Project: Design and implementation. Public Health Rep. 2007;122(1):62-72. Available from: https://journals.sagepub.com/doi/10.1177/003335490712200109
8. Henderson SA, Edwards RG. Chiasma frequency and maternal age in mammals. Nature. 1968;218(5136):22-8. Available from: https://www.nature.com/articles/218022a0.
9. Hassold T, Hunt P. To err (meiotically) is human: the genesis of human aneuploidy. Nat Rev Genet. 2001;2(4):280-91. Available from: https://www.nature.com/articles/35066065
10. Antonarakis SE, Petersen MB, McInnis MG, Adelsberger PA, Schinzel AA, Binkert F, et al. The meiotic stage of nondisjunction in trisomy 21: determination by using DNA polymorphisms. Am J Hum Genet. 1992;50(3):544-50.
11. Sherman SL, Allen EG, Bean LH, Freeman SB. Epidemiology of Down syndrome. Ment Retard Dev Disabil Res Rev. 2007;13(3):221-7. Available from: https://onlinelibrary.wiley.com/doi/10.1002/mrdd.20157
12. Ghosh S, Feingold E, Dey SK. Etiology of Down syndrome: Evidence for consistent association among altered meiotic recombination, nondisjunction, and maternal age across populations. Am J Med Genet A. 2009;149A(7):1415-20. Available from: https://onlinelibrary.wiley.com/doi/10.1002/ajmg.a.32932
13. Witters G, Van Robays J, Willekes C, Coumans A, Peeters H, Gyselaers W, et al. Trisomy 13, 18, 21, Triploidy and Turner syndrome: the 5T's. Look at the hands. Facts Views Vis Obgyn. 2011;3(1):15-21.
14. Sánchez-Pavón E, Mendoza H, Garcia-Ferreyra J. Trisomy 21 and assisted reproductive technologies: A review. JBRA Assist Reprod. 2022;26(1). Available from: https://www.jbra.com.br/trab/pub/download_trabalho.php?fileSource=/var/www/vhosts/jbra.com.br/media/trab/arq_3185&fileName=19%20-%201753%20-%20Trisomy.pdf&id_trabalho=1109
15. Duncan FE, Hornick JE, Lampson MA, Schultz RM, Shea LD, Woodruff TK. Chromosome cohesion decreases in human eggs with advanced maternal age. Aging Cell. 2012;11(6):1121-4. Available from: https://onlinelibrary.wiley.com/doi/10.1111/j.1474-9726.2012.00866.x
16. Touati SA, Wassmann K. How oocytes try to get it right: spindle checkpoint control in meiosis. Chromosoma. 2016;125(2):321-35. Available from: http://link.springer.com/10.1007/s00412-015-0536-7
17. PMC. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4454629/pdf/nihms646562.pdf
18. Templado C, Vidal F, Estop A. Aneuploidy in human spermatozoa. Cytogenet Genome Res. 2011;133(2-4):91-9. Available from: https://karger.com/CGR/article/doi/10.1159/000323795.
19. Sotonica M, MackicDjurovic M, Hasic S, Kiseljakovic E, Jadric R, Ibrulj A. Association of parental age and the type of Down syndrome on the territory of Bosnia and Herzegovina. Med Arh. 2016;70(2):88.
20. Kovaleva NV. Sex ratio in Down syndrome. Tsitol Genet. 2002;36(6):54-69.
21. Kovaleva NV. Germ-line transmission of trisomy 21: Data from 80 families suggest an implication of grandmaternal age and a high frequency of female-specific trisomy rescue. Mol Cytogenet. 2010; 3:7.
22. Kovaleva NV, Butomo IV, Verlinskaia DK, Il'iashenko TN, Pantova IG, Prozorova MV, et al. Karyological characteristics of Down's syndrome: clinical and theoretical aspects. Tsitologiia. 1999;41(12):1014-21.
23. Paul P, Chouhan P. Socio-demographic factors influencing utilization of maternal health care services in India. Clin Epidemiol Glob Health. 2020;8(3):666-70. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2213398420300075
24. Dey S, Raheem E, Sarkar P. Identifying the factors influencing institutional and non-institutional delivery practices in slums of Shillong city. Health Popul Perspect Issues. 2014;37:76-87.

