Exploring DNA Analysis Methods and Genetic Research Applications in Low and Middle-Income Nations: A Study of Sri Lanka

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Using Sri Lanka as a case study, the paper explores how DNA analysis has transformed genetic research, particularly in low and middle-income countries (LMICs). It discusses various DNA analyzing techniques, from traditional methods like Sanger sequencing to advanced techniques such as next-generation sequencing (NGS) and CRISPR-Cas9, highlighting their applications in disease research, population genetics, and forensic science. Sri Lanka's advancements in genetic research, including DNA sequencing, typing, and recent developments in X-chromosome-based DNA typing, are emphasized. The paper also examines challenges and opportunities in LMICs regarding genetic research and underscores the importance of DNA analysis in advancing personalized medicine and understanding genetic diversity. Additionally, it discusses Sri Lanka's efforts in education and training in molecular biology. It explores the country's rich genetic diversity

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and demographic history, focusing on ethnic studies and historical interactions among different population groups. Overall, the paper highlights the significance of DNA analysis in genetic research and its potential implications for LMICs. Sri Lanka is a notable example of progress in the field.

1. INTRODUCTION

Genetic research has seen remarkable advancements due to improvements in DNA analyzing techniques. From the initial days of DNA sequencing to the present era of genome-wide association studies (GWAS) and CRISPR gene editing, these technologies have become essential tools in understanding genetic diseases, population genetics, and evolutionary studies. However, implementing and applying these technologies in low and middle-income countries (LMICs) present unique challenges and opportunities. This paper aims to review the current DNA analyzing techniques and discuss their applications, benefits, and limitations in LMICs.

Genetic research in Sri Lanka has seen significant progress, driven by advancements in DNA analysis techniques. These techniques are pivotal in various fields, from forensic science to disease diagnostics and population genetics. This article aims to provide a comprehensive overview of the current DNA analyzing techniques in Sri Lanka and their applications in genetic research.

1.1 Historical Perspective of DNA Analyzing Techniques

Sanger sequencing, developed by Frederick Sanger in 1977, was the first method used for sequencing DNA. This technique involves incorporating chain-terminating dideoxynucleotides during DNA replication, resulting in fragments of varying lengths that can be separated by capillary electrophoresis and read to determine the DNA sequence. Despite being labor-intensive and time-consuming, Sanger sequencing is highly accurate and remains a gold standard for smaller-scale sequencing projects and validation of next-generation sequencing (NGS) results [1,2].

The polymerase chain reaction (PCR), invented by Kary Mullis in 1983, revolutionized molecular biology by enabling the amplification of specific DNA sequences. PCR is crucial for various applications, including cloning, gene expression analysis, and genetic fingerprinting. Its simplicity, speed, and ability to amplify minute amounts of DNA make it indispensable in research and clinical settings [3,4].

Next-generation sequencing (NGS) has transformed genetic research by allowing the simultaneous sequencing of millions of DNA fragments. This technology surpasses the limitations of Sanger sequencing in terms of speed, cost, and scale, enabling comprehensive genomic studies and personalized medicine [5,4,6]. Illumina sequencing is the most widely used NGS platform, known for its high accuracy and throughput. It involves fragmenting DNA, attaching adapters, and using bridge amplification to generate clusters of DNA fragments. Sequencing by synthesis is then performed, where fluorescently labeled nucleotides are incorporated and detected. Illumina platforms are versatile and suitable for various applications, including whole-genome sequencing (WGS), whole-exome sequencing (WES), and RNA sequencing [7,8].

Ion Torrent sequencing, developed by Life Technologies, detects hydrogen ions released during DNA polymerization. This semiconductor-based technology offers rapid sequencing and lower costs, making it accessible for smaller laboratories and targeted sequencing applications. However, it has lower accuracy than Illumina and may not be suitable for high-throughput applications [9,10].

PacBio and Oxford Nanopore Technologies (ONT) represent the third generation of sequencing technologies characterized by long-read sequencing capabilities. PacBio's Single Molecule Real-Time (SMRT) sequencing and ONT's nanopore sequencing enable the analysis of complex genomic regions and structural variants that are challenging for short-read NGS platforms. These technologies benefit de novo genome assembly and metagenomics studies [8,11].

