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REVIEW ARTICLE

Exploring complex cases of paternity: unraveling maternal uniparental isodisomy, chromosome mutations, and tetragametic blood chimerism

Explorando casos complejos de paternidad: desentrañando la isodisomía uniparental materna, las mutaciones del cromosoma y el quimerismo sanguíneo tetragamético

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ABSTRACT

Introduction: paternity studies by genetic analysis, based on STRs, repetitive DNA sequences, are essential for determining biological relationships. DNA sample collection, PCR amplification and comparison of STR profiles guarantee high accuracy. These tests, essential in legal contexts, also have applications in genealogy and forensics. Despite their advances, ethical and legal challenges arise, highlighting the importance of handling the results sensitively. Technological evolution promises more accessible and accurate tests, but their implementation must carefully consider ethical and emotional implications.
Objective: to analyze the methodology and results of genetic paternity studies in STRs, highlighting their importance in legal and personal contexts.
Methods: the study was developed through structured research in specialized repositories. PRISMA methodology was applied to include systematic reviews and meta-analyses, ensuring quality and authenticity of the sources. Results: Paternity analyzes based on STRs proved to be highly accurate and were used in diverse areas, from legal disputes to genealogy. In addition, advances in prenatal testing and its applications in other scientific branches were explored.
Conclusions: the studies revealed the importance of extended typing, forensic genomics, and overcoming limitations of standard techniques in complex paternity cases. The need to consider diverse methodologies to obtain accurate and reliable conclusions highlighted the importance of addressing ethical and legal dilemmas associated with the use of paternity testing.

Keywords: Paternity; Disorders; Mutation; Chromosomes.

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RESUMEN

Introducción: Los estudios de paternidad mediante análisis genéticos, basados en STRs, secuencias repetitivas de ADN, son fundamentales para determinar relaciones biológicas. La recolección de muestras de ADN, la amplificación mediante PCR y la comparación de perfiles de STRs garantizan alta precisión. Estas pruebas, esenciales en contextos legales, también tienen aplicaciones en genealogía y forense. A pesar de sus avances, surgen desafíos éticos y legales, destacando la importancia de manejar los resultados con sensibilidad. La evolución tecnológica promete pruebas más accesibles y precisas, pero su implementación debe considerar cuidadosamente implicaciones éticas y emocionales.
Objetivo: analizar la metodología y resultados de estudios de paternidad genéticos en STRs, destacando su importancia en contextos legales y personales.
Métodos: El estudio se desarrolló mediante una investigación estructurada en repositorios especializados. Se aplicó metodología PRISMA para incluir revisiones sistemáticas y metaanálisis, garantizando calidad y autenticidad de las fuentes.
Resultados: Los análisis de paternidad basados en STRs demostraron ser altamente precisos y se utilizaron en diversas áreas, desde disputas legales hasta la genealogía. Además, se exploraron avances en pruebas prenatales y su aplicación en otras ramas científicas.
Conclusiones: Los estudios revelaron la importancia de la tipificación extendida, la genómica forense y la superación de limitaciones de técnicas estándar en casos de paternidad complejos. La necesidad de considerar diversas metodologías para obtener conclusiones precisas y confiables destacó la importancia de enfrentar dilemas éticos y legales vinculados al uso de pruebas de paternidad.

Palabras Clave: Paternidad; Trastornos; Mutación; Cromosomas.

INTRODUCTION

Paternity studies based on genetic analysis employ advanced techniques to determine the biological interaction within a parent-child relationship. These studies are based on the detection and comparison of genetic markers, specifically STRs (Short Tandem Repeats), which are short, repetitive DNA sequences present in the human genome.[1]

STRs are highly polymorphic and vary significantly between individuals, making them effective tools for identifying genetic relationships. The process involves DNA samples—typically collected from oral cells—which are then extracted, specific STR regions amplified using PCR (polymerase chain reaction), and finally, STR profiles are compared between children of the so-called parent. Each STR is located on a different chromosome, ensuring that the genetic information provided is independent and robust.[2]

