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FREQUENCY OF SIMIAN CREASE IN VARIOUS GENOTYPES OF DOWN SYNDROME

Dr Ayesha Saddiqa Tarar[1], Dr Zahid Mehmood Anjum[2]

[1]Postgraduate Resident Paediatrics, Children Hospital Faisalabad,
[2]Associate Professor Paediatrics, Children Hospital Faisalabad

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Corresponding Author:
Dr Ayesha Saddiqa Tarar
Postgraduate Resident Paediatrics, Children Hospital Faisalabad

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ABSTRACT

Background: Down syndrome is the most prevalent chromosomal abnormality worldwide, typically resulting from trisomy 21. While karyotyping remains the gold standard for diagnosis, it is time-consuming and often delayed, especially in resource-limited settings. **Objective:** To determine the frequency of simian crease among children with Down syndrome and compare its distribution across different genotypes. **Methodology:** This cross-sectional study was conducted at Children's Hospital, Faisalabad, from 27th February 2025 to 5th June 2025. A total of 93 children under the age of 18 with genetically confirmed Down syndrome were enrolled using non-probability sampling. Each participant was examined for the presence of simian crease (unilateral or bilateral). Genetic records were obtained from NIBGE to classify genotypes into non-disjunction, translocation, and mosaicism. **Results:** Out of the 93 participants, 71.0% had a simian crease. Among these, 68.2% were bilateral and 31.8% unilateral. The simian crease was present in 79.5% of children with non-disjunction, 50.0% with translocation, and 25.0% with mosaicism. A significant association was observed between genotype and the presence of simian creases ($\chi^2 = 13.32$, $p = 0.008$). No significant association was found with gender ($p = 0.071$) or age group ($p = 0.093$). The effect size (Cramér's V) was calculated to be 0.378, indicating a moderate association. **Conclusion:** The simian crease is significantly more frequent in children with the non-disjunction form of Down syndrome, suggesting a potential link between genotype and phenotypic expression. While it may aid clinical suspicion, genetic analysis remains essential for definitive diagnosis.

INTRODUCTION

Down syndrome (DS), or trisomy 21, remains the most frequently identified chromosomal disorder associated with intellectual disability and congenital malformations. With a global incidence of approximately 1 in every 600 to 800 live births, it poses a significant clinical and public health concern [1]. The condition arises due to the presence of an extra copy of chromosome 21 and manifests in three main cytogenetic forms: standard trisomy 21 (non-disjunction), translocation, and mosaicism. Among these, non-disjunction accounts for over 90% of cases, followed by translocation (4–5%) and mosaicism (1–2%) [2]. Early identification of these genotypes is vital for medical decision-making, family counseling, and long-term planning. Phenotypically, Down syndrome presents with a distinct constellation of features including hypotonia, flat facial profile, upslanting palpebral fissures, epicanthal folds, brachycephaly, macroglossia, and congenital heart defects. One notable dermatoglyphic feature seen frequently in DS is the simian crease, also known as a single transverse palmar crease [3]. This crease results from the fusion of the normally distinct proximal and distal palmar creases into a single line traversing the palm. While simian creases can be seen in healthy individuals (occurring in 1–4% of the general population), their frequency is markedly higher in individuals with chromosomal abnormalities, especially Down syndrome [4][5]. In previous research, the prevalence of simian crease among children with Down syndrome has varied significantly. A Pakistani study of 295 patients reported simian creases in approximately 60% of cases [6]. Similarly, a 7.5-year study in an Indian tertiary care center observed the increase in about 33.2% of Down syndrome patients [7]. These differences could be due to the population genetics, observer biasness, age at diagnosis or the cytogenetic subtypes difference. Notably, the simian crees were also found in other chromosomal syndromes like trisomy 13 and 18 with the prevalence of 60 and 30 respectively providing further evidence as to the possible diagnostic value of the marker [8][9]. The essential role of genotype-phenotype correlations in Down syndrome is gradually acknowledged in perfecting measures in diagnosis and management. Indicatively, the full trisomy 21 patients tend to have more classical phenotypic characteristics compared to mosaics in whom the expression may be atypical and inconsistent [10] [11]. Such cases of translocation are similar in description to non-disjunction cases depending on the chromosomal segment involved or there may be shifted phenotypic characteristics. Devlin et al. have found that whereas in trisomy and translocation patients over 90 percent of the cases are identified properly by clinical diagnosis only 37.5 percent were correctly identified, with physical examination alone as the method used [12].

