Maternal Isodisomy of Chromosome 13: A Case Study Linking Genetic Inheritance, Nutrition-Related Traits, and Sustainable Health Outcomes

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Abstract. A rare genetic disorder known as Uniparental disomy (UPD) occurs when both chromosomal copies are received by the child from one parent and not following the Mendelian inheritance laws. Although, UPD primarily investigated within the domains of medical genetics and forensic science, but it also carries important implications for food, nutrition, and healthcare practices. The present observation of maternal UPD of chromosome 13 in a child, identified during routine forensic parentage analysis using autosomal STR and Y-STR profiling, highlights the broader relevance of such rare genetic events beyond inheritance anomalies. Since, chromosome 13 harbors genes related to growth regulation, metabolic pathways, immune function, and disease susceptibility. Therefore, nutritional needs, growth patterns and long-term health consequences are indirectly impacted by aberrant inheritance patterns like UPD which can influence gene dosage, imprinting effects, and recessive disease expression. From a healthcare perspective, nutritional planning and dietary interventions may need to be tailored in individuals with chromosomal abnormalities to support optimal growth and metabolic balance. In public health contexts, awareness of rare genetic mechanisms such as maternal isodisomy of chromosome 13 underscores the need for interdisciplinary approaches linking genetics, nutrition, and preventive medicine. Despite its potential significance, research connecting UPD with nutritional status and healthcare strategies remains limited. Addressing this gap could enhance understanding of genotype–phenotype relationships and support evidence-based practices in food sustainability, nutritional counseling, and healthcare planning. Thus, forensic genetic findings not only resolve legal questions but also offer valuable insights relevant to holistic health and nutrition frameworks.

Keywords: Maternal uniparental disomy, Chromosome 13, Paternity testing, Forensic case, Nutritional genomics, Population health genetics, STRs (Short Tandem Repeats).

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1 Introduction

Paternity testing simply means establishing fatherhood. The earliest scientific report in journal for paternity test can be track down to 1956 (Henninghsen, 1956). DNA testing is incredibly reliable and foremost approach of confirming as well refuting familial ties (Jolly, 2000). As we all are born with a distinct set of genetic instructions called as DNA. The genetic characterization of a child is decided by the genetic makeup of the biological father and mother. Consequently, by establishing biological relationships DNA profiling conclusively and definitively answers difficult questions, also helps to resolves disputes and streamline court proceedings. When there is no match between the child's DNA and alleged parent, the alleged individual is completely excluded as the child's biological parent. A DNA match is regarded to have a probability of 99% or above, and so defining a biological connection in the process, as concluded by Klein, 2005.

DNA profiling by highly polymorphic genetic markers (Short Tandem Repeats) is largely used in field of forensic investigation including paternity and kinship testing. For the paternity testing, the thumb rule of genetic inheritance laws states that a single allele from each parent is passed down to the child. But to verify parenthood by the use of STRs is confusing and even challenging in the situations which results in transgressions of Mendel's inheritance principles due to genetic mutation. Uniparental disomy (UPD) is a phenomenon in which one parent, as opposed to both, is the source of a complete or a part of a homologous chromosomal region. UPD can lead to altered gene dosage and extensive homozygosity, thereby unmasking recessive variants or modifying the expression of genes involved in metabolic and nutrition-related pathways (Robinson, 2000). Chromosome 13 contains several genes of metabolic relevance, including IRS2, which plays a critical role in insulin signaling and glucose homeostasis, DGKH, associated with lipid-mediated cellular signaling, and MIPEP, involved in mitochondrial energy metabolism (Withers et al. 1998). In 1980, Engel introduced the theoretical concept of uniparental disomy (UPD), prompted by the high frequency occurrences of disomy and nullisomy events across various chromosomes in human gametes. Based on the various studies done by Cavalheiro et al (2020), Benn P (2021), Yamazawa et al. (2010), Eggermann (2020) and Chein et al (2022), UPD can be categorized as uni or hetero-disomy and depending on its origin, it may be paternal (patUPD) or maternal UPD (matUPD). According to a study conducted by Benn (2021), Eggermann (2020), Nakka et al (2019) and Scuffins (2021), involving 4 million healthy individuals, it was observed that one out of every 2000 births had UPD overall, with mat-UPD incidence being more common than pat-UPD. However, this may be an under-emphasized genetic condition because mostly reported cases of UPD are with clinical phenotypes.