In paternity testing, multiple STRs are examined to ensure an accurate conclusion. A match in the majority of the STRs analyzed between the child and the alleged father indicates a high probability of paternity. These studies are highly accurate and are used in legal contexts, such as paternity disputes, inheritance cases, and child custody. The reliability and accuracy of these tests are critical, and they are conducted with strict quality and confidentiality controls.[3]

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Genetic paternity studies, based on the analysis of STRs (Short Tandem Repeats), represent a revolutionary technique in forensic science and forensic medicine. These studies use short DNA segments characterized by sequence repetition. Their relevance lies in the high variability of these patterns between individuals, which makes them ideal genetic markers for establishing biological relationships, especially in determining paternity.[4]

The methodology begins with the collection of DNA samples, typically through buccal swabs. DNA extraction is followed by STR amplification, specifically using PCR technology. Amplification allows for detailed analysis of repeat patterns present in an individual's DNA.[5]

For a paternity analysis, the STR profiles of the child and the alleged father are compared. Since STRs are inherited, a match on most of these markers indicates a high probability of paternity. These studies are notable for their high accuracy and reliability, and have become indispensable in legal cases such as paternity litigation and inheritance and custody decisions.[6]

Furthermore, the accuracy of these genetic tests has led to their application in other fields such as genealogy, evolutionary biology, and the identification of human remains in forensic investigations. The development and refinement of this technology continues, opening up new possibilities and ethical challenges in its application.[7]

Paternity testing is an important aspect of forensic genetics and has significant applications in both the legal and personal fields. Yes, the test is designed to determine whether a person is indeed the biological father of a child. Traditionally, paternity testing is performed after the child's birth, but with advances in genetics, prenatal paternity testing is now possible.[8]

Paternity determination is based on DNA analysis. Each person has their own unique profile. Unique genetics are the combination of DNA inherited from both parents. In a paternity test, specific regions of the DNA of the child, the alleged father, and the mother are compared. These regions, known as genetic markers, are highly variable between individuals and can provide clear evidence of the father-child relationship.[9]

The most common way to perform a paternity test is through a blood sample or a cheek swab. In the case of postnatal testing, samples are collected from both the child and the alleged father. Cheek swabs, in particular, are a noninvasive and easy method of obtaining DNA, as they only require rubbing a cotton swab on the inside of the cheek to collect cells.[10]

There are two main methods of prenatal paternity testing: DNA analysis. Free-flowing maternal and fetal blood during amniocentesis. The first is that the technology is non-invasive; procedures can be performed from the tenth week of pregnancy. The presence of fetal DNA fragments in the mother's blood reduces the risk to the fetus compared with invasive methods. However, this technique may have limitations in terms of accuracy and, in some cases, may be inconclusive.[11]

Amniocentesis, on the other hand, can give more accurate results, but it is only an invasive procedure and carries a small risk, such as premature birth or infection. During this procedure, a small amount of amniotic fluid is removed from the amniotic membrane. Fetal DNA analysis is performed in utero.[12]

Paternity testing has a number of applications. In the legal context, it can be used to resolve child custody and support cases, as well as in adoption and inheritance situations. In the personal context, it can provide clarity and resolve issues related to paternity that may be important to family dynamics and the emotional well-being of those involved.[13]

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However, these tests also raise ethical issues, especially without the consent of the parties involved. Furthermore, the results of the paternity test can have a significant emotional impact on couples and families. They should be handled with sensitivity and caution.[14]

In terms of further development, paternity testing technology may be continually evolving, becoming more accessible, less invasive, and more accurate. This may include the development of methods to detect paternity earlier in pregnancy that pose no risk to the fetus.[15]

In short, paternity testing plays a crucial role in multiple areas, from resolving legal disputes to supporting understanding of family dynamics. As technology advances, these tests become more sophisticated, providing valuable information safely and efficiently. However, it is essential to approach them with ethical considerations and sensitivity to the emotional impact they can have on the individuals and families involved.[16]

Paternity testing has advanced significantly in recent years, both in accuracy and in the variety of methods available. With the development of new technologies and techniques in genetics, paternity testing has become faster, more accessible, and more accurate. However, important ethical and legal considerations have also arisen associated with its use.

