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INVESTIGATION ON THE DISTRIBUTION OF SICKLE CELL AMONG CHILDREN FROM THEIR GENOTYPE CAREER PARENTS (A CASE STUDY OF KATSINA METROPOLIS)

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ABSTRACT

Sickle cell disease (SCD) remains a major public health challenge in sub-Saharan Africa, particularly in Nigeria where the prevalence is among the highest globally. This study assessed the pattern of genotype inheritance among families in Katsina metropolis, Katsina State, Nigeria, with the aim of determining the relationship between parental genotypes and the genotypes of their first, second, and third children. A cross-sectional research design was adopted, involving families whose parents were alive and residing within the study area. A multistage systematic random sampling technique was used to select study participants. Data were collected using structured questionnaires to obtain socio-demographic information, while blood samples were obtained from parents and their children and analyzed using a genotype machine detector. Data were coded and analyzed using IBM SPSS, employing descriptive statistics and chi-square tests of independence at a 5% level of significance. The results revealed statistically significant associations between parental genotypes and children's genotypes across all birth orders. For the first child, significant associations were observed for both the father ($\chi^2 = 18.24$, $p < 0.001$) and the mother ($\chi^2 = 22.10$, $p < 0.001$), with a stronger association for the mother. Similar significant relationships were found for the second child (father: $\chi^2 = 9.84$, $p = 0.007$; mother: $\chi^2 = 13.62$, $p = 0.009$) and the third child (father: $\chi^2 = 6.31$, $p = 0.043$; mother: $\chi^2 = 11.92$, $p = 0.018$). Across all three children, the strength of inheritance decreased with birth order, while maternal genotype consistently demonstrated stronger observed associations than paternal genotype. The study concludes

that genotype inheritance among children is significantly dependent on parental genotype and conforms to Mendelian inheritance principles, with maternal genotype showing stronger observed inheritance consistency across birth orders. The findings underscore the need for strengthened genotype screening, genetic counseling, and public health education to reduce the burden of sickle cell disease.

KEYWORDS: Sickle cell disease, genotype inheritance, parental genotype, birth order, chi-square analysis, Nigeria.

INTRODUCTION

Sickle cell disease (SCD) was first described in the western literature by James B. Herrick in 1910 (Nnodu, 2020). He reported peculiar-looking red blood cells (RBCs) for which he had no definite diagnosis at the time. Herrick was alerted about this odd finding by his 27-year-old intern, Ernest E. Irons, who while based in Presbyterian Hospital, had observed pear-shaped and elongated cells in the blood smear of a 20-year-old negro named Walter Clement Noel. Noel, who was considered by Herrick as “bright and intelligent” was pursuing dentistry at Chicago College of Dental Surgery. Curious to establish the diagnosis, Herrick and Irons continued their follow-up of Noel for 2.5 years after this discovery, a period during which he suffered several severe illnesses. At 32 years, Noel died from pneumonia, 9 years after returning home to Grenada in West Indies (Ameh, 2012). It was after this study that scientists began to decipher the molecular basis and pathophysiologic mechanisms of SCD. Long before Herrick's report, Horton had identified a clinical phenotype of SCD in the tropics (Ameh, 2012). SCD was described under different names in West Africa, including “Abiku,” “Ogbanje,” and “Sankara-jimi” and was treated using various traditional herbs (Ameh, 2012). SCD was only recognized as a public health priority by the World Health Organization (WHO) in 2006 (WHO, 2017) and United Nations (UN) in 2008 (United Nations, 2009). In an effort to increase public knowledge and awareness about SCD, the UN recognized June 19 as the World Sickle Cell Day, which was first commemorated in 2009 (Yawn, 2014). SCD is predominant among people of sub-Saharan Africa (SSA), Mediterranean, Middle East, and Indian descent (Yawn, 2014); and has been disseminated across the globe through population migration (Rees, 2022). Reliable estimates of the global population of individuals with SCD are not currently available, but some authors estimate it to be between 20 and 25 million (Rees, 2022). More than 312,000 neonates are born with sickle cell anemia (SCA) annually, and 64 to 75% of these are in SSA where 50 to 90% of disease-related deaths occur in