The acrocentric chromosomes (13, 14, 15, 21, 22) are more susceptible for the prevalence of UPD due to their propensity to form Robertsonian translocations, which are chromosomal translocations in which two acrocentric chromosomes fuse their long arms and centromeres while losing some of their short arm material.

Herein, we present a case report to add on the literature on mUPD13 by emphasizing the dilemma faced by the forensic investigators and contextualizing its relevance to

nutrition-associated genetic traits. In addition, the variation in Mendelian inheritance has captivated more attention for paternity testing. Moreover, case studies by Fridman et al, (2025), in forensic context, have demonstrated that uniparental disomy may lead to false exclusions in paternity or maternity cases. This problem is more worsen when dealing with forensic databases, where alleles from both parents are assumed to contribute equally to the genetic profile of child. Studies by Priya et al, (2023) argue that forensic evidence involving genetic testing must be interpreted with caution, especially when genetic anomalies like UPD are involved. The literature suggests that forensic practitioners need to be trained to recognize the signs of chromosomal anomalies and account for them during the analysis and interpretation of genetic evidence. The lack of specific guidelines or protocols addressing uniparental disomy in forensic science is a significant gap that needs to be addressed through updated policies and the integration of more advanced genetic techniques.

2 Case Presentation

We present a case of a girl who was eloped from his home two years ago and later found living with a man who was alleged to be the father of her child. The State Forensic Science Laboratory's DNA section in Jaipur, Rajasthan accepted the related exhibits of the case for standard examination. We have received forensic samples comprising of garments of victim (Alleged mother) along with blood sample of child and alleged father on FTA card. The FTA card, developed by Flinders Technology Associates, is a bio-sample collection card. A free radical scavenger and chemical denaturants present in the FTA® cards firmly bond to the DNA while the remaining proteins and inhibitors are removed by washing (Krambrich 2022). In our case study, the victim (Alleged mother) was refused to undergo medical examination so we don't receive any control sample of victim (Alleged mother) to identify her profile. This poses a challenge for forensic examiners to infer her profile from available exhibits.

3 Materials and Methods

Paternity testing were performed using Powerplex®-Fusion 6C (Promega) kit with standard laboratory norms. Sum of total 23 autosomal polymorphic loci were genotyped along with Amelogenin and three other male originated loci. Further, GlobalFilerTM (Applied Biosystems), Powerplex® Y23 (Promega) and Investigator® Argus X-12 QS (Qiagen) were utilized to confirm the paternity among the samples.
The cutting from exhibits was taken in 1.5ml centrifuge tube. The Maxwell FSC Extraction System (Promega) was used to extract the DNA using the Casework Extraction Kit. The extracted DNA was then amplified using multiplex PCR system kits but for half reaction on Eppendorf AG 22331 Hamburg Mastercycler Nexus X2. DNA fragment of the PCR amplicons were run through the Genetic Analyser 3500 (Applied Biosystems). Fragment analysis of the data obtained was performed by

GeneMapperTM ID-X software v1.6. All the examination procedures were run under the protocol recommended by the manufacturer.

4 Result and Findings

The primary genotyping was carried out using Promega's Powerplex®-Fusion 6C kit. Table 1 displays the outcomes of the amplification of 23 autosomal STRs and the gender defining protein Amelogenin. Akhteruzzaman et al, 2012 reported false paternity on the basis of one or two mismatches. Genotype at the locus D13S317 in garment of victim (Alleged mother), child and alleged father was 8/9/11, 8/8 and 11/11 respectively. Therefore, it can be assumed that at D13S317, at garment of victim, allele calling 8/9/11 is from both victim (Alleged mother) and alleged father, in which 11(homozygous) is of alleged father, hence 8/9 is of the victim (Alleged mother). The expected allele of the child at locus D13S317 should be either 8/11 or 9/11 as case suppose to follow Mendelian inheritance rules. Half of the child's DNA comes from his father and the other half from her alleged mother. But, it was observed that the child has allele calling of 8/8 at D13S317 and allele 11 from father is not expressed (Figure 1). Initially, results of Powerplex®-Fusion 6C (Promega) kit denied patrilineal relation to the presumed father owing to genetic disparities at loci D13S317. Nonetheless, we performed supplementary testing using GlobalFilerTM (Applied Biosystems) kit (Table 2). Based on the samples' STR data analysis, genotyped through Powerplex®-Fusion 6C (Promega) and GlobalFilerTM (Applied Biosystems) kits, it could be concluded that alleles of DNA profile of a male, derived from a blood sample of alleged father are accounted in the composite DNA profile retrieved from victim's garment (Alleged mother) (Table 1 and 2).

