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Research Article

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Paediatric Genomic Medicine: Facilitators, Barriers and Implementation Strategies for Whole Exome Sequencing (WES) Adoption at a Malaysian Tertiary Teaching Hospital

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ABSTRACT

Next-generation sequencing incorporating whole exome sequencing (WES) is still a relatively new diagnostic test in Malaysian paediatric clinical medicine, having been adopted less than a decade ago. However, how Malaysian paediatricians and medical officers perceive WES remains largely unexplored. This study aims to address this gap. Semi-structured interviews were conducted for 12 participants, including 6 paediatricians with ongoing or completed subspecialty training, inclusive of fellowship programmes and 6 paediatric medical officers in their third and fourth year of their postgraduate paediatric master's study. Four themes were identified via reflexive thematic analysis of the transcribed data. (1) In the perception of WES, all twelve participants acknowledged the significance of precision medicine and the role of WES as a diagnostic tool. (2) In the perceived facilitators, eight participants noted that WES assisted in family planning and prenatal counselling, while half highlighted its good diagnostic yield. (3) In the perceived barriers, all participants mentioned the financial aspect and the result interpretation, while half emphasised limited accessibility to WES services. (4) In the proposed strategies for WES implementation, ten participants highlighted financial assistance, while nine participants suggested educating policymakers and healthcare providers. Two participants suggested having more local labs, while half mentioned having a dedicated in-house genetic team and multidisciplinary teams. This study outlines the current status of WES implementation at Hospital TABTAR and recommends policy changes to enhance WES in Malaysian hospitals. Future research should include diverse participants from other Malaysian tertiary teaching hospitals to better understand WES as a diagnostic tool.

Keywords: Whole Exome Sequencing, Paediatric, Perceptions, Reflexive Thematic Analysis, Perceived Facilitators And Barriers

Introduction

In all viable births, around 2 to 3% have been presented to be affected with paediatric genetic diseases (PGDs) [1]. There are more than 7,000 distinct PGDs, and whilst respectively they are rare, occurring in fewer than 1 in 2,000 individuals, altogether more than 350 million people from all over the world are affected [1]. Although PGDs have over 7,000, at best, 5% of treatments are accessible for these diseases. Genetic conditions are the dominant cause of death in infants as well as children in industrialised nations [2].

Medical genetic services had been integrated into Malaysian healthcare around a decade ago. From this time on, the genetic services were made better with accessibility of genetic counselling, testing and diagnosis. The expansion in the funds for genetic services and Clinical Genetics, acknowledged as a subspeciality, promotes the rise of genetic testing in Malaysia. The diagnosis of rare genetic conditions has been revolutionised by technologies of next-generation sequencing (NGS), incorporating whole exome sequencing (WES), which is getting more accessible as clinical tests [2].

WES is the targeted sequencing of almost every protein-coding region of the genome.

Protein-coding variants that are either hereditary or acquired are regarded as the major part of disease-causing variants,

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representing more than 60% of all established causative genomic variation. Generally, a hybridisation capture or multiplex primer-based amplification is either utilised to construct libraries of exonic sequences that can be mapped to the reference genome to search for variants. The ampleness of protein-coding genes as opposed to other regions in the genome, WES utilised well-sequenced and mapped areas of the genomes via in silico conjuncture of protein function.

Important scientific findings and technology evolution guided by the promising completion of the Human Genome Project, whereby the entire human genome has been sequenced, facilitate the introduction of the field of personalised medicine. The genomic advancement lays the foundation for further individualised, predictive, and pre-emptive medicine approaches, essentially reforming the way we diagnose and treat patients (NHS England 2017). Precision medicine, according to the National Institutes of Health of the United States (2018), is interpreted as a medicine route towards prevention of disease, diagnosis and treatment whereby it involves a patient's genetic code, environment and lifestyle specifics.

Materials and Methods

Study Design and Participants

This research study utilised an exploratory qualitative design, grounded in an interpretivist paradigm, aimed towards fostering an in-depth understanding of participants' subjective meaning-making, thoughts, experiences, interpretations, and perceptions of whole exome sequencing. The researchers' worldview aligned with the interpretivist outlooks, which ratified that there were multiple realities, and that knowledge was established through social interactions and individual interpretations. The study was conducted based on semi-structured, in-depth one-to-one interviews. The length of the interview varied, with the minimum duration being 20 minutes, while the maximum duration was 58 minutes. The interviews were conducted in English and audio recorded with consent from the participants and saved onto a password-protected cloud.