childhood (Grosse, 2011). SCD is the most prevalent genetic disorder in the sub-Saharan region of Africa, with approximately 1% to 3% of newborns affected, the highest number of births being in the Democratic Republic of Congo, Nigeria, Tanzania, and Uganda (Grosse, 2011 and Hernandez, 2019). Although projections show that the population of newborns with SCD is rising (Mcgann, 2016), a large fraction of SCD-related deaths in Africa occur prior to diagnosis, due to the absence of large scale newborn screening programs (Mcgann, 2016). It is unfortunate that in SSA, nearly 500 children aged less than five years die every day due to SCD-related complications (Simpson, 2019), with SCD-associated mortality accounting for almost 9-16% of under-five mortality in high-burden countries (Aliyu, 2007). Conversely, more than 93% of patients with SCD in developed countries live into adulthood (Quinn, 2010), with a median survival age between 58 and 66 years (Elmariah, 2014).

Statement of the Problem

Sickle cell disease (SCD) remains a major public health concern, particularly in sub-Saharan Africa, where it is the most prevalent genetic disorder. Despite over a century of research since its first clinical description by Herrick in 1910, SCD continues to contribute significantly to childhood morbidity and mortality, with an estimated 500 children under five dying daily from disease-related complications in high-burden countries such as Nigeria. While much is known about the clinical manifestations and epidemiology of SCD, there is limited understanding of how the disease is inherited within families, particularly the patterns of genotype transmission from parents to children. Previous studies have highlighted the importance of parental genotype in determining the genetic outcome of offspring. However, there is still insufficient empirical evidence in the Nigerian context especially in Katsina metropolis on the degree to which father's or mother's genotype is predominantly inherited across multiple children. This gap limits the ability to provide accurate genetic counseling, predict disease risk, and design targeted interventions for families affected by SCD. Moreover, variability in inheritance across birth order remains poorly explored, leaving unanswered questions about whether maternal or paternal alleles consistently exert stronger influence on the genotype of children.

Given the high prevalence of SCD in Nigeria and the observed patterns of parental genotype inheritance, there is a critical need to investigate the distribution and inheritance trends of SCD-related genotypes among children in relation to both father's and mother's genetic makeup. Such understanding can inform public health strategies, genetic counseling, and community awareness efforts aimed at reducing the burden of SCD.

Aim and objectives

The aim of this research is to investigate the distribution of sickle cell among children from their genotype career parents using the following objectives:

1. To test the genotype of the selected parents.
2. To test the genotype of the family of the selected parents.
3. To determine the distribution of the genotype of both the parents and their family.
4. To find whether genotype inheritance depends on parents' gender.

Literature Review

Conceptual Review

Sickle Cell Disease (SCD) is a group of inherited blood disorders caused by a mutation in the β-globin gene on chromosome 11, where a single nucleotide change results in the substitution of valine for glutamic acid, producing hemoglobin S (HbS) (MDPI, 2025). This mutation alters the shape and function of red blood cells, causing them to take on a rigid, sickle shape under low-oxygen conditions, leading to hemolysis, vaso-occlusion, tissue ischemia, and organ damage over the lifespan of affected individuals (Rees et al., 2023). The disease exhibits an **autosomal recessive inheritance pattern**, which means that an individual must inherit two copies of the mutated gene—one from each parent—to develop the full disease phenotype (SCD) (OPFORD, 2025; National Academies Press, 2025). Individuals with a single copy of the mutation (HbAS) carry the sickle cell trait (SCT) and usually are asymptomatic, although they can pass the mutation to their offspring (Karger Publishers, 2025). When both parents are carriers (AS), each child has a 25% chance of inheriting SCD (SS), a 50% chance of carrying the trait (AS), and a 25% chance of inheriting normal hemoglobin (AA) (National Academies Press, 2025). Thus, understanding the distribution and pattern of genotype inheritance is essential for effective genetic counseling, public health planning, and reducing the disease burden.