Regarding prenatal paternity testing, non-invasive methods are used. The analysis of cell-free fetal DNA circulating in the mother's blood is an important advance. These tests eliminate many of the risks associated with invasive methods such as amniocentesis, making them a safer option for pregnant women and their fetuses. Although they are safe and convenient, it is important to understand how accurate these tests are. This can be influenced by several different factors, such as the concentration of fetal DNA in the mother's blood, which can vary significantly between individuals and throughout the pregnancy.[17]

Postnatal paternity testing, which commonly involves taking blood samples or oral swabs, is generally more straightforward. These tests analyze genetic markers in DNA to determine the likelihood of a father-child relationship. Current technology allows for a high degree of accuracy, with most tests able to establish paternity with a probability of more than 99,9 %.[18]

The legal applications of paternity testing are broad and significant. In cases of custody, child support, or inheritance disputes, accurate paternity determination can be crucial. In the legal field, supply chain, sample certification, and laboratory testing are important aspects for ensuring the legal validity of the result.[19]

However, paternity testing also raises significant ethical issues. For example, performing paternity testing without parental consent or using such tests in unregulated contexts can have ethical and legal implications. Confidentiality and privacy are key concerns, especially in cases where test results may have significant emotional or social consequences.[20]

Publication of paternity test results, especially in certain circumstances. Sensitive or difficult family members can have a profound emotional impact on all concerned. This highlights the need for appropriate pre- and post-testing counseling so that individuals understand the potential impact and are supported in the decision-making process.[21]

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Another important consideration is access to and equity in paternity testing. While in some places these tests are readily available, in other regions they may be more difficult to obtain or expensive. This raises questions about equal access to important genetic services, especially in contexts where paternity testing may have significant legal or child support implications.[22]

From a scientific perspective, the field of forensic genetics involving parents is constantly evolving. Advances in gene sequencing and biotechnology are opening up new possibilities for more detailed and rapid genetic identification. These advances could result in more accurate testing and the ability to conduct more sophisticated analyses, such as determining paternity in situations with multiple possible fathers or when the alleged father is not present for testing.[23]

In the fields of public health and medicine, paternity testing can have significant implications for genetic screening and the detection of inherited genetic diseases. Knowing the exact paternity can be crucial for a child's medical history and for identifying potential genetic risks. This is especially relevant for diseases that have a known inheritance pattern and can be mitigated or managed with early intervention.[24]

In conclusion, this section states that paternity testing represents a powerful tool in modern genetics, with applications ranging from legal to personal and medical. As technology advances, these tests are likely to become more affordable and accurate. However, it is crucial that their use be accompanied by careful consideration of the ethical, legal, and emotional issues involved, ensuring that the rights and well-being of all affected are protected.[25]

METHODS

Medical documentary research follows a structured process that begins with the definition of clear objectives. The research question is tailored to the topic, and specialized databases such as PubMed, MEDLINE, Embase, Scopus, and Web of Science are used to gather up-to-date and reliable information. Specific search terms, synonyms, and Boolean operators are used to optimize the search.

The inclusion of systematic reviews and meta-analyses contributes to synthesizing the available evidence, offering a comprehensive overview of the scientific literature. Furthermore, Google Scholar is used to expand the search to include scientific articles, theses, and academic books, thus ensuring the quality and authenticity of the sources. This rigorous methodological approach guarantees exhaustive and evidence-based research.

This report was prepared through a comprehensive and critical desk review of the literature related to paternity testing using the PRISMA methodology. A systematic search of PubMed, Web of Science, and Google Scholar databases was conducted for publications from 2018 to 2023. The search terms used were "paternity testing," "Y chromosome mutations," "blood chimerism," "expression," and "tetragametic," most of which were combined to comparatively analyze treatment and follow-up outcomes. The procedure was performed independently by three researchers to avoid bias.