Before the interview took place, each participant who was purposively selected was invited via email. Participant information sheet (PIS) will be included in the invitation email. They will be given time to read and ask questions through the email exchange. If they agreed to volunteer to participate in the research, a consent form will be provided in the follow-up email. Their consent will be obtained through their digital signature. A copy of the signed form will be saved in the password-protected cloud as proof that they consented to participate in the research. A time, date and Zoom link for the online interview were set for each participant. The primary researcher collected the signed consent form and conducted the interviews for study participants. The figure below shows the standard protocol flowchart of the study.

Inclusion Criteria

Eligible participants were all general paediatricians and paediatricians with ongoing or completed subspecialty training, inclusive of fellowship programmes. Included participants were also paediatric medical officers at least in their third and fourth year of their postgraduate paediatric master's study on campus.

Exclusion Criteria

Selected participants who were ineligible were paediatric medical officers in their first and second year of their postgraduate paediatric master's study, and participants who had not consented to participate in the study.

Selection of Participants

Purposive sampling was employed in this qualitative study to recruit participants who had adequate knowledge about WES and had experience in utilising WES in their current practice. This approach ensured that the selected participants based on the inclusion criteria were appropriate and aligned with the study's objective. Based on Kelly (2010), purposive sampling was utilised to choose participants who were most presumably to yield appropriate and rich data. The participants were identified from the professional networks and official website of the Department of Paediatrics at Universiti Kebangsaan Malaysia (UKM).

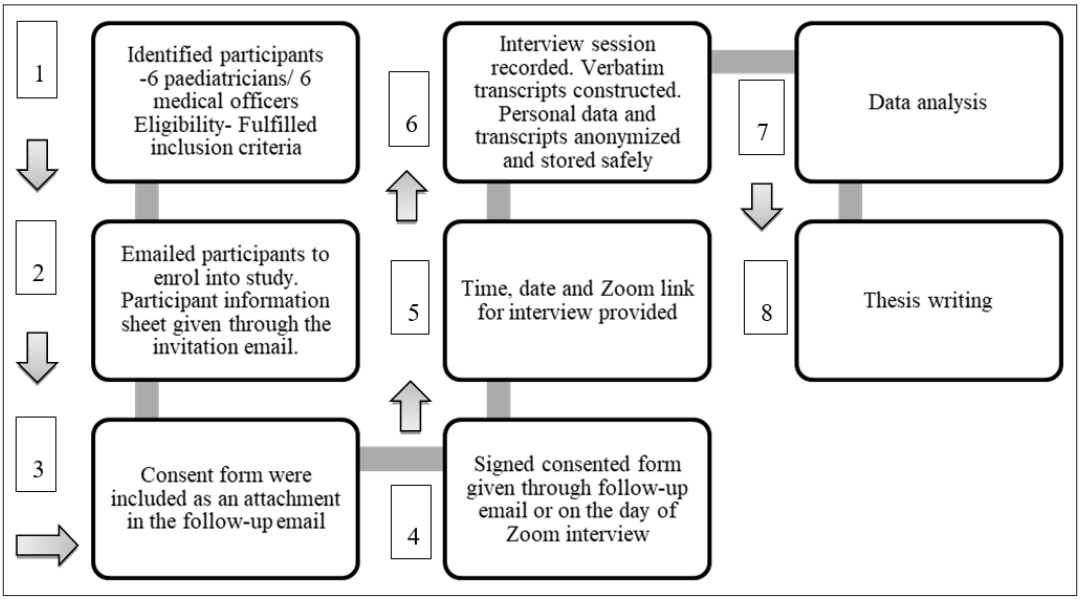

Figure 1: Standard Protocol Flowchart

Sample Size

A total of 12 purposively selected participants, which included 6 paediatricians with ongoing or completed subspecialty training, inclusive of fellowship programmes and 6 paediatric medical officers at least third and fourth years of their postgraduate paediatric residency. Guest et al. revealed that in homogeneous studies using purposeful sampling, like many qualitative studies, a minimum of 12 interviews should be enough to achieve data saturation [3].