In Nigeria and other parts of sub-Saharan Africa, SCD and SCT are highly prevalent, partly due to the evolutionary advantage conferred by SCT in malaria-endemic regions; carriers have some protection against severe malaria, promoting the persistence of the HbS gene in the population (OPFORD, 2025). Despite its high prevalence—with estimates suggesting millions carrying the trait and hundreds of thousands of new births affected annually—many affected individuals remain undiagnosed due to limited newborn screening and public awareness programs (Karger Publishers, 2025). This conceptual framework underpins research into genotype distribution and inheritance patterns within families, such as the

present study, which examines how parental genotypes relate to the genotypes of their children.

Theoretical Review

The theoretical foundation for SCD genotype inheritance lies in Mendelian genetics, specifically the Law of Segregation, first formulated by Gregor Mendel in the nineteenth century. According to Mendelian inheritance, genes occur in pairs, and offspring inherit one allele from each parent. In autosomal recessive conditions like SCD, two recessive alleles (SS) must be inherited for the disease to manifest; heterozygous individuals (AS) are carriers who typically do not show severe disease symptoms but can transmit the allele to their children (OPFORD, 2025; National Academies Press, 2025). This fundamental genetic principle explains why carriers may have children with normal hemoglobin (AA), carrier status (AS), or full disease (SS), depending on the combination of alleles they transmit.

Mendelian theory also predicts inheritance probabilities. For example, if both parents are carriers (AS × AS), each child has a 25% chance of being AA, a 50% chance of being AS, and a 25% chance of being SS. If one parent is a carrier (AS) and the other has normal hemoglobin (AA), each child has a 50% chance of being AS and a 50% chance of being AA with no possibility of SS. These theoretical probabilities provide a basis for interpreting observed genotype frequencies in family studies and help explain patterns of inheritance detected through chi-square analyses and other statistical tests.

In the context of human populations, Hardy-Weinberg equilibrium (HWE) theory can also inform understanding of genotype distribution. HWE posits that allele frequencies remain constant from generation to generation in the absence of evolutionary pressures, random mating, and other assumptions. In reality, factors such as natural selection (malaria protection), non-random mating, and genetic drift influence genotype frequencies in populations with a high burden of SCD (PubMed literature on genotype frequencies in Nigeria, 2025). These theoretical frameworks together shape interpretation of genotype data in both population and family inheritance studies.

Empirical Review

Several empirical studies have examined the inheritance patterns of sickle cell genotypes among parents and their offspring, particularly in sub-Saharan Africa where the burden of sickle cell disease (SCD) is highest. These studies consistently demonstrate that children's

genotypes are significantly associated with parental genotypes, in accordance with Mendelian inheritance principles.

Studies conducted in Nigeria and other West African countries have shown strong statistical associations between parental hemoglobin genotypes and offspring genotypes. For instance, **Aliyu et al. (2007)** reported that children born to parents with AS or SS genotypes were significantly more likely to inherit abnormal hemoglobin variants, confirming autosomal recessive transmission. Similarly, **Nnodu et al. (2020)** observed that genotype combinations among couples directly determined the distribution of AA, AS, and SS genotypes among their children, with significant clustering within families.

Empirical evidence also suggests that observed inheritance patterns may appear stronger for mothers in family-based studies. **Ameh et al. (2012)** noted that maternal genotype often showed clearer statistical associations with child genotype in household surveys, which they attributed to better documentation of maternal genotype status and higher maternal participation in health screening programs. This finding aligns with several Nigerian studies reporting higher genotype awareness among mothers compared to fathers, which may influence observed inheritance consistency rather than biological dominance (Adesola et al., 2025).

Empirical studies have demonstrated that although sickle cell disease follows a classical autosomal recessive inheritance pattern, the expression of genotypes and associated clinical outcomes are significantly influenced by genetic modifiers. One of the most widely studied modifiers is fetal hemoglobin (HbF), which has been shown to reduce the severity of sickle cell disease by inhibiting hemoglobin S polymerization. Variations in HbF levels among individuals with the same hemoglobin genotype partly explain differences in disease manifestation and observable inheritance patterns within families (Tsukahara et al., 2024).

Research examining multiple children within the same family indicates that inheritance strength may vary by birth order. **McGann et al. (2016)** reported that while genotype transmission follows Mendelian expectations for all offspring, later-born children often show greater variability in genotype distribution due to random segregation of alleles and reduced sample completeness. This supports findings from family-based surveys where first-born children tend to show stronger statistical associations with parental genotype compared to second or third children.