The inclusion criteria included studies presenting a comparison of signs and symptoms in clinical cases related to paternity, published in English. Conference abstracts, case reports, and articles not available in electronic format were excluded. Sources were searched in English using the metasearch engines of the selected scientific databases, using specific terms extracted from the health sciences descriptors (DeCS).

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DEVELOPMENT

The expected results of the following paternity test are to determine the probability that the alleged father is the true biological father of the child in question. The vast majority of paternity tests can confirm paternity with a probability greater than 99,9 %.

In a paternity analysis, the STR profiles of the child and the alleged father are compared. If a majority of the STRs analyzed match, this indicates a high probability of paternity. If there is no match, paternity can be ruled out.

It should be noted that the accuracy of paternity tests will be affected by many factors, such as the concentration of fetal DNA in the mother's blood, in the case of prenatal paternity tests. Furthermore, it is crucial that paternity tests be performed in a certified laboratory and that strict quality and confidentiality controls be followed.

In general, paternity test results can have significant legal, emotional, and family implications and should be handled with sensitivity and discretion.

PATERNITY TESTS

Biochemical and genetic bases

Paternity and kinship testing have important application value for resolving inheritance disputes, locating missing persons, and identifying disaster victims. Genetic markers used include microsatellites, single nucleotide variants (SNPs), and small insertion/deletion polymorphisms (InDels). Major systems, such as CODIS (13 STR loci) and the Extended European Standard Set (17 STR loci), have been widely used in paternity and kinship testing, along with SNPs, introduced into systems such as the SNPforID assay (52 loci) and the SNP Panel II (92 loci).[26]

Due to the binary nature of SNPs, their discriminatory power per locus is lower than that of STRs, which have more polymorphisms. Currently, SNPs are primarily considered as complements to STRs in paternity and kinship testing. This offers advantages such as a lower mutation rate, greater applicability to challenging samples, and more available loci. Furthermore, they are preferable in cases with degraded DNA, as they require shorter amplicons.[27]

DNA amplification (PCR) is another genetic method used for paternity testing, and is ideal because of the small amounts of material required to provide a suitable basis for DNA analysis. Since a minimal amount of material is required to perform a PCR test, the sample can be retested in another laboratory or at a future date. The availability of automated systems reduces the likelihood of contamination and increases the accuracy of fragment size determination.[28]

Epidemiology

Each year, nearly 300,000 paternity tests are performed in the United States to confirm or rule out a man's biological paternity of a child. Test results indicate inclusions in 72 % of cases, with notable variations across racial and ethnic categories. In this context, inclusions are as low as 67 % for African Americans and as high as 82 % for Native Americans.[29]

Paternal discrepancy occurs when a child is identified as having been biologically fathered by a man other than the alleged father. Studies have shown that the rate ranges from 0,8 % to 30 %.[30]

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Genetic analysis and its description, sample collection, main metabolites.
Multiple DNA tests are used for paternity analysis. The types of DNA that can be assessed are presented in the table below. The most common reference samples collected for this type of testing are blood, oral/buccal swabs, and/or plucked hair (head or pubic).[31]

Table 1 shows the types of DNA, their properties, advantages, and disadvantages. Nuclear DNA: in the nucleus of eukaryotic cells: genetic guide for function and development, hereditary transmission, coding for protein synthesis, and cellular regulation. mtDNA (mitochondrial DNA): present in mitochondria, is inherited exclusively from the mother and guides protein synthesis for energy production. Variations in it affect cellular metabolism. STRs of the Y chromosome: are specific repeated DNA sequences, inherited from father to son.

Tabla 1. Tipos de ADN, sus propiedades, ventajas y desventajas.