Interview Guide

In-depth, semi-structured interviews were conducted using an interview guide. Having a prepared interview guide benefited an interviewer in several ways. Aiding the interviewer to focus on the important topics that needed to be covered during the interview and tailoring questions to the interview context or situation and study participants [4,5]. Moreover, keeping the interview session organised through marking the questions as addressed to prevent any repetition and ensuring all the participants received the same questions devised by the interviewer. The interview guide (Appendix 1) was constructed by the researchers based on the research objectives and research questions. The interview guide incorporated three main components, which were perceptions on the understanding and importance of WES as a tool for investigating paediatric genetic conditions, perceived facilitators and barriers to perform WES in a tertiary paediatric teaching hospital and proposed strategies for WES implementation as an investigative tool for paediatric genetic conditions.

Data Collection

Personal information data collected included their role, subspeciality and years of medical practice for descriptive data analysis. All online interviews were audio recorded through the Zoom platform and transcribed verbatim by the primary researcher. Once the interview transcripts were generated, it was reviewed and carefully reread for verification and accuracy [6]. The audio recordings were deleted once verified. To ensure confidentiality, the transcripts were pseudonymised by labelling e.g. "Participant 1". Personal information data and interview transcripts that were anonymised were stored in the password-protected Google Cloud UKM drive and made strictly accessible only to researchers.

Data Analysis

Interview data were analysed on the basis of a constructivist approach, perceiving that reality is subjective, owing to individual perspectives of participants involved in the study and allowing for various interpretations. ATLAS.ti (Scientific Software Development GmbH, version 9) was used to analyse the qualitative data. Six steps of reflexive thematic analysis were employed [6]. Thematic analysis in this study established and interpreted patterns or themes in the qualitative data set. The first step involved the primary researcher being familiarised with the transcript data, and preliminary themes were identified through delving into the participant's perspective of WES thoroughly. Quotes were then selected from all interview transcripts. Secondly, similar patterns or terms were recognised and delegated as keywords. Furthermore, codes were generated representing the data's core message or significance. Keywords contributed an important role in coding as they shaped the analysis and converted raw data into structured and meaningful insights. Subsequent to that, themes were developed that required organising codes into relevant groups and provided insights into the research question. Fifthly, themes were refined and renamed, corresponding with the research study. The final step involved was report writing [7].

Results

We conducted semi-structured online interviews with 12 participants from Hospital Tunku Ampuan Besar Tuanku Aishah Rohani, Hospital Pakar Kanak-kanak UKM (Hospital TABTAR) from April to May 2025. Among the study participants recruited, there were general paediatricians and paediatricians with subspecialties (n=6), while the rest were paediatric medical officers in their postgraduate paediatric training (n=6). Their mean years of medical practice were 13.2 years (7 – 33 years) as shown in Figure 4.1.

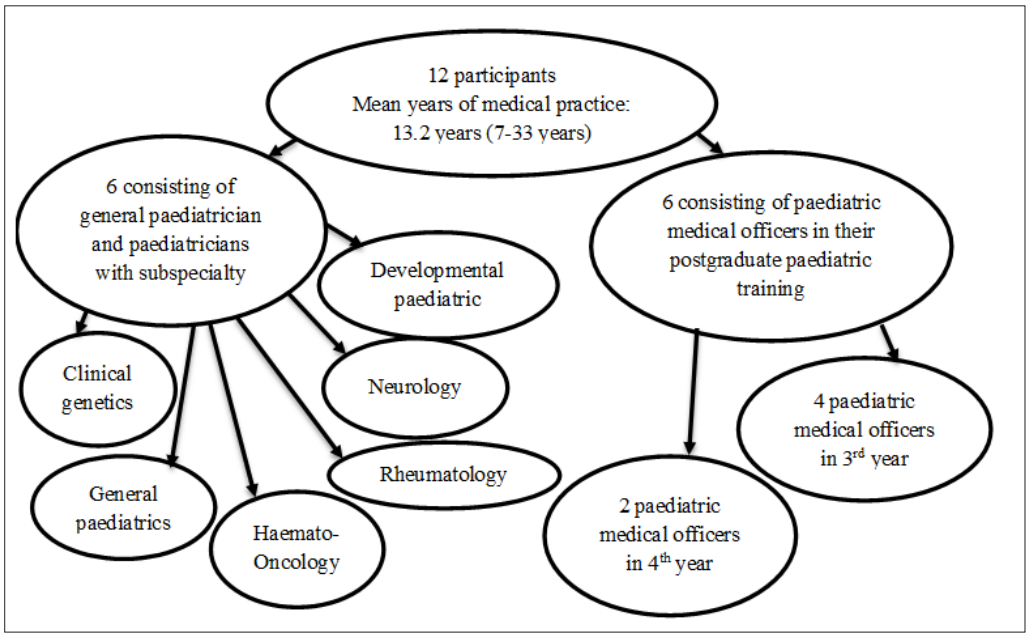

Figure 2: Demographic Profile of Participant

Four themes were elicited from the reflexive thematic analysis of the transcribed data. The thematic map generated below showed the relationship between themes and subthemes.