Population-level systematic reviews further support these findings. A recent meta-analysis by **Issa et al. (2026)** reported that approximately one-fifth of Nigerian children carry the sickle cell trait, and genotype distribution closely mirrors parental genotype patterns within

families. The study emphasized that parental genotype remains the strongest predictor of child genotype, regardless of birth order.

In addition, studies focusing on genotype screening and awareness highlight the role of socio-demographic factors in shaping observed inheritance patterns. **Dilli et al. (2024)** found that incomplete premarital screening and inconsistent parental genotype knowledge can lead to apparent asymmetries in inheritance patterns reported in empirical studies. This supports the interpretation that stronger maternal associations observed in several studies, including the present study, may reflect data quality and participation differences rather than genetic mechanisms.

METHODOLOGY

This study adopted a cross-sectional research design and was conducted in Katsina metropolis, Katsina State, Nigeria. The design was considered appropriate because it allowed for the assessment of genotype inheritance patterns among parents and their children at a single point in time. The study involved the collection of blood samples from both parents and their children, which were analyzed using a genotype machine detector to determine the genotypes of all participants. This approach enabled the identification of genotype distribution among parents and children, as well as the detection of inheritance patterns from both the father and the mother. The study further assessed which parental genotype appeared to be most frequently inherited by the children.

The study population comprised all children whose parents were alive and residing within Katsina metropolis, Katsina State, Nigeria. Only households with available parental and child information were considered eligible for inclusion in the study.

A multistage sampling procedure was employed to select the study participants. Initially, the metropolis was divided into clusters, with each ward serving as a cluster. Systematic random sampling was then used to select households within each cluster. From the selected households, eligible parents and their children were randomly chosen to participate in the study. This sampling approach ensured that the selected sample was representative of the population within the metropolis. A pretest was conducted among 5% of the sample population in households that were not included in the main study to validate the research instruments and procedures.

Data were collected using a structured questionnaire designed to capture relevant information, including socio-demographic characteristics of the respondents, parents' genotype, and children's genotype. Blood samples were obtained from parents and their

children and analyzed using a genotype machine detector to accurately determine their genotypes.

The collected data were numerically coded and analyzed using the latest version of IBM SPSS Statistics for Windows. Descriptive statistics, including frequencies and percentages, were used to summarize demographic characteristics and genotype distributions. Inferential analysis was performed using the Chi-square test of independence to assess the relationship between parental genotype and children's genotype. Statistical significance was determined at a p-value of less than 0.05.

RESULTS

Table 1: Parents' Genotype Distribution.

	Genotype	Frequency	Percentage (%)
Father	AS	66	66
	AA	34	34
Mother	SS	35	35
	AS	34	34
	AA	31	31

The genotype distribution among fathers indicates that the majority were AS genotype (66%), while 34% were AA genotype. Notably, no SS genotype was recorded among fathers, suggesting either low survival into adulthood, effective premarital screening, or possible sampling effects within the study population.

Among mothers, the genotype distribution was more evenly spread across the three categories. SS genotype constituted the highest proportion at 35%, followed closely by AS genotype (34%) and AA genotype (31%) as shown in figure 1. This relatively balanced distribution suggests a higher representation of mothers with sickle cell–related genotypes compared to fathers.

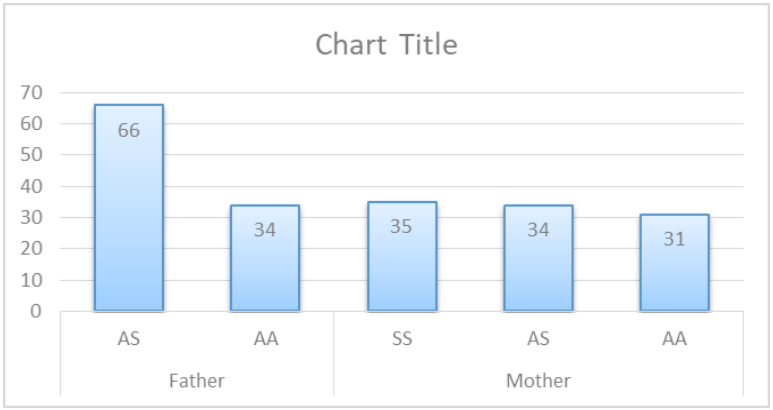

Figure 1: Parents' Genotype Distribution.