Table 1. Allelic data analysis by Powerplex®-Fusion 6C (Promega) Kit

Locus	Blood sample of alleged father on FTA card	Blood sample of child on FTA card	Garment of victim (Alleged mother)
AMELOGENIN	**XY**	**XY**	**XY**
D3S1358	15,17	15,17	15,16,17
D1S1656	16,16.3	14,16.3	12,14,16,16.3
D2S441	11,14	11,11	10,11,14
D10S1248	14,16	15,16	13,14,15,16
D13S317	**11,11**	**8,8**	**8,9,11**
Penta E	12,12	12,13	5,12,13
D16S539	11,13	9,11	9,11,12,13
D18S51	12,16	12,14	12,13,14,16
D2S1338	18,20	19,20	18,19,20,23
CSF1PO	11,12	11,11	11,12

Penta D	11,14	8,11	8,11,12,14
TH01	6,7	7,9.3	6,7,9.3
vWA	18,19	14,19	14,17,18,19
D21S11	30,32.2	30,32.2	28,30,32.2
D7S820	12,12	9,12	9,11,12
D5S818	12,13	12,13	12,13
TPOX	8,8	8,11	8,11
D8S1179	11,14	13,14	11,12,13,14
D12S391	18,22	20,22	18,20,21,22
D19S433	13,14.2	13,14	13,14,14.2,15
SE33	17,31.2	18,31.2	17,18,31.2
D22S1045	11,15	15,15	11,15
DYS391	10	10	10
FGA	19,23	19,21	19,21,23,25
DYS576	17	17	17
DYS570	17	17	17

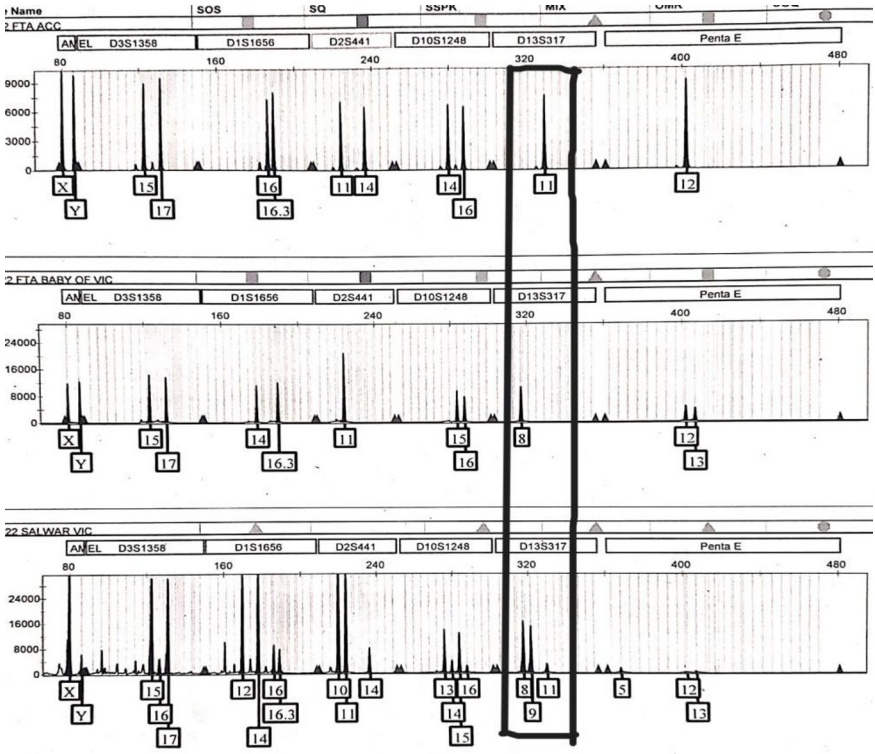

Fig1. Genotype electropherogram at text locus D13S317 of the alleged father, child and the alleged mother