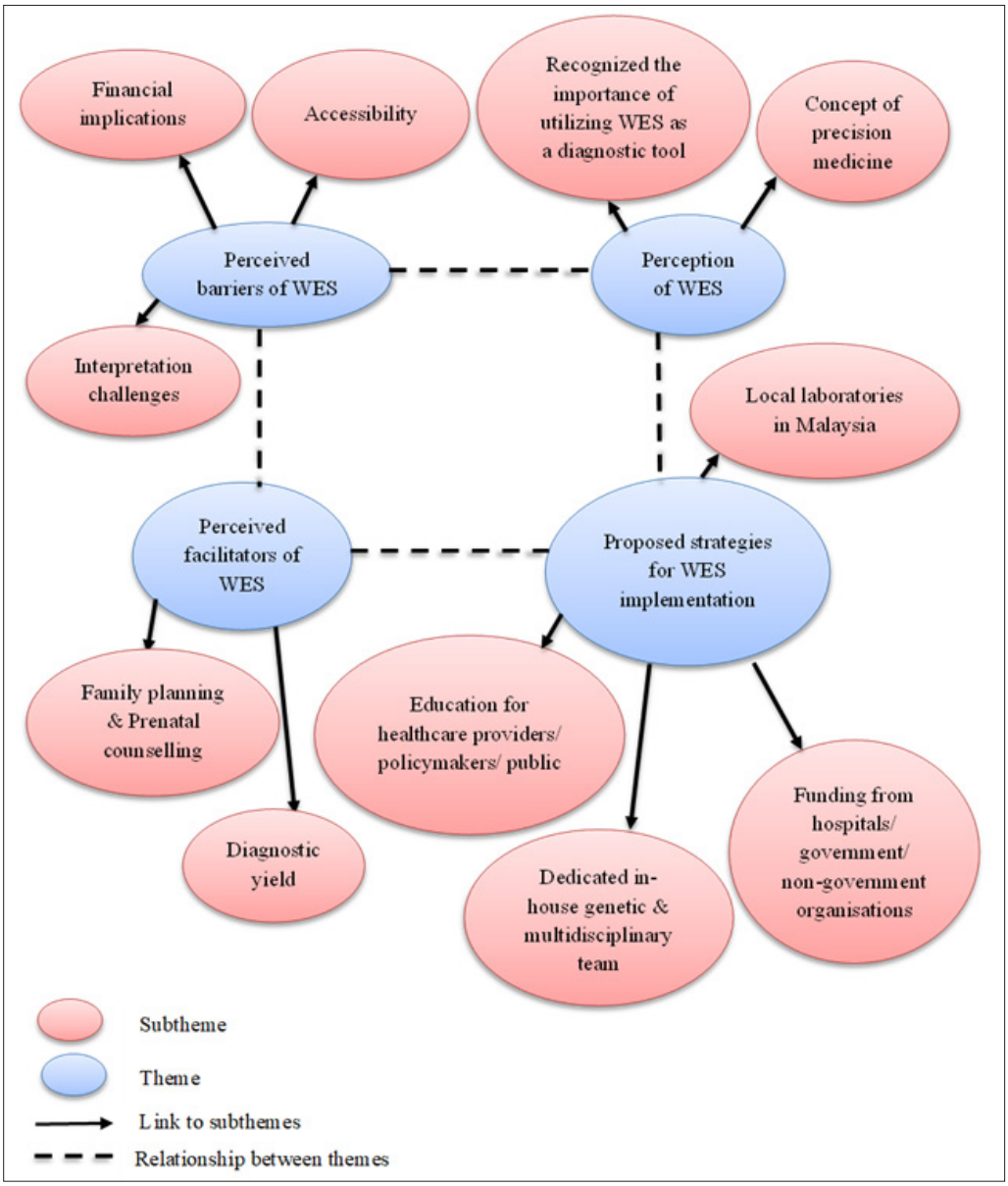

Figure 3: Thematic Map

Theme 1: Perception of WES by Malaysian Paediatricians and Medical Officers

Precision Medicine

We explored the participants' perception and understanding of WES in paediatric clinical medicine; all twelve participants mentioned the concept of precision medicine. It highlighted the approach to medicine changes over time, introducing newer technology like WES, which is able to diagnose individuals, and the treatment would be more precise.