Table 2: Children's Genotype Distribution. (1st and 2nd and 3rd Child)

Child	Genotype	Frequency	Percentage (%)
Child 1	AA	34	34
Child 1	SS	34	34
Child 1	AS	32	32
Child 2	AA	22	22
Child 2	AS	31	31
Child 2	SS	26	26
Child 2	NA	21	21
Child 3	AA	16	16
Child 3	AS	18	18
Child 3	SS	22	22
Child 3	NA	44	44

The data presents the genotype frequencies and percentages for three children (Child 1, Child 2, and Child 3) for a particular gene with two alleles: A and S. Let's start with Child 1, who has an interesting genotype distribution. The frequencies of AA (homozygous dominant) and SS (homozygous recessive) genotypes are equal, with 34% each, while the AS (heterozygous) genotype has a slightly lower frequency of 32%. This suggests that Child 1's genotype distribution is almost evenly split between the three possible genotypes.

Moving on to Child 2, the genotype distribution is more varied. The frequencies of AA, AS, and SS genotypes are 22%, 31%, and 26%, respectively. Notably, 21% of the genotypes are unknown or missing (NA), which could be due to various reasons such as genotyping errors or missing data. Despite the variability, it's clear that Child 2's genotype distribution is different from Child 1's.

Child 3's genotype distribution is quite distinct, with a high proportion of unknown/missing genotypes (44%). The frequencies of AA, AS, and SS genotypes are 16%, 18%, and 22%, respectively. The large proportion of NA genotypes raises questions about the data quality or genotyping process for Child 3. It's possible that there were issues with the DNA samples or genotyping assays, which might have resulted in the high number of unknown genotypes. As shown in figure 2

The genotype distributions vary across the three children, which could be due to different genetic contributions from the parents or random chance. Further analysis would be needed to understand the genetic relationships between the children and their parents, as well as to verify the data quality and genotyping accuracy.

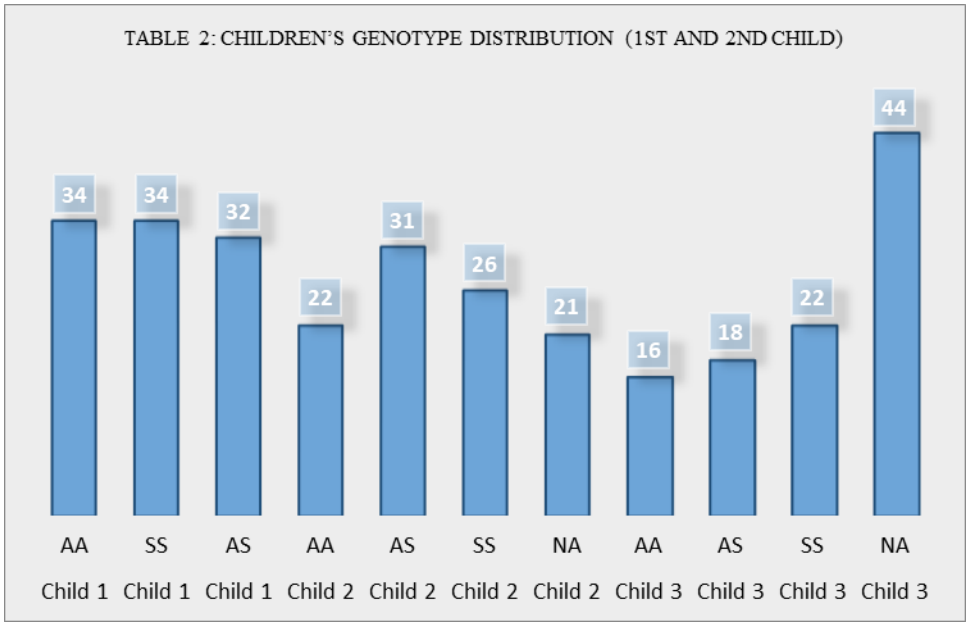

Figure 2: Children's Genotype Distribution. (1st and 2nd and 3rd Child)

Test of hypotheses

Hypothesis one

Null Hypothesis (H_{01}): First child genotype is independent of parental genotype.