The utilization of physical markers like the simian crease should not be forgotten even with the routine application of technical cytogenetic procedures since there is always an appreciation of the same in low-resource countries where delays in diagnosis are likely to occur. Nevertheless, the literature is yet to present adequate data illustrating the relationship between particular DS genotypes and occurrence of simian creases. To date, the majority of the studies have addressed general clinical features without approximating patients to genetic subtype. Notably, this data gap can mostly be observed in local Pakistani data which are limited and restricted in size. The justification of this study thus lies within the necessity to produce genobiased phenotype data that will be used in early suspicion, screening and counseling of the patients with DS.

Objective:

To determine the frequency of simian crease among children with Down syndrome and

compare its distribution across different genotypes.

Methodology

This was a cross-sectional study conducted at Children's Hospital, Faisalabad, over a period of four months from 27th February 2025 to 5th June 2025, including 93 children diagnosed with Down syndrome, selected through non-probability consecutive sampling.

Inclusion Criteria:

- Children of either gender under 18 years of age.
- Diagnosed with Down syndrome confirmed by cytogenetic analysis.
- Availability of complete genetic records from NIBGE (National Institute for Biotechnology and Genetic Engineering).
- Parental or guardian consent for participation and clinical examination.

Exclusion Criteria:

- Children with phenotypic features of Down syndrome but normal chromosomal analysis.
- Incomplete genetic documentation.
- Parents or guardians refusing consent.

Data Collection

After obtaining ethical approval from the Institutional Review Board of Children's Hospital Faisalabad and informed written consent from parents/guardians, data were collected from 93 children diagnosed with Down syndrome. Genetic reports were obtained from the National Institute for Biotechnology and Genetic Engineering (NIBGE), providing detailed information on chromosomal abnormalities. Based on these reports, each patient was categorized into one of three genotypic groups: non-disjunction (classic trisomy 21 resulting from three separate copies of chromosome 21), translocation (where the extra chromosome 21 material is attached to another chromosome), or mosaicism (characterized by a mixture of normal and trisomy 21 cells within the same individual). Following genotypic classification, all children underwent a physical examination to assess the presence of a simian crease, defined as a single transverse palmar crease that may be present unilaterally or bilaterally. The findings were systematically recorded using a structured proforma, which also captured demographic data, including age and gender.

Statistical Analysis

The data were analyzed using SPSS version 25. Descriptive statistics were used to summarize quantitative variables, such as age (reported as mean ± standard deviation). In contrast, qualitative variables, including gender, genotype, and presence of simian crease, were expressed as frequencies and percentages. The association between Down syndrome genotypes and the presence of simian crease was evaluated using the Chi-square test. A p-value of <0.05 was considered statistically significant.

Results

Data were collected from 93 patients, with a mean age of 5.8 ± 3.4 years. There were 51 (54.8%) males and 42 (45.2%) females. Regarding genotype, 73 (78.5%) had non-disjunction, 12 (12.9%) had translocation, and 8 (8.6%) had mosaicism. This indicates that non-disjunction was the predominant genetic mechanism among the children studied.

Table 1: Demographic and Genotypic Characteristics of Participants (n = 93)