"I think from the words itself, it means a medicine that is more accurate as the technology advance." (Participant 5)

"For instance, the one that I use, this precision medicine…We will cater the genetic result of this patient so as to individualize the risk factor for the type of leukemia that he has. 'Each patient using these genetic factors and also the risk that he has, meaning to say if the child has a certain genetic predisposition or genetic enzyme that we noted during the genetic testing, we will give a different type of medication." (Participant 12)

Understanding the importance of WES as a diagnostic tool

We explored the participants' understanding of WES in paediatric clinical medicine; all twelve participants recognised the importance of utilising WES as a diagnostic tool.

"I mean it is a very good investigation and also quite a new investigation to Malaysians… more accessible in the current years. So, it's actually helping us to get a diagnosis in lots of diagnosis dilemmas or undiagnosed patients." (Participant 2)

"So, basically, we are actually sequencing the coding region of our genome, meaning we are sequencing all the exomes of coding genes. So, this is actually basically just sequencing

maybe one to two percent of our DNA. But it is actually quite cost effective because 80 percent of the known genetic mutations are actually located within this coding region called exomes. I think as a clinical geneticist, the main role is actually for the diagnostic purposes." (Participant 6)

Theme 2: Perceived Facilitators of WES in Investigating Paediatric Genetic Conditions Among Malaysian Paediatricians and Medical Officers

Family Planning and Prenatal Counselling

We explored the participants' facilitators utilising WES in paediatric clinical medicine; eight participants emphasised that WES assisted in family planning and prenatal counselling.

"I think it can help them giving genetic counselling for patients, and also help them to explain to the patient in regards to the inheritance patterns for future children, so that they can plan a family decision. For example, let's say a patient comes with Beckwith-Wiedemann syndrome (BWS)...has high genetic predisposition, or this can occur sporadically. So, you can also give, manage reproductive planning. I think most of the time we do in vitro fertilisation (IVF) and the other one is called villus sampling once the mother is already in the pregnancy." (Participant 12)

A different participant described that WES facilitated family planning.

"Yeah. For example, you have an index case that is… positive of… that it's complementary to whatever the diagnosis is. So, you want to screen the parents to see if the parents are carriers, or the parents carry some mutations. And then, um, this would then help you to know whether this is actually inherited disease, or is it de novo… kind of mutation…for future pregnancies for the parents." (Participant 11)

Diagnostic Yield

We explored the participants perceived facilitators utilising WES in paediatric clinical medicine, and half of the participants mentioned that WES provide good diagnostic yield.

"Okay, when you talk about the diagnostic yield…I think the average diagnostic yield for neurological disease…depends on the centre and are you doing a screening or just targeted diagnostic approach. But again, I don't screen for every patient... Because the selection of my patient is targeted, that's why the diagnostic yield is quite high, 50 to 70%." (Participant 1)

Theme 3: Perceived Barriers of WES in Investigating Paediatric Genetic Conditions Among Malaysian Paediatricians and Medical Officers

Financial Implications

We explored the participants perceived barriers to utilising WES in paediatric clinical medicine; all twelve participants consistently highlighted the financial implications of whole exome sequencing (WES) as a key barrier to its use in paediatric clinical settings.

"Sometimes because of course the cost is another thing needs to be considered…we need to consider the financial burden to the parents as well. We have to outweigh the cost and the significance of the result to the parents." (Participant 5)

"So, who want to pay for it…Is insurance going to pay for it? Which I don't think average families are happy to pay for the cost…It may not give you the diagnosis 100%. In general, in Malaysia, the insurance doesn't cover inherited, congenital disease." (Participant 7)

This illustrates how clinicians weigh clinical utility against affordability, particularly when dealing with families who may not have the financial means to access advanced genomic testing.