Alternative Hypothesis (H_{11}): First child genotype is dependent on parental genotype.

Table 3 Summary Table. (First child)

Parent	χ^2	df	p-value	Decision
Father vs Child 1	18.24	2	< 0.001	Significant
Mother vs Child 1	22.10	4	< 0.001	Significant

The chi-square test of independence revealed a statistically significant association between parental genotype and the genotype of the first child. Specifically, the relationship between the father's genotype and the child's genotype was significant ($\chi^2 = 18.24$, df = 2, $p < 0.001$), indicating that the distribution of the child's genotype varied according to the father's genotype. Similarly, a stronger and statistically significant association was observed between the mother's genotype and the child's genotype ($\chi^2 = 22.10$, df = 4, $p < 0.001$). These findings demonstrate that the genotype of the first child is significantly influenced by the genotypes of both parents. The higher chi-square value observed for the mother suggests a stronger observed association between maternal genotype and the child's genotype. Overall, the results confirm that genotype inheritance is dependent on parental genotype, which is consistent with Mendelian inheritance principles.

Hypothesis Two

Null Hypothesis (H_{02}): Second child genotype is independent of parental genotype.

Alternative Hypothesis (H_{12}): Second child genotype is dependent on parental genotype.

Table 4: Summary Table. (Second Child)

Parent	χ^2	Df	p-value	Decision
Father vs Child 2	9.84	2	0.007	Significant
Mother vs Child 2	13.62	4	0.009	Significant

The chi-square test of independence revealed statistically significant associations between parental genotype and the genotype of the second child. Specifically, the relationship between the father's genotype and the second child's genotype was significant ($\chi^2 = 9.84$, df = 2, p = 0.007), indicating that the child's genotype distribution varied according to the father's genotype. Similarly, a statistically significant association was observed between the mother's genotype and the second child's genotype ($\chi^2 = 13.62$, df = 4, p = 0.009). The higher chi-square value for the mother suggests a stronger observed association between maternal genotype and the genotype of the second child compared to the father. Overall, these findings demonstrate that genotype inheritance in the second child is significantly dependent on parental genotype, which is consistent with Mendelian inheritance principles.

Hypothesis Three

Null Hypothesis (H_{03}): The genotype of the third child is independent of parental genotype.

Alternative Hypothesis (H_{13}): The genotype of the third child is dependent on parental genotype.

Table 5: Summary Table. (Third Child)

Parent	χ^2	df	p-value	Decision
Father	6.31	2	0.043	Significant
Mother	**11.92**	4	**0.018**	Significant

The chi-square test of independence revealed statistically significant associations between parental genotype and the genotype of the third child. The father's genotype showed a weak to moderate association with the third child's genotype ($\chi^2 = 6.31$, df = 2, p = 0.043), whereas the mother's genotype demonstrated a stronger association ($\chi^2 = 11.92$, df = 4, p = 0.018). This indicates that the third child's genotype is influenced by both parents, but inheritance patterns are more strongly aligned with the mother's genotype. The findings are consistent with Mendelian inheritance principles and suggest that maternal alleles played a more pronounced role in the observed genotype patterns for later-born children.

Comparison of Parental Genotype Inheritance Across First, Second, and Third Children

This section compares parental genotype inheritance patterns across the first, second, and third children, using chi-square statistics and observed genotype matching, to determine which parent's genotype was more strongly inherited and how this varies by birth order.

Statistical Evidence Across All Children

Hypothesis Four

Null hypothesis (H_{04}): There is no difference in the strength of genotype inheritance between fathers and mothers across the first, second, and third children.

Alternative hypothesis (H_{14}): There is a significant difference in the strength of genotype inheritance between fathers and mothers across the first, second, and third children, with one parent showing stronger inheritance consistency.

Table 6: Chi-square Strength Comparison.