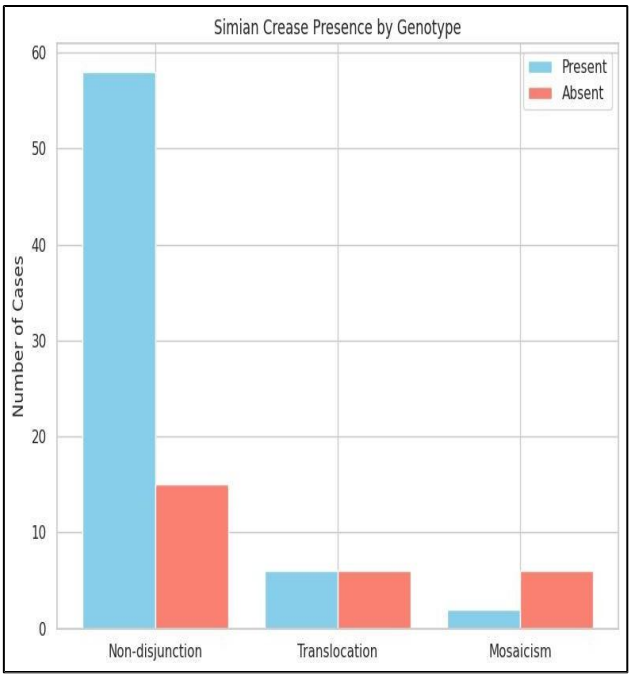
Variable	n (%) or Mean ± SD
Age (years)	5.8 ± 3.4
Gender	
• Male	51 (54.8%)
• Female	42 (45.2%)
Genotype	
• Non-disjunction	73 (78.5%)
• Translocation	12 (12.9%)
• Mosaicism	8 (8.6%)

Simian crease was present in 66 (71.0%) out of 93 children. In the non-disjunction group, 58 (79.5%) had a crease, with 41 (56.2%) bilateral and 17 (23.3%) unilateral. In the translocation group, 6 (50.0%) had the crease—3 (25.0%) bilateral and 3 (25.0%)

unilateral. Among those with mosaicism, only 2 (25.0%) had a crease, each with one bilateral and one unilateral case. This suggests the strongest association between simian crease and non-disjunction.

Table 2: Frequency and Laterality of Simian Crease by Genotype

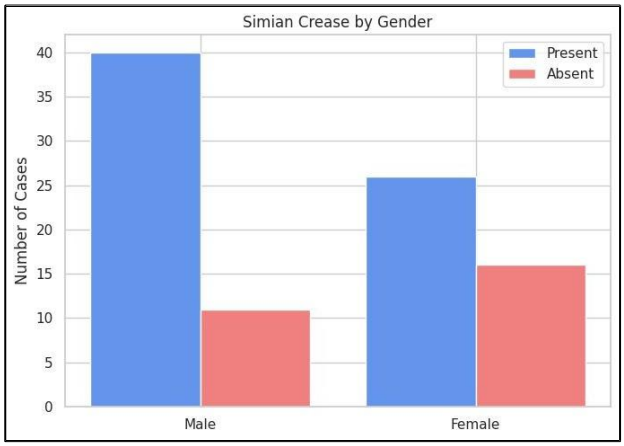
Genotype	Total (n)	Simian Crease Present	Simian Crease Absent	Bilateral Crease	Unilateral Crease
Non-disjunction	73	58 (79.5%)	15 (20.5%)	41 (56.2%)	17 (23.3%)
Translocation	12	6 (50.0%)	6 (50.0%)	3 (25.0%)	3 (25.0%)
Mosaicism	8	2 (25.0%)	6 (75.0%)	1 (12.5%)	1 (12.5%)
Total	**93**	**66 (71.0%)**	**27 (29.0%)**	**45 (48.4%)**	**21 (22.6%)**



40 (78.4%) of males had a simian crease, compared to 26 (61.9%) of females. Regarding age, simian crease was found in 30 (78.9%) children under 5 years, 24 (70.6%) aged 5–10 years, and 12 (57.1%) above 10 years. Although the frequency decreased with age, this trend did not reach statistical significance.

Table 3: Distribution of Simian Crease by Gender

Gender	Total (n)	Simian Crease Present	Simian Crease Absent
Male	51	40 (78.4%)	11 (21.6%)
Female	42	26 (61.9%)	16 (38.1%)
Total	**93**	**66 (71.0%)**	**27 (29.0%)**
Age Group (Years)			
< 5	38	30 (78.9%)	8 (21.1%)
5–10	34	24 (70.6%)	10 (29.4%)
> 10	21	12 (57.1%)	9 (42.9%)
Total	**93**	**66 (71.0%)**	**27 (29.0%)**



There is significant association between simian crease and genotype ($\chi^2 = 9.63$, $p = 0.008$). The associations with gender ($\chi^2 = 3.25$, $p = 0.071$) and age group ($\chi^2 = 4.78$, $p = 0.093$) were not statistically significant. This highlights that genotype, particularly non-disjunction, is the most relevant factor associated with simian crease presence in these children.