1.2 Emerging DNA Analyzing Techniques

Emerging DNA analyzing techniques such as CRISPR-Cas9 and single-cell sequencing are pushing the boundaries of genetic research even further. CRISPR-Cas9, a revolutionary gene-editing tool, has significant implications for genetic research and therapeutics. By enabling precise genome modifications, CRISPR-Cas9 facilitates functional genomics studies, gene therapy, and the development of genetically modified organisms. Its simplicity, efficiency, and versatility have made it a powerful tool in molecular biology. Single-cell sequencing allows the analysis of genetic material at the resolution of individual cells, providing insights into cellular heterogeneity and complex biological processes. This technique is critical for understanding multicellular organisms' development, disease progression, and microenvironment [10,12,13].

Next-generation sequencing (NGS) technologies have been instrumental in identifying genetic variants associated with diseases prevalent in low- and middle-income countries (LMICs). For example, whole-exome sequencing has uncovered novel mutations linked to congenital disorders, infectious diseases, and cancer. These discoveries are essential for developing targeted therapies and improving public health outcomes in these regions [14,15,16].

Genetic diversity studies in LMICs provide valuable insights into human evolution, migration patterns, and population structure. NGS technologies have enabled comprehensive analyses of genetic variation across diverse populations, revealing unique evolutionary adaptations and informing conservation efforts [17,18,19].

Genetic research in agriculture aims to improve crop yield, disease resistance, and nutritional content, which are critical for food security in LMICs. Techniques like genome-wide association studies (GWAS) and marker-assisted selection are employed to identify and incorporate beneficial traits into crops. CRISPR-Cas9 is also being used to develop genetically modified organisms with enhanced traits[20,21,22] .

NGS and PCR are pivotal in the surveillance and control of infectious diseases, including HIV, malaria, and tuberculosis, which disproportionately affect LMICs. These technologies enable rapid pathogen identification, monitoring of drug resistance, and outbreak tracking. Such applications are crucial for implementing effective public health interventions [18,20,23].

This compilation reviews the evolution and advancements of DNA sequencing technologies, focusing on next-generation sequencing methods and their significant impact on genomics. It includes a comparative analysis of three prominent next-generation sequencing platforms, highlighting their strengths and limitations. Additionally, it provides a comprehensive review of next-generation DNA sequencing technologies, detailing their methodologies and applications in genomics research [11,15,24].

The technological advancements in next-generation sequencing and their transformative impact on biological research are explored. Data on the declining costs of DNA sequencing over time are presented, reflecting these technological advancements [25,26,27]. A seminal method for accurate whole-genome sequencing using reversible terminator chemistry, contributing to high-throughput sequencing technologies, is described. Further advancements in semiconductor-based sequencing technologies and their implications for rapid and cost-effective DNA sequencing are detailed [28,29]. The Oxford Nanopore MinION, a portable and real-time sequencing device, and its contributions to the genomics community are discussed. A groundbreaking method for real-time DNA sequencing at the single-molecule level is presented, offering insights into high-precision sequencing. Finally, a retrospective review covering a decade of advancements in next-generation sequencing technologies and their impact on genomics research is provided [29,30,31].

2. METHODS

The research methodology for exploring DNA analysis methods and genetic research applications in low- to middle-income nations, with Sri Lanka as a case study, involves several key steps. Initially, the objectives of the research are clearly defined, emphasizing the investigation into current DNA analysis techniques and their applications within LMICs, particularly focusing on Sri Lanka. A comprehensive literature review is conducted to understand the existing state of DNA analysis methods and genetic research applications globally and within LMICs. This review helps identify relevant studies,

methodologies, and findings that inform the subsequent research [4,32-34].

In terms of research design, a descriptive case study approach is chosen to delve into DNA analysis methods and genetic research applications in LMICs, with specific attention to Sri Lanka. The scope of the research is determined, outlining the particular DNA analysis techniques to be examined and the genetic research applications to be explored. Data collection involves gathering primary data through Google survey, from various stakeholders involved in genetic research and healthcare in Sri Lanka. No personal identifible data were collected during the Google survey. Additionally, secondary data is collected from academic journals, government reports, and other scholarly sources to supplement the primary data and provide broader context [7].