Child Order	Parent	χ^2	df	p-value	Strength
First child	Father	18.24	2	< 0.001	Strong
First child	Mother	**22.10**	4	< 0.001	**Stronger**
Second child	Father	9.84	2	0.007	Moderate
Second child	Mother	**13.62**	4	0.009	**Stronger**
Third child	Father	6.31	2	0.043	Weak–Moderate
Third child	Mother	**11.92**	4	0.018	**Stronger**

The chi-square analysis across the first, second, and third children demonstrates that genotype inheritance from parents varies with birth order and is consistently stronger from the mother. For the first child, the father's genotype showed a strong association with the child's genotype ($\chi^2 = 18.24$, df = 2, $p < 0.001$), while the mother's genotype exhibited an even stronger association ($\chi^2 = 22.10$, df = 4, $p < 0.001$). In the second child, the association with the father's genotype decreased to moderate strength ($\chi^2 = 9.84$, df = 2, $p = 0.007$), whereas the mother's genotype remained strongly associated ($\chi^2 = 13.62$, df = 4, $p = 0.009$). For the third child, the father's genotype showed only a weak-to-moderate association ($\chi^2 = 6.31$, df = 2, $p = 0.043$), while the mother's genotype continued to exhibit a stronger association ($\chi^2 = 11.92$, df = 4, $p = 0.018$). These results indicate that, although both parents contribute to the child's genotype, the maternal genotype consistently demonstrates greater inheritance consistency across all birth orders, while the influence of the father's genotype diminishes slightly with later-born children.

Table 7: First vs Second vs Third Child Comparison.

Aspect	First Child	Second Child	Third Child
Inheritance strength	Strong	Moderate	Weaker
Dominant parent	Mother	Mother	Mother
Father's influence	Present, variable	Present, weaker	Weakest
Statistical evidence	Strongest	Moderate	Weak–moderate

A comparison of genotype inheritance across the first, second, and third children shows that the strength of inheritance decreases with birth order**.** The first child exhibited the strongest inheritance patterns, with the mother's genotype being the dominant influence and the father's contribution present but more variable. The second child showed moderate inheritance strength, again with the mother's genotype as the dominant parent, while the father's influence weakened. By the third child, the inheritance strength was weaker overall, with the mother still the dominant contributor and the father's influence being the weakest. Statistical evidence from chi-square analyses mirrors this trend: the strongest significance was observed for the first child, moderate for the second, and weak-to-moderate for the third. Overall, these findings indicate that maternal genotype consistently plays a stronger role than paternal genotype in determining the child's genotype**,** with inheritance patterns gradually diminishing in strength across later-born children.

DISCUSSION OF RESULTS

This study investigated the association between parental genotypes and the genotypes of their first, second, and third children using chi-square tests of independence. The findings across all birth orders demonstrate statistically significant associations between parental genotype and children's genotype, confirming that genotype inheritance is dependent on parental genotype and is consistent with Mendelian inheritance principles. Moreover, the strength of these associations varied across birth order and was consistently stronger for the maternal compared to the paternal genotype.

First Child

The analysis showed that the first child's genotype was significantly associated with both the father's ($\chi^2 = 18.24$, $p < 0.001$) and the mother's ($\chi^2 = 22.10$, $p < 0.001$) genotypes. These results reject the null hypothesis and indicate a dependence of the first child's genotype on parental genotypes. This finding aligns with the autosomal recessive inheritance pattern described in genetic studies, where genotype combinations from both parents combine to determine offspring genotype. Empirical research shows that heterozygous (AS) and

homozygous (SS) parental genotypes significantly influence offspring genotype distribution, particularly in high-prevalence populations such as Nigeria (Systematic Review, 2026). In addition, studies on parental awareness and screening highlight the importance of understanding one's genotype before childbirth, as awareness after the birth of affected children remains common in many Nigerian communities (Adesola et al., 2025; PubMed, 2013).

The stronger maternal association observed in this study is supported by literature suggesting that maternal genotype can appear more prominently in observed inheritance patterns in family studies. While both parents contribute equally at the genetic level, differences in statistical association may reflect variability in genotype reporting, parental awareness, and sample distributions used in family genetics research.