Table 2. Allelic data analysis by GlobalFilerTM (Applied Biosystem) kit

Locus	Blood sample of alleged father on FTA card	Blood sample of child on FTA card	Garment of victim (Alleged mother)
D3S1358	15,17	15,17	15,16,17
Vwa	18,19	14,19	14,17,18,19
D16D539	11,13	9,11	9,11,13
CSF1PO	11,12	11,11	11,12
TPOX	8,8	8,11	8,11
Y-indel	2	2	1,2
Amelogenin	**XY**	**XY**	**XY**
D8S1179	11,14	13,14	11,12,13,14
D21S11	30,32.2	30,32.2	28,29,30,32.2
D18S51	12,16	12,14	12,14,16
DYS391	10	10	10
D2S441	11,14	10,11	10,11,13
D19S433	13,14.2	13,14	13,14,15
THO1	6,7	7,9.3	7,8,9.3
FGA	19,23	19,21	19,21,23,25
D22S1045	11,15	15,15	11,15
D5S818	12,13	12,13	12,13
D13S317	**11,11**	**8,8**	**8,9,11**
D7S820	12,12	9,12	9,11,12
SE33	17,31.2	18,31.2	17,18,31.2
D10S1248	14,16	15,16	11,13,14,15
D1S1656	16,16.3	14,16.3	12,14,16,16.3
D12S391	18,22	20,22	19.3,20,20.3,21
D2S1338	18,22	19,20	18,19,20,23

Furthermore, X-STR analysis was carried out in the present investigation because, in incidences of paternity evaluation where a disparity was emerged at just one locus, additional approaches to analysis have to be further employed to validate the parental connection. For establishing motherly relationship of the victim (Alleged mother) and the child we employed Investigator® Argus X-12 QS (Qiagen) kit (Table 3). The genotype obtained after the analysis of the data collected by the software revealed that the victim (Alleged mother) is biologically related to the origin of the DNA profile that was taken from the child's sample. Using more than one kit invariably increases the discrimination power and hence the 12 X-STR. An ideal match was found in the outcomes that included the 12 STR loci on X-chromosome of alleged mother and

child. Therefore, this case study emphasizes the intrinsic significance of X-chromosomal STR data for analyzing ambiguous paternity instances.

Table 3. Allelic data analysis by Investigator Argus X-12 QS (Qiagen) Kit

Locus	Blood sample of alleged father on FTA card	Blood sample of child on FTA card	Garment of victim (Alleged mother)
QS1	Q	Q	Q
AMELOGENIN	**XY**	**XY**	**XY**
DXS10103	16	20	16,19,20
DXS8378	12	9	9,11,12
DXS10101	33	32	27.2,32,33
DXS10134	36	35	33,35,36
DXS10074	17	19	17,18,19
DXS7132	14	13	13,14
DXS10135	28	27	27,28,29
DXS7423	15	15	14,15
DXS10146	28	27	27,28,29
DXS10079	16	19	16,19
HPRTB	14	12	10,12,14
DXS10148	20	18	18,20
D21S11	30,32.2	30,32.2	28,29,30,32.2

The child was a male and his paternity could be established using Y chromosome STR marker kit. The DNA profile procured from provided blood sample of child and alleged father on FTA card is biologically related, is established by using Powerplex® Y23 (Promega) kit (Table 4).

Table 4. Allelic data Analysis of Powerplex Y23 (Promega) kit

Locus	Blood sample of alleged father on FTA card	Blood sample of child on FTA card	Garment of victim (Alleged mother)
DYS576	17	17	17
DYS389I	13	13	13
DYS448	18	18	18
DYS389II	29	29	29
DYS19	15	15	15

DYS391	10	10	10
DYS481	24	24	24
DYS549	13	13	13
DYS533	11	11	11
DYS438	11	11	11
DYS437	16	16	16
DYS570	17	17	17
DYS635	24	24	24
DYS390	23	23	23
DYS439	12	12	12
DYS392	10	10	10
DYS643	10	10	10
DYS393	13	13	13
DYS458	17	17	17
DYS385a/b	12,19	12,19	12,19
DYS456	15	15	15
Y-GATA-H4	11	11	11

5 Discussion

The foundation of paternity testing is the Mendelian principle of inheritance. Especially when testing a single chromosomal marker and if short tandem repeat (STR) markers have genotypic flaws that deviate from Mendelian principle of inheritance, we perpetually elucidate them as silent alleles or slippage mutations as opposed to UPD.