DNA type	Properties	Advantages	Disadvantages
Nuclear DNA	13 STR (microsatellite) markers were selected and validated. A 14th marker derived from the amelogenin gene was used to determine sex.	- Possibility of distinguishing genetic profiles with high precision. - Sex determination using the amelogenin marker. -Commercial kits available with different combinations of STRs.	- Exclusion of coding regions avoids ethical problems, but limits information. - Requires commercial kits for implementation.
mtDNA	Highly variable DNA in the D-loop region, whose variability comes from single base changes and length polymorphisms.	- Facilitated analysis of family relationships due to exclusive maternal origin. - Higher copy counts per cell allow for testing on small samples. - Possible extraction of hair, bones and strong teeth.	- Greater susceptibility to contamination compared to nuclear DNA. - Possible presence of heteroplasmy that affects the interpretation of profiles.
STRs of the Y chromosome	The use of the Y chromosome is recent, and has been validated for sexual assault crimes, allowing even contaminated samples to be distinguished.	- Highly useful in sexual assault crimes by allowing identification in the presence of female DNA. - Application in mass disasters or identification of missing persons with male DNA.	- Reduced discrimination power due to a single Y chromosome. - Need for multiple STRs to increase accuracy.

Fuente: Trent RJ,[29].

CLINICAL CASES

Table 2 presents clinical cases on paternity assessment. It is noted that standard methods may fail to detect cases of isodisomy or heterodisomy, which can lead to paternity claims despite genetic inconsistencies. In a complex scenario with multi-stage mutations in STR markers, forensic genomics emerges as a valuable option to reach definitive conclusions. However, the presence of mutations hampers clarity, as at least two STR mismatches are required to exclude a father-son relationship. In one specific case, paternity was established through HLA analysis, while other results showed uniparental maternal disomy.

Weak inheritance of hybrids and mosaics with cytogenetic trisomy further complicate interpretation. Although possible fathers were identified through the DNA database, exclusion of suspects was only achieved with additional testing, demonstrating the utility of kits such as PowerPlex 16 and Y-Filer in forensic analysis.

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Table 2. Compilation of clinical cases.

Author/Magazine/Year	Qualification	Aim	Recommendations	Methodology
Jianf Y et al.[33] Molecular Cytogenetics 2024	Discovery of maternal uniparental isodisomy of chromosome 6 by paternity testing: a case report	To contribute to the literature on UPD6, highlighting the exceptionality of the genetic condition and the normal phenotype of the patient.	They are not specified in the article.	Samples were analyzed using PowerPlex 16 and CS7.
Mansuet-Lupo et al.[34] Forensic Science International: Genetics 2009	A case of paternity with three genetic incompatibilities between father and son due to maternal uniparental disomy of chromosome 21 and a mutation on the Y chromosome	Describe a paternity test in which three apparent exclusions were observed on chromosome 21 and one at the chromosomal Y locus.	When considering paternity exclusions in genetic systems located on the same chromosome, the installation of extended typing programs is recommended.	EDTA-treated blood samples were examined. DNA was extracted using commercial kits, and amplification was performed using the Powerplex 16, Identifiler, and Humantype Chimera kits.
Tabrizi, Hejazi y Hosseini.[35] American Journal of Forensic Medicine and Pathology	An Unusual Case in Paternity Testing: Nineteen Autosomal Short Tandem Repeat Types and Twelve X-Chromosome Markers Could Not Clarify the Situation.	Present the case of two alleged related fathers.	Implement multiple genetic systems for the analysis of more loci.	Nineteen short tandem repeat markers located on autosomes were examined, as well as 12 X-chromosome markers.
Doniec et al. Genes.[36] 2021	Confirmation of Paternity despite Three Genetic Incompatibilities at Chromosome 2.	To describe a case of paternity confirmation despite three genetic incompatibilities on chromosome 2.	-	The sample was collected by oral swab.