25. Windsperger K, Hoehl S. Development of Down syndrome research over the last decades–what healthcare and education professionals need to know. Front Psychiatry. 2021 Dec 14; 12:749046. Available from: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.749046/full
26. Verma PK, Akhil M, Gaire H. Evaluation of clinical profile to diagnose Down syndrome with respect to karyotyping as gold standard: A cross-sectional study. Int J Contemp Pediatr. 2022 Oct 27;9(11):1027. Available from: https://www.ijpediatrics.com/index.php/ijcp/article/view/5097
27. Kava MP, Tullu MS, Muranjan MN, Girisha KM. Down syndrome: Arch Med Res. 2004 Jan;35(1):31-5.
28. Kumar RK, Delatycki M. Down syndrome. In: Gupte S, editor. Recent advances in pediatrics—Special volume 9: Neurology. New Delhi, India: Jaypee Brothers; 2001. p. 1-13.
29. Jones KL. Down syndrome (Trisomy 21 syndrome). In: Smith's recognizable patterns of human malformations. 5th ed. Philadelphia, PA, USA: W. B. Saunders Co.; 1997. p. 8-13.
30. Fryns JP. Chromosome 21, trisomy 21. In: Buyse ML, editor. Birth defects encyclopedia. USA: Center for Birth Defects Information Services, Inc. and Blackwell Scientific Publications; 1990. p. 391-3.
31. Balwan WK, Kumar P, Raina TR, Gupta S. Double trisomy with 48, XXX+21 karyotype in a Down's syndrome child from Jammu and Kashmir, India. J Genet. 2008 Dec;87(3):257-9. Available from: http://link.springer.com/10.1007/s12041-008-0039-x
32. Park VM, Bravo RR, Shulman LP. Double non-disjunction in maternal meiosis II giving rise to a fetus with 48, XXX, +21. J Med Genet. 1995 Aug 1;32(8):650-3. Available from: https://jmg.bmj.com/lookup/doi/10.1136/jmg.32.8.650
33. Tsvetkova M, Levkova M, Tsvetkova S, Hachmeriyan M, Kovachev E, Angelova L. Double aneuploidy 48, XXX, +21 of a Bulgarian newborn with Down phenotype: a case report. Egypt J Med Hum Genet. 2020 Dec;21(1):25. Available from: https://jmhg.springeropen.com/articles/10.1186/s43042-020-00068-2.
34. Gatinois V, Bigi N, Mousty E, Chiesa J, Musizzano Y, Schneider A, et al. Mosaic complete tetrasomy 21 in a fetus with complete atrioventricular septal defect and minor morphological variations. Mol Gen Gen Med. 2019 Nov;7(11):e00895. Available from: https://onlinelibrary.wiley.com/doi/10.1002/mgg3.895.
35. Trevisan P, Moraes FN de, Mattos VF de, Graziadio C, Rosa RFM, Paskulin GA, et al. Cytogenetic profile of patients with Down syndrome in southern Brazil. Sao Paulo Med J. 2014;132(4):253-4.
36. Verma IC, Mathew S, Elango R, Shukla A. Cytogenetic studies in Down syndrome. Indian Pediatr. 1991 Sep;28(9):991-6.
37. Kang H, Wang L, Li X, Gao C, Xie Y, Hu Y. Application of chromosome microarray analysis and karyotyping in diagnostic assessment of abnormal Down syndrome screening results. BMC Pregnancy Childbirth. 2022 Nov 4;22(1):813. Available from: https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-022-05139-3.
38. Jyothy A, Kumar KS, Rao GN, Rao VB, Swarna M, Devi BU, et al. Cytogenetic studies of 1001 Down syndrome cases from Andhra Pradesh, India. Indian J Med Res. 2000 Apr; 111:133-7.
39. Kaur A, Singh JR. Chromosomal abnormalities: Genetic disease burden in India. Int J Hum Genet. 2010 Mar;10(1-3):1-14. Available from: https://www.tandfonline.com/doi/full/10.1080/09723757.2010.11886079
40. Ćatović A, Kendić S. Cytogenetic findings at Down Syndrome and their correlation with clinical findings. Bosn J Basic Med Sci. 2005;5(4):61-67.
41. Antonarakis SE, Lyle R, Dermitzakis ET, Reymond A, Deutsch S. Chromosome 21 and Down syndrome: from genomics to pathophysiology. Nat Rev Genet. 2004 Oct;5(10):725-38.
42. Sinet PM, Théophile D, Rahmani Z, Chettouh Z, Blouin JL, Prieur M, et al. Mapping of the Down syndrome phenotype on chromosome 21 at the molecular level. Biomed Pharmacother. 1994 Jan;48(5-6):247-52. Available from:

https://linkinghub.elsevier.com/retrieve/pii/0753332294901406
43. Pritchard MA, Kola I. The "gene dosage effect" hypothesis versus the "amplified developmental instability" hypothesis in Down syndrome. J Neural Transm Suppl. 1999; 57:293-303.
44. Korbel JO, Tirosh-Wagner T, Urban AE, Chen XN, Kasowski M, Dai L, et al. The genetic architecture of Down syndrome phenotypes revealed by high-resolution analysis of human segmental trisomies. Proc Natl Acad Sci USA. 2009 Jul 21;106(29):12031-6. Available from: https://pnas.org/doi/full/10.1073/pnas.0813248106

How to cite this article: Abhilasha Chaudhary, Komal Uppal, Rinmi Kasar, Himangi Dayal, Ankur Jindal, Sunil Kumar Polipalli et.al. Clinical and genetic profile of Down syndrome: Insights from 10 years of experience at a tertiary care center. *Int J Health Sci Res.* 2025; 15(4):1-10. DOI: *10.52403/ijhsr.20250401*

******