UPD is frequently culminates from two non-disjunction instances, meiosis was site of the first instance and the second one occurred during the process of mitosis. Non disjunction (homologous chromosomes fail to split from one another) occurs in Meiosis I, raised the likelihood of having two distinct uniparental heterodimers or simply homologous chromosomes from a single parent. The non-separated chromosomes in the zygote when fertilized with a normal haploid gamete may arise to be monosomic or trisomic. Secondly, non- disjunction could happen after the zygote formation, in which mitosis with aneuploidy brought off by duplication of a monosomic chromosome (monosomic rescue) or the deletion of third chromosome (trisomic rescue) (Del Gaudio D et al 2020). It was studied that trisomies with one paternal and two distinct maternal chromosomes are more prevalent during maternal meiosis I, when the majority of non-disjunction events takes place. In later stages, the deletion of a chromosome from paternal parent causes trisomic rescue, which makes the maternal heterodimers increasingly prevalent. Consequently, as previously mentioned in this article's background, we discovered that the UPD13 is maternal UPD13. However, it is not apparent what exactly on chromosome 13 causes maternal

UPD in this instance. Based on the mechanism of UPD being generated specified above, two explanations seem possible in this case that eventually leads to UPD. At first assumption, a nullisomic sperm might have fertilized a disomic ovum, turning out a diploid zygote with 45 chromosomes. Alternatively, when a typical sperm cross with an ovum containing the isochromosome, it could have been trisomic for chromosome 13. There could have been a subsequent "rescue" of the post zygotic embryo due to the deletion of the paternal chromosome 13.

Maternal isodisomy of chromosome 13 may have implications extending into the domain of nutritional genomics, as chromosomal homozygosity can influence genes involved in nutrient metabolism and energy balance. Homozygosity arising from isodisomy may therefore modify individual metabolic responses to nutrients, potentially affecting susceptibility to nutrition-related metabolic disorders. Although the present study did not evaluate dietary intake or metabolic phenotype, the incidental forensic detection of such genetic events highlights how forensic datasets may intersect with broader nutritional health considerations. Uniparental disomy (UPD) poses significant challenges in forensic paternity testing, as it can lead to false exclusions in parentage determinations. It is feasible that a negligence to acknowledge the allelic variations evidential of UPD in practice could result in a number of serious consequences, possibly erroneous omission from paternity tests, diminished database searches for people gone missing, and IBD (identical by descent) analysis intervention in forensic genetic genealogy (FGG). Consequently, when a forensic analyst stumbles upon inconsistent genotyping, the existence of UPD should be taken into account. Antioxidants found in traditional fermented drinks shield cells from harm brought on by free radicals. [29,30,33].

6 Conclusion

The identification of maternal isodisomy of chromosome 13 in this case highlights not only its forensic relevance but also its potential nutritional and metabolic implications. Isodisomy results in extended regions of homozygosity, which may unmask recessive variants or alter the dosage of genes involved in nutrient metabolism and energy regulation. Chromosome 13 harbors several genes of metabolic importance. Alterations in the pathways have been linked to impaired nutrient utilization and metabolic dysregulation at the population level (DeFronzo & Ferrannini, 1991). Although no direct nutritional phenotype was assessed in the present forensic investigation, the incidental detection of such chromosomal anomalies underscores the broader public-health relevance of forensic genetic data. The study conclusively supported the biological mother–child relationship and but the mismatch at locus D13S317 in the child and the alleged father might be credited to UPD and the child is biologically beyond doubt son of the alleged parents. Seeing as conventional laboratory protocols may overlook the possibility of both isodisomy and heterodisomy, the emergence of UPD, particularly asymptomatic, has implications for paternity testing. When anomalous paternity results occur, this atypical inheritance

pattern should be appropriately taken into consideration. It is not anticipated from a paternity testing lab to drawn up substantial number of tests for such a case, however, additional research was necessary to address the primary discrepancies. Our studies suggest that likewise supplementary method such as Chromosomal Microarray (CMA) could be used to validate our study. A very effective method, Next Generation sequencing could help investigators to detect UPD, to draw conclusions in parentage testing.

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Conflicts of Interest

Authors disclosed that they have no conflicting interests.

Approval by Ethics

Per the “Helsinki declaration” signed informed consent was acquired for study.

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