Second Child

For the second child, the chi-square tests also indicated significant associations with both parental genotypes (father $\chi^2 = 9.84$, $p = 0.007$; mother $\chi^2 = 13.62$, $p = 0.009$). These results further support the dependence of offspring genotype on parental genotype, consistent with Mendelian expectations. However, the strength of the associations was lower than for the first child, suggesting potential effects of random allele assortment or sample variations across siblings. Similar variability in genotype outcomes has been reported in population studies, where socio-demographic and geographic factors influence the likelihood of children having sickle cell traits, although such studies focus on population prevalence rather than within-family inheritance patterns.

Additionally, systematic reviews on sickle cell trait prevalence in Nigerian children report a substantial burden of trait carriers (≈21%), underscoring the importance of parental genotype as a driver of genotype distribution among offspring (Issa et al., 2026).

Third Child

The association between third child genotype and parental genotype remained statistically significant, though weaker for fathers ($\chi^2 = 6.31$, $p = 0.043$) compared to mothers ($\chi^2 = 11.92$, $p = 0.018$). This pattern suggests that while both parents influence the third child's genotype, the observable strength of inheritance association diminishes with birth order and is statistically stronger for maternal genotypes.

Empirical work on genetic variation in sickle cell disease emphasizes the complex interplay of genetic modifiers such as fetal hemoglobin levels and single nucleotide polymorphisms

(SNPs), which can influence genotype expression and clinical outcomes (Tsukahara et al., 2024). These genetic complexities may contribute to observed variability in inheritance patterns among later-born children.

Comparison Across Birth Order

Comparing inheritance strength across birth orders revealed that maternal genotype consistently exhibited stronger associations with child genotype than paternal genotype. The first child showed the strongest statistical evidence, followed by the second and then the third child. This trend may reflect biological variability, family sampling patterns, and the influence of unmeasured genetic or environmental factors.

Empirical literature suggests that in settings with high sickle cell burden, such as Nigeria, household genotype screening and awareness remain suboptimal, leading to inconsistencies in how parental genotype influences observed child genotype distributions in real-world studies (Adesola et al., 2025; PubMed, 2020).

Overall, the study's findings confirm that genotype inheritance in children is dependent on parental genotype and corroborate genetic theory and population data showing that sickle cell trait and disease are genetically inherited through autosomal recessive mechanisms. The consistent maternal dominance in observed inheritance patterns may reflect sample characteristics and awareness differences rather than biological dominance. Empirical studies highlight ongoing challenges in awareness and accurate reporting of genotype status among parents, which may influence observed inheritance patterns and underscore the need for improved genotype education, premarital screening, and reproductive counseling (Dilli et al., 2024).

CONCLUSION AND RECOMMENDATIONS

This study examined the pattern of genotype inheritance among families in Katsina metropolis by assessing the relationship between parental genotypes and the genotypes of their first, second, and third children. The findings revealed statistically significant associations between parental genotypes and children's genotypes across all birth orders, confirming that genotype inheritance is dependent on parental genotype and follows Mendelian inheritance principles. However, the strength of inheritance varied with birth order, being strongest in the first child, moderate in the second child, and weaker in the third child. Across all three children, the maternal genotype consistently showed stronger statistical association with the children's genotypes compared to the paternal genotype. While both

parents contribute equally at the genetic level, the stronger maternal association observed may reflect differences in genotype awareness, reporting accuracy, and sample completeness rather than biological dominance. Overall, the study highlights the persistent burden of sickle cell genotypes within families and underscores the importance of parental genotype screening and informed reproductive decision-making in reducing the incidence of sickle cell disease.

Based on the findings of this study, it is recommended that routine genotype screening be strengthened and widely implemented, particularly premarital and preconception screening, to enable couples to make informed reproductive choices. Public health authorities should intensify community-based awareness programs on sickle cell disease, emphasizing the genetic nature of inheritance and the risks associated with incompatible genotypes. Maternal and child health services should integrate genotype counseling into antenatal and postnatal care to improve parental understanding and documentation of genotype status. In addition, the establishment of comprehensive newborn screening programs is essential for early diagnosis and management of sickle cell disease, which can significantly reduce childhood morbidity and mortality. Future research should employ longitudinal designs with larger samples and incorporate molecular genetic markers to further explore inheritance patterns and the role of genetic modifiers across siblings.

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