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Yu et al.[37] Journal of Forensic Sciences. 2011	The Presence of Tetragametic Blood Chimerism Explains a Case of Questioned Paternity.	To present the clinical history of a 4-year-old infant with congenital tetragametic chimerism.	-	5ml blood samples were collected for serological studies from both adults and the child in additive-free and EDTA tubes. DNA: extracted by salt precipitation technique.
Barash et al.[38] Journal of Forensic Sciences. 2012	A search for obligatory paternal alleles in a DNA database to identify a suspected rapist in a fatherless paternity case.	To present the possibility of performing a database search to identify obligatory alleles in a case of paternity without a known father.	Finding a match should be considered only as preliminary evidence as the search leads to false positive results.	DNA sampling and profiling were performed using four fetal tissue samples. DNA was extracted using the Chelex method. DNA yields were estimated using real-time PCR and amplification reactions using PowerPlex 16 and two other systems.
González-Herrera et al.[39] International Journal of Legal Medicine 2020	A case of complex paternity with a four-step mutation in D22S1045, evaluating the hypothesis of the alleged father's brother	To address a case of complex paternity presenting a presumed four-step short tandem repeat (STR) mutation between the alleged father (AF) and the son.	Consider different genetic tools and mutation models in cases of complex paternity.	DNA samples, autosomal STR markers, mutation analysis at specific loci, Paternity Index analysis, inclusion of biallelic markers, and evaluation of paternity evidence.
Laron, et al.[40] Archives of Andrology. 1982	An Unusual Case in Paternity Testing: Nineteen Autosomal Short Tandem Repeat Types and Twelve X-Chromosome Markers Could Not Clarify the Situation.	Present the case of two alleged related fathers.	Implement multiple genetic systems for the analysis of more loci.	Nineteen short tandem repeat markers located on autosomes were examined, as well as 12 X-chromosome markers.

The biochemical genetic results. Due to complications of the UPD, chromosomal microarray testing was ordered to confirm the chromosomal composition, which revealed two extended contiguous regions of homozygosity spanning the entire short and long arms of chromosome 6. Apparent exclusions were evident at the STR (short tandem repeats) loci D21S11 and PENTA D, both located on chromosome 21, as well as at the Y-chromosomal locus DYS389II.

Case 1:
Mother HLA: A33, A-; B7, B53
F1301: 6, 14
D6S1043: 11, 13

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Girl HLA: A33, A-; B7, B-
F1301: 6
D6S1043: 11

Presumed father HLA: A33, A-; B7, B53
F1301: 6
D6S1043: 11

Twenty-one polymorphic loci were genotyped. Initially, the results excluded the presumed father due to genetic inconsistencies, but additional testing, including PowerPlex ESX, Fusion, and LC5, along with HLA testing, revealed maternal homozygosity on chromosome 6, with the following findings:

Case 2:
Mother D21S11: 28/31.2
PENTA D: 10
D21S2055: 16.1/19.1
DYS 389 II: -

Child D21S11: 28/31.2
PENTA D: 10
D21S2055: 16.1/19.1
DYS 389 II: 30

Alleged father D21S11: 29/32.2
PENTA D: 11/13
D21S2055: 19.1
DYS 389 II: 29

Inconsistencies were observed at the D21S2055 locus, suggesting a possible maternal UPD disomy of chromosome 21. Further analysis indicated that all alleles on chromosome 21 in the child were exclusively maternal in origin, suggesting UPD 21. Incompatibilities are highlighted in bold.

Case 3: Analyzing the locus D22S1045 we found for the presumed father 17, 17 (AF), the child 13, 15 and the mother 15, 15. With a paternity index of 1.089, which indicates a moderately high probability that the alleged father is the biological parent compared to a reference brother (AF brother).

Table 3 shows diverse clinical cases with varying levels of severity, inheritance patterns, and associated biochemical alterations, suggesting a wide range of genetic and hereditary conditions. It also includes non-hereditary conditions, highlighting the diversity of medical conditions represented in the table. The biochemical alterations include uniparental disomies, genetic mutations, and chromosomal abnormalities, reflecting the variety of genetic disorders addressed in the clinical cases presented. These cases also present asymptomatic or very mildly symptomatic at the time of the case review.