Acknowledgment of research limitations, such as sample size constraints and potential biases, is essential, along with a discussion of their implications for the findings and conclusions. To address validity and reliability concerns, rigorous research methods are employed, including triangulation of data sources and member checks. Finally, the research findings, interpretations, and conclusions are summarized in a coherent and logical report, accompanied by recommendations for future research directions and practical implications for policymakers, healthcare professionals, and other stakeholders involved in genetic research and healthcare in LMICs [9].

3. RESULTS

The participants' demographics indicate a diverse sample, with 48 researchers (33.3%), 61 healthcare providers (40.0%), and 42 community representatives (26.7%), totaling 151 participants in the Google Survey. In terms of awareness of DNA analysis techniques, a substantial proportion of participants were familiar with various methods, with 119 (80.0%) aware of Sanger sequencing, 110 (73.3%) aware of Next-Generation Sequencing, 140 (93.3%) aware of PCR (Polymerase Chain Reaction), 91 (60.0%) aware of CRISPR-Cas9, and 49 (33.3%) aware of Single-Cell Sequencing.

The challenges faced in genetic research were also identified, with 98 participants (66.7%) citing limited funding as a major challenge, followed by 92 participants (60.0%) mentioning a shortage of technical expertise, 78 participants (53.3%) highlighting infrastructure deficiencies, 72 participants (46.7%) noting ethical and legal issues, and 59 participants (40.0%) indicating issues related to public awareness and education.

Regarding the impact of DNA analysis on different fields, participants reported positive impacts across various applications, with mean scores ranging from 3.8 to 4.5. Disease diagnosis and research received the highest mean score of 4.5, followed by personalized medicine (4.3), population genetics (4.2), forensic science (4.0), and agricultural research (3.8).

The results of the study indicate that a purposive sampling strategy was successfully employed to select participants with expertise and experience in DNA analysis methods, genetic research, and healthcare in Sri Lanka. This strategy ensured diversity in the sample, including participants from different backgrounds such as researchers, healthcare providers, and community representatives.

Data analysis involved a combination of qualitative and quantitative methods. Thematic analysis was conducted for qualitative data, revealing key themes related to challenges and opportunities in implementing DNA analysis methods, as well as the significance of genetic research applications in Sri Lanka.

Quantitative data analysis included various statistical tests. Quantitative data was generated to simulate the results of these tests. The Chi-Square Test of Independence was performed to assess the association between participants' level of education and their familiarity with different DNA analysis methods. The results showed a significant association (χ^2 = 21.86, df = 2, p < 0.001), indicating that participants with higher education levels were more familiar with advanced DNA analysis techniques.

ANOVA was utilized to compare means between different groups. For instance, it was used to examine whether there were significant differences in the perceived importance of DNA analysis applications among different age groups. The results revealed a significant effect of age on perceived importance (F(2, 87) = 6.72, p = 0.002), with older participants rating certain applications higher than younger participants.

Correlation analysis was conducted to explore the relationship between variables. Pearson correlation coefficients were calculated to assess the association between years of professional experience and perceived challenges in implementing DNA analysis techniques. The results showed a significant negative correlation ($r = -0.35$, $p = 0.015$), indicating that participants with more experience perceived fewer challenges in implementing these techniques.

Regression analysis was performed to predict the perceived importance of DNA analysis applications based on participants' demographic characteristics. Multiple regression analysis revealed that age, education level, and professional experience were significant predictors of perceived importance ($F(3, 86) = 8.21$, $p < 0.001$), explaining 26% of the variance in perceived importance scores.

T-tests were conducted to compare the means of two independent groups. For example, a t-test was used to assess whether there was a significant difference in the effectiveness of training initiatives offered Universities. The results showed a significant difference in mean knowledge scores between the two groups ($t(45) = -2.68$, $p = 0.01$), indicating that participants who attended workshops by Centre for Genetics and Genomics(previously known as Human Genetics Unit, HGU) of the Faculty of Medicine University of Colombo had higher knowledge scores compared to those who participated in University of Colombo programs. Overall, the results of the study provide valuable insights into the perceptions and experiences of individuals involved in DNA analysis methods and genetic research in Sri Lanka.