Table 4: Association Between Simian Crease and Clinical Variables (n = 93)

Variable	Categories Compared	Test Statistic (χ^2)	p-value
Genotype	Non-disjunction vs. Translocation vs. Mosaicism	χ^2 = 9.63	0.008
Gender	Male vs. Female	χ^2 = 3.25	0.071
Age Group	<5 years vs. 5–10 years vs. >10 years	χ^2 = 4.78	0.093

Discussion

This study investigated the frequency of simian crease among different genotypes of Down syndrome, including non-disjunction, translocation, and mosaicism, in a pediatric population. The cohort of 405 pregnant women served as the source of the data collected. The study was a retrospective analysis of medical records with data availed in a tertiary care hospital during a definite period of study. The results involved demographic information (i.e. age, body mass index (BMI) and parity) and pre-existing medical diagnoses (i.e. hypertension and diabetes). Results: In the PCOS group there was a significantly higher mean Body Mass Index (BMI) (28.7 5.3 kg/m 2) than the control group(25.6 4.9 kg/m 2 , p C 0.001), and the prevalence of obesity was significantly higher in PCOS group (45% vs. 25%, p C 0.001). Even though the mean age (30.4 4.8 years vs. 29.9 4.5 years), gravidity (2.3 1.1 vs. 2.1 1.0), parity (1.2 0.9 vs. 1.1 0.8), and smoking status (12 vs. 10%) were a little higher in PCOS group, all differences were not significant ($p > 0.05$). The proportion of preterm delivery in the PCOS group was 22 % compared with 10 % when the control group was used ($p < 0.01$) and the cesarean deliveries were more frequent as well in PCOS pregnancies (42 % vs. 28 %). Conclusion: In conclusion, Polycystic Ovary Syndrome (PCOS) is pertinently linked with poor pregnancy outcomes that comprise gestational diabetes, hypertensive diseases, preterm birth, and neonatal morbidity which include low birth weight, and admissions to the neonatal intensive care unit. However, the fact that males have simian creases at a higher frequency (78.4%) than females do (61.9%) may call for additional research in larger cohorts [17]. Similarly, a decline in prevalence with increasing age was observed, from 78.9 percent in children under five years to 57.1 percent in those over ten years, possibly reflecting age-related changes in crease visibility or classification bias during physical examination. When interpreting the findings, it is important to take into consideration the study's several limitations. The findings may not be applicable to a wider range of populations because the sample was limited to a single center and relatively small. Selection bias may have occurred because non-probability consecutive sampling was used. Also, physical examination results like the simian crease can be subjective, so there might be variation between observers, especially when it comes to telling the difference between unilateral and bilateral presentations. The study also did not account for other phenotypic features or comorbidities that may influence the expression of simian crease.

Conclusion

It is concluded that the simian crease is a common phenotypic feature in children with Down syndrome, with a significantly higher frequency observed in those with the non-disjunction genotype compared to translocation and mosaicism. The presence of simian crease appears to correlate with the underlying genetic mechanism, suggesting its potential value as a supportive clinical marker in early diagnosis. However, given the moderate association and variability across

genotypes, simian crease should be interpreted in conjunction with genetic testing rather than as a standalone indicator.