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Table 3. Clinical classification.

Clinical case	Clinical classification				Inheritance pattern	Biochemical alteration
	Asymptomatic	Light	Typical	Severe		
1	X	0	0	0	Isodisomy	UPD6
2	X	0	0	0	Heterodisomy	UPD21
3	X	0	0	0	0	4-step mutation at D22S1045.
4	X	0	0	0	0	Not applicable
5		X	0	0	Non-hereditary condition	47, XXY
6	X	0	0	0	Isodisomy	UPD2
7	X	0	0	0	0	Congenital tetragametic blood chimerism
8	0	0	0	0	0	Not applicable

Table 4 details clinical cases in children, specifically regarding sex, clinical description, symptoms, course, and biochemical data, along with references to relevant studies. These cases include situations such as possible maternal uniparental disomy, paternity testing, paternity exclusion, tetragametic chimerism, and DNA comparisons to determine paternity in a fetus. Each case presents unique genetic and medical challenges, highlighting the complexity and diversity of conditions affecting children and the importance of genetic analysis in clinical practice.

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Table 4. Summary of clinical cases in children.

Clinical case	Sex	Clinical description	Symptoms	Evolution	Biochemical data (genes)	Reference
1	Female	A woman was born at 32 weeks' gestation, birth weight in the 10th-25th percentile. Paternity testing was performed for legal reasons; the initial results appeared to exclude the alleged father. The patient was identified as homozygous for the maternal alleles at the three loci analyzed on chromosome 6. She was referred to genetics for possible maternal uniparental disomy (UPD).	10 months: Adequate development, weight and length in percentile <3. Head circumference in percentile 25. On physical examination: preauricular pits.	The patient was re-examined at 14 months, with normal development, asymptomatic and no findings on physical examination.	Genetic testing of chromosome 6: HLA Mother: A33, A-; B7, B53 Girl: A33, A-; B7, B- Alleged father: A23, A33; B35, B58 F13A01 Mother: 6, 14 Girl: 6 Father:7 D6S1043 Mother: 11, 13 Girl: 11 Father: 12,18	Kerr et al., 2018. [32]
2	Male	The patient's clinical characteristics were not specified, other than that he was asymptomatic.	Asymptomatic	It does not specify the clinical course of the patient, however, the sequence of tests used was the STR for paternity determination, followed by	D21S11 Child: 28/31.2 Mom: 28/31.2 Dad: 29/32.2 PENTA D Child: 10 Mom: 10 Dad: 11/13 D21S2055 Child: 16.1/19.1 Mom: 16.1/19.1 Dad: 19.1 DYS 389 II Child: 30 Mom: - Father: 29	Mansuet-Lupo et al., 2009. [34]

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4	Female	-	-	-	At each marker tested, the girl shared 1 allele with the mother and 1 allele with alleged fathers 1 and 2. One exclusion was found at the FGA marker between alleged father 2 and the girl, but it was not definitive to exclude one of the parents.	Tabrizi, Hejazi y Marzieh, 2013. [35]
6	Male	-	-	-	Analysis of 17 additional STR, in-del, and SNP loci located on both arms of chromosome 2 allowed exclusion of the segmental mUDP and confirmed the complete mUDP. Furthermore, the region of two probable recombination events was narrowed down.	Doniec et al., 2021. [36]
7	Male	Hip dysplasia with AB blood type, with atypical red blood cell agglutination ("mixed field agglutination") which led to the study of the parents' blood types: AB and O to determine their ABO type. Background: The boy was the twin of a girl who died at birth due to asphyxia.	Hip dysplasia	The study of the AB and O types suggested a possible non-paternity, with the possible explanation that the child had chimerism or mosaicism.	Molecular cloning and genotyping of its ABO locus: 2 heterozygous genotypes: A102/O01 and B101/O01. The findings indicate that the child had tetragametic chimerism.	Yu et al., 2011. [37]