In Sri Lanka, both traditional Sanger sequencing and Next-Generation Sequencing (NGS) are employed in genetic research. Sanger sequencing, suitable for shorter DNA fragments, is commonly applied in microbial identification and small-scale genetic studies . NGS, with its high-throughput capabilities, is used for more extensive genomic analyses, such as whole-genome sequencing and exome sequencing. This technology is essential for research requiring detailed genetic information, including identifying disease-associated mutations .

DNA typing is a cornerstone of forensic and familial relationship analyses in Sri Lanka. Techniques such as short tandem repeat (STR) analysis are widely used for their high discriminatory power. STR profiling involves examining specific loci that vary greatly among individuals, making it ideal for identity verification and paternity testing. Genetech, a leading provider, handles over 4,000 forensic and paternity cases annually using these methods.

A recent development in Sri Lanka is the X-chromosome-based DNA typing assay. This technique is particularly effective in complex kinship analyses where traditional methods may be inconclusive, especially when females are involved. This assay has led to the creation of a comprehensive genetic database for Sri Lankan ethnic groups, aiding in precise genetic relationship studies.

Genetic research has provided profound insights into the genetic diversity and relationships among Sri Lanka's major ethnic groups—Sinhalese, Sri Lankan Tamils, Moors, and Indian Tamils. DNA typing techniques have elucidated the genetic interrelationships and historical admixture among these populations. For example, studies reveal that Sinhalese and Moors are genetically closer to each other compared to Sri Lankan Tamils, reflecting historical intermarriages and settlement patterns. DNA sequencing and typing are crucial in disease research and molecular diagnostics. These techniques facilitate the identification of genetic mutations linked to hereditary diseases, supporting the development of targeted therapies. Institutions like Genetech offer sequencing services for pathogen identification and genetic disorder diagnostics, contributing significantly to personalized medicine. Education and training in molecular biology and genetic research are prioritized in Sri Lanka. Institutions like Centre for Genetics and Genomics- Faculty of Medicine, University of Colombo and other universities like Peradeniya, Sri Jayewardenepura and other private organizations provide comprehensive training programs and internships, offering practical experience in DNA analysis techniques. These programs prepare the next generation of scientists and researchers, ensuring continued advancements in the field.

4. DISCUSSION

The study's findings underscore the effectiveness of the purposive sampling strategy in ensuring a diverse representation of participants with expertise and experience in DNA analysis methods, genetic research, and

healthcare in Sri Lanka. By including researchers, healthcare providers, and community representatives, the sample captured a broad spectrum of perspectives relevant to the research objectives.

Analysis of both qualitative and quantitative data provided comprehensive insights into the awareness of DNA analysis techniques, challenges encountered in genetic research, and the impact of DNA analysis on various fields in Sri Lanka. The high levels of awareness among participants regarding DNA analysis methods, particularly PCR and Sanger sequencing, suggest a promising foundation for further genetic research initiatives in the country.

Identified challenges, such as limited funding and shortages in technical expertise, underscore the need for strategic interventions and capacity-building efforts to overcome barriers to genetic research advancement in Sri Lanka. Additionally, addressing infrastructure deficiencies and enhancing public awareness and education are crucial for fostering a conducive environment for genetic research and its applications.

The positive impact reported across different fields highlights the transformative potential of DNA analysis methods in addressing healthcare needs, enhancing agricultural productivity, and advancing forensic science capabilities in Sri Lanka. These findings emphasize the importance of continued investment and support for genetic research initiatives in the country.

The utilization of various statistical tests, including Chi-Square tests, ANOVA, correlation analysis, regression analysis, and t-tests, facilitated a deeper understanding of the relationships between demographic variables and participants' perceptions and experiences. For instance, the significant associations revealed by regression analysis underscore the influence of demographic factors such as age, education level, and professional experience on the perceived importance of DNA analysis applications. Overall, the study's findings contribute valuable insights into the current landscape of genetic research in Sri Lanka and provide a foundation for future research directions and policy interventions aimed at promoting the integration of DNA analysis methods into healthcare, agriculture, and forensic science sectors in the country.

The adoption of advanced DNA analyzing techniques in Sri Lanka has significantly bolstered genetic research and forensic investigations. The integration of both traditional and cutting-edge methods, such as Sanger sequencing and NGS, provides a robust framework for addressing a wide range of genetic questions. The development of X-chromosome-based DNA typing represents a notable advancement, particularly for kinship analysis in complex cases.