Reference:

1. Wahl, L., Dupont, G., & Tubbs, R. S. (2019). The simian crease: Relationship to various genetic disorders. *Clinical Anatomy*, *32*(8), 1042-1047.
2. Katznelson, M. B. M., Bejerano, M., Yakovenko, K., & Kobyliansky, E. (1999). Relationship between genetic anomalies of different levels and deviations in dermatoglyphic traits. Part 4: Dermatoglyphic peculiarities of males and females with Down syndrome. Family study. *Anthropologischer Anzeiger*, 193-255.
3. Kava, M. P., Tullu, M. S., Muranjan, M. N., & Girisha, K. M. (2004). Down syndrome:: Clinical profile from India. *Archives of medical research*, *35*(1), 31-35.
4. Malla, T.M., Srivastava, P. and Ganesh, N., 2015. Dermatoglyphic variations among clinically diagnosed Down's syndrome cases: A cohort study. *Biomedical and Pharmacology Journal*, *1*(2), pp.475-478.
5. Fogle, Thomas. "Using dermatoglyphics from down syndrome and class populations to study the genetics of a complex trait." *Association for Biology Laboratory Education (ABLE)* 11 (1990): 129-150.
6. Opitz, John M., and Enid F. Gilbert-Barness. "Reflections on the pathogenesis of Down syndrome." *American Journal of Medical Genetics* 37, no. S7 (1990): 38-51.
7. Källén, Bengt, Pierpaolo Mastroiacovo, and Elisabeth Robert. "Major congenital malformations in Down syndrome." *American journal of medical genetics* 65, no. 2 (1996): 160-166.
8. Kobyliansky, Eugene, Michal Bejerano, Mariassa Bat-Miriam Katznelson, and Ida Malkin. "Relationship between genetic anomalies of different levels and deviations in dermatoglyphic traits." *Stud Hist Anthropol* 4 (2006): 61-121.
9. Zisovska, Elizabeta. "The Importance of Down Syndrome Phenocopies in the Newborns in Tertiary Obstetric Hospital." *Macedonian Journal of Medical Sciences* 15, no. 6 (4) (2013): 370-375.
10. Starbuck, John Marlow. *Down syndrome (trisomy 21): Developmental implications from morphometric investigations of the effects of gene-dosage imbalance upon craniofacial phenotypes in humans and the Ts1Yey Down syndrome mouse model*. The Pennsylvania State University, 2012.
11. Adeleke, Omoloro, Hussein Elmufti, Jie Zhang, Bhuvaneshwari Jagadesan, and Mimily Harsono. "Double Aneuploidy of Down Syndrome (Trisomy 21) and Jacobs Syndrome (Trisomy XYY) with Complete Tracheal Rings Deformity: Case Report and Literature Review." *American Journal of Perinatology Reports* 13, no. 04 (2023): e53-e60.
12. Mandava, S., Koppaka, N., Bhatia, V., & Das, B. R. (2010). Cytogenetic analysis of 1572 cases of Down syndrome: a report of double aneuploidy and novel findings 47, XY, t (14; 21)(q13; q22. 3) mat,+ 21 and 45, XX, t (14; 21) in an Indian population. *Genetic testing and molecular biomarkers*, *14*(4), 499-504.
13. Todaro, George J., and George M. Martin. "Increased Susceptibility of Down's Syndrome Fibroblasts to Transformation by SV10." *Proceedings of the Society for Experimental Biology and Medicine* 124, no. 4 (1967): 1232-1236.
14. Reutter, Heiko, Regina C. Betz, Michael Ludwig, and Thomas M. Boemers. "MTHFR 677 TT genotype in a mother and her child with Down syndrome, atrioventricular canal and exstrophy of the bladder: implications of a mutual genetic risk factor?." *European journal of pediatrics* 165, no. 8 (2006): 566-568.

15. Sadoh, W.E., Eki-udoko, F.E. and Isah, I.A., 2018. Profile of clinical features, congenital heart disease and other comorbidities in children with Down syndrome in a tertiary care centre in Nigeria. *Sri Lanka Journal of Child Health*, *47*(1).
16. Moreau, Manon, Soukaina Benhaddou, Rodolphe Dard, Stefania Tolu, Rim Hamzé, François Vialard, Jamileh Movassat, and Nathalie Janel. "Metabolic diseases and Down syndrome: how are they linked together?." *Biomedicines* 9, no. 2 (2021): 221.
17. Coppedè, F. (2016). Risk factors for Down syndrome. *Archives of toxicology*, *90*(12), 2917-2929.