Interpretation Challenges

Participants identified result interpretation as a major barrier to the clinical application of WES in paediatrics. In particular, all twelve participants highlighted the challenge of interpreting variants of uncertain significance (VUS) and communicating their relevance to families.

"Sometimes we do get this variance of insignificance (VUS). So, in this one, we probably may not be able…have some trouble in telling the parents because we're not sure whether…this certain variance is the cause of the disease or not. And sometimes these variances were not reported worldwide. So, it can be a new found variant that probably needs further studying and probably need to be repeated later. You cannot interpret..." (Participant 4)

Accessibility

We explored participants perceived barriers to utilising whole exome sequencing (WES) in paediatric clinical practice. Half of the participants reported limited accessibility to WES, with logistical challenges particularly in resource-limited or remote settings, which further constrain its use.

"I think the first one is not all hospital offer this WES because first one i think, if let's say we go to the district hospital…Rarely we offer this kind of a test for the patient. Usually, we're going to refer to the tertiary hospital or we're going to call our geneticist to ask opinion about it." (Participant 8)

"Sending the sample, and we have a specific day to send, and we need to call in the patients from very rural area to come in for blood taking. The delivery service that we use sometimes…, uh, there's a specific time, that need to reach airport…to fly off." (Participant 10)

Theme 4: Proposed Strategies of WES Implementation as an Investigative Tool for Paediatric Genetic Conditions in Malaysian Hospitals

Funding From Hospitals/ Government/ Non-Government Organisations

We explored participants perceived strategies to enhance the implementation of WES as a diagnostic tool in Malaysian hospitals. Ten participants emphasised the need for financial assistance, particularly in the form of government subsidies or institutional support schemes.

"I think it's the funding. I know we should have more funding actually, at least from the government. Maybe they can

subsidize half of the amount of the test, then we use it more widely...Honestly speaking, most of the time, the patients pay themselves." (Participant 12)

Echoing this, another participant mentioned financial assistance or subsidies from companies.

"Well, I think if there is organization that can help to support the cost, that will be helpful…the company can give us discounts and all, or even I think research, if there's a collaboration for certain disease...If the public service…Zakat or those welfare support can maybe help with the subsidizing costs for this WES, so it can help, at least parents won't think twice if we counsel to send. This is one of the suggestions…meaning financial aid for this." (Participant 4)

Local Laboratories in Malaysia

Two participants proposed development of local infrastructure and services as a strategy to improve access to WES in Malaysia. These suggestions included establishing WES capabilities within government laboratories and promoting local industry involvement to reduce reliance on overseas testing services.

"Actually, we try to get funding to create WES in government labs. So, I think recently Institute for Medical Research Malaysia (IMR) has managed to get some funding to set up WES" (Participant 6)

"My suggestion is maybe we can have the first one. So far, we don't have any local that can do the WES. So, maybe we should have more local company that can offer more WES." (Participant 8).

These recommendations reflect a broader call for capacity building within the Malaysian healthcare system to improve the affordability, accessibility, and sustainability of genomic diagnostics.

Educating healthcare providers, policymakers and public

Nine participants emphasised the need to improve knowledge and awareness of WES among healthcare professionals, policymakers, and the general public.

A recurring concern was the inappropriate or uninformed use of WES due to insufficient understanding of its indications, limitations, and ethical implications.

"Nurturing the knowledge also…to a paediatric MOs…to a paediatrician, like how and why we want to send…" (Participant 2)

Another separate participant mentioned educating not just the clinicians about WES but also the policymakers and the public.

"Yeah, you have to educate people…people on top…politicians…directors... And also, the lay people, like the parents. And the doctors, because… many doctors are not aware of this…A suggestion is for every general paediatrician or a paediatric trainee to go through a genetic posting. The thing is not all hospitals have it." (Participant 11)

Dedicated In-House Genetic and Multidisciplinary Team

We explored the participants' proposed strategies to implement WES as an investigation tool in Malaysian hospitals; half of the participants mentioned having an in-house genetic team. They emphasised the need for multidisciplinary collaboration in the implementation and interpretation of WES within clinical settings. The complexity of genomic data and its disease-specific implications were seen as requiring coordinated input from a range of clinical and laboratory specialists.