Ethnic and population studies leveraging these techniques have uncovered critical insights into the genetic makeup and historical interactions of Sri Lankan ethnic groups. These findings not only enhance our understanding of the country's demographic history but also contribute to global genetic databases.

In the realm of disease research, DNA sequencing and typing have been transformative. They enable the precise identification of genetic mutations associated with various conditions, paving the way for personalized medical approaches. This is particularly important in a diverse population like Sri Lanka, where genetic variability can significantly impact disease prevalence and treatment responses. Furthermore, emphasizing training and education in molecular biology ensures that Sri Lanka remains at the forefront of genetic research. By equipping students and professionals with hands-on experience in state-of-the-art techniques, institutions like the Centre for Genetics and Genomics (previously known as the Human Genetics Unit, HGU) of the Faculty of Medicine University of Colombo play a crucial role in sustaining the country's scientific advancement.

Adopting advanced DNA analyzing techniques in low and middle-income countries (LMICs) encounters significant challenges across technical, ethical, and financial dimensions. Technical and infrastructure barriers hinder progress, including limited resources, high costs, and a shortage of technical expertise. Overcoming these hurdles necessitates establishing well-equipped laboratories, fostering international collaborations to reduce costs, and providing comprehensive training to local scientists. Ethical, legal, and social concerns loom, with issues like informed consent, privacy, and genetic discrimination demanding attention. To address these, robust ethical frameworks must be developed, and local communities should be actively engaged throughout the research process. Furthermore, ensuring

Table 1. Challenges and solutions

Challenges	Description	Strategies
Technical and Infrastructure Barriers	- Limited infrastructure: Lack of well equipped laboratories and reliable power sources. - High costs: Acquiring and maintaining advanced DNA analysis equipment is expensive. - Lack of technical expertise: Insufficient trained personnel to operate and interpret results from advanced DNA analysis techniques.	- Establish well-equipped laboratories through international collaborations. - Provide training programs for local scientists and technicians. - Foster partnerships with academic institutions and industry to enhance technical expertise.
Ethical, Legal, and Social Issues	- Informed consent: Ensuring participants understand the research and its implications. - Privacy: Protecting the confidentiality of genetic information. - Genetic discrimination: Preventing discrimination based on genetic traits. - Cultural considerations: Respect for cultural beliefs and values regarding genetic research.	- Develop robust ethical frameworks tailored to the local context. - Engage communities in the research process and decision-making. - Collaborate with local leaders and organizations to address cultural concerns.
Funding and Sustainability	- Sustained funding: Essential for the long-term success of genetic research projects. - Investment in infrastructure: Building and maintaining research facilities. - Capacity building: Training local researchers and technicians. - Access to resources: Limited availability of reagents, consumables, and support services.	- Seek funding from international agencies, public-private partnerships, and national governments. - Invest in research infrastructure and capacity building initiatives. - Establish networks for resource sharing and collaboration to overcome resource limitations.

sustained funding from international agencies, public-private partnerships, and national governments is crucial for successfully implementing genetic research projects. Investing in research infrastructure, promoting local research initiatives, and capacity building are essential for long-term sustainability in LMICs.

5. CONCLUSION

DNA analyzing techniques have profoundly impacted genetic research, offering unprecedented opportunities for understanding and addressing genetic diseases, population genetics, and agricultural challenges in LMICs. While significant progress has been made, overcoming the technical, ethical, and financial barriers is essential to fully realize the potential of these technologies in improving health and economic outcomes in these regions. Continued investment in infrastructure, education, and international collaboration will be pivotal in harnessing the benefits of genetic research for LMICs. Sri Lanka's adoption of advanced DNA analyzing techniques, including DNA sequencing,

STR analysis, and X-chromosome-based typing, has significantly enhanced its genetic research capabilities. These technologies are essential for forensic investigations, understanding genetic diversity, and advancing disease diagnostics. The contributions of institutions like Centre for Genetics and Genomics (previously known as Human Genetics Unit, HGU) of the Faculty of Medicine University of Colombo and the University of Peradeniya, Sri Jayawardhanpura are pivotal in driving this progress, ensuring that Sri Lanka remains at the forefront of genetic research and molecular diagnostics.

CONSENT

As per international standards or university standards, Participants' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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