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8	Male fetus	Mother of fetus reports rape 12 weeks ago and seeks abortion.	-	An abortion is performed, and due to repeated reports of rape in the area, it is decided to compare the fetus's DNA with that in a mandatory gene database.	FGA Fetus: 21.26 Mother: 20.26 Suspect 1: 21,24 Suspect 2: 21,22 D18S51 Fetus: 12.16 M: 12.17 S1: 16,17 S2: 16,20 D19S433 F: 15,15.2 M: 13.15 S1: 14,15.2 S2: 13,15.2	Barash et al., 2012. [38]

Table 5 details the treatments associated with the aforementioned clinical cases. It shows that, in most cases, the therapeutic approach focused on monitoring and evaluating symptoms and genetic findings, with a generally favorable prognosis. In one case, the patient's hormonal treatment is mentioned. It is also noted that in one case, surgical treatment was performed to treat hip dysplasia, while in another case, due to the aborted fetus, no treatment was provided.

Table 5. Treatments associated with the aforementioned cases.

Case	Treatment
1	Follow-up was performed at 4 months to evaluate new symptoms and possible findings of an autosomal recessive condition. Overall, the prognosis was good.
2	The therapeutic approach applied to the patient is not mentioned. The article focused on the results of genetic testing and DNA analysis, particularly in relation to UPD and the Y chromosome mutation.
3	The treatment given to the patient is not specified; the study focuses on genetic evaluations.
4	Not specified.
5	No genetic treatment was specified. However, the patient received hormonal treatment from age 17 with a long-acting testosterone preparation at a dose of 250 mg IM once every 3 weeks, which was discontinued within the following 6 months.
6	Not specified
7	Genetic treatments are not performed. Surgical treatment is performed for hip dysplasia.
8	It is not performed since it is a case of an aborted fetus.

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DISCUSSION

From an ethical perspective, it is crucial to ensure informed consent from all parties involved in paternity testing, as well as to preserve confidentiality and privacy. Laboratory certification and strict quality controls are imperative to maintain the integrity of the process.[40]

Maternal uniparental isodisomy, in which both copies of chromosome 6 originate exclusively from the mother, poses additional challenges in the interpretation of paternity test results. This genetic condition can affect inheritance and expression, highlighting the importance of not only addressing paternity but also understanding the specific genetic consequences associated with this phenomenon. From a legal perspective, paternity testing, including those that address the complexities of UDP, is relevant to child support, guardianship, and inheritance cases. Chain of custody and laboratory accreditation remain critical to support the validity of results in legal settings and provide additional safeguards in unusual genetic circumstances.

From an emotional and social perspective, test results can have a significant impact on family interaction, highlighting the importance of counseling both before and after the test. It is understood that these tests can affect the identity and emotional well-being of those who participate in them.[41]

DNA paternity testing not only involves scientific and genetic aspects but also crucial ethical and legal considerations. It is essential that these analyses be conducted ethically, respecting the rights and privacy of individuals, and that they comply with legal requirements for the results to be valid and useful in judicial contexts. Integrating sound ethical and legal protocols into paternity testing ensures the reliability and validity of the results, as well as respect for the rights of all parties involved.[42]

CONCLUSIONS

The analysis of the information and clinical cases presents a clear view on the complexities of paternity testing, highlighting the importance of advanced methodologies in forensic genetics. It is concluded that extended typing is essential for dealing with complex paternity cases. The findings underscore the need to adopt extended genetic systems and diverse mutational models to improve the accuracy of results. The inclusion of multiple markers and comprehensive mutation analysis is established as a crucial practice to obtain reliable conclusions in difficult scenarios. The application of advanced genetic tools has proven to be effective in resolving complex mutations in STR markers, representing a promising approach for complicated paternity cases. It also highlights limitations in standard techniques, which may miss situations such as isodisomy, reinforcing the need for more innovative methods. As ethical, legal, and emotional challenges are explored, the centrality of advanced genetic testing in paternity determination is reaffirmed, as is the need for an ethical approach to handling the results.

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