"You can't have this without the specific team for me. The genetic team would be the most important person to for in-house, or maybe in… uh, will be available for us to consult in case we face challenges." (Participant 9)

"So, a team that expert in those diseases…I think autism, then the developmental paediatricians or geneticists will be someone that who is helpful. Like cancer…oncologist, a geneticist, the laboratory haematologist or pathologist will be the person that will need to be well versed on that area to read the gene. It's so diverse… is not something that…geneticist can solve all the problem…I don't think it can be one person read everything (Participant 7)

Discussion

This research study offers insights into how two groups of paediatricians with subspecialties and paediatric medical officers in their postgraduate paediatric master's study perceive WES, what facilitates their utilisation of WES as a diagnostic tool, what barriers they faced utilising WES in investigating paediatric genetic conditions and their proposed strategies for WES implementation in Malaysian hospitals.

Participant Recruitment and Interview Timeframe

Purposive sampling employed during the recruitment of the study participants was crucial, considering this method is a well-established approach in qualitative research aimed at selecting and identifying data-rich cases for optimal use within constrained resources. This implies identifying and choosing ones who are well-versed or have experience with the area of interest. Besides possessing the knowledge as well as being experienced, Bernard and Spradley (1979) illustrated the significance of availability and having the intention to participate, and being capable of conveying experiences and points of view with depth and clarity. On that account, the selection of my study participants was not biased; however, it was appropriate and intended, given the exploratory type of research.

Reflecting on the timeframe of all the interviews with the two groups of study participants, paediatricians and medical officers, there was a huge variation in the interview length. The level of experience of the participants and those who were more well-versed in the area of interest influenced the interview duration, deriving from the group of general paediatricians with subspecialties providing richer insights, therefore resulting in longer interviews compared to the group of medical officers. However, participants from the group of medical officers with lesser experience provided shorter yet insightful responses.

Navigating The Perception of WES

The theme perceptions of WES among Malaysian paediatricians and medical officers revealed that all twelve participants associated WES with the advancement of precision medicine. Participants recognised that the evolving landscape of clinical practice increasingly emphasises personalised and targeted treatment approaches. By identifying the specific genetic variant as the pathogenic basis for a patient's condition through WES, clinicians are better positioned to administer variant-targeted therapies, thus aligning care with the principles of precision medicine. This finding is consistent with those of Chung et al., who reported that WES significantly reduces diagnostic timelines compared to sequential traditional investigations [8]. Earlier diagnosis, in turn, facilitates timely and personalised treatment. The researchers highlighted the potential for integrating WES into paediatric and adolescent clinical pathways to support the broader adoption of precision medicine [8]. The coherence of the findings between the two studies suggests that the implementation of WES could facilitate the application of precision medicine in patients' care.

In addition, toward their understanding of WES, all twelve participants recognised the importance of utilising WES as a diagnostic tool in their current practice. In the paediatric setting, there are undiagnosed patients or diagnosis dilemma cases in which conventional diagnostic methods were unable to find the actual cause of their disease. Utilising WES as their next diagnostic test would assist in finding a diagnosis. This resonates with findings led by Shakiba & Keramatipour, revealing that implementing WES as an investigative tool is regarded as a revolution in the diagnosis of complex cases, where other investigations, including biochemical tests, have yet to yield a diagnosis. The utility of WES in diagnosing genetic conditions has increased, reducing the cost of running a series of tests. They found WES effective in diagnosing metabolic and neurogenetic conditions, particularly challenging and unresolved cases of patients. The parallel findings across both studies suggest the views of healthcare providers on WES can reduce diagnostic odyssey attributed to them, considering it a significant tool in paediatric clinical medicine.

Consideration of Facilitators in Using WES

The theme perceived facilitators of WES in investigating paediatric genetic conditions describes the view expressed by eight participants, highlighting that it assists in family planning and prenatal counselling for the parents of the patient. As some parents may plan for future pregnancies, obtaining a diagnosis through WES may inform them of the recurrent risk for their next child and may help them understand the risk of carriers for a particular genetic condition. This finding aligns with a previous study by Iglesias et al., who reported that WES utility precisely predicts the recurrent risk for parents and their relatives, and also accurately identifies any other family members harbouring the mutation to allow for preventative medical care and prenatal counselling [9]. The swift diagnosis through WES has a significant impact on individuals who are distressed about recurrent risk, especially those cautious of planning for subsequent children before diagnosis confirmation [9]. The agreement observed in both studies reinforces WES's capability of providing information on the diagnosis of genetic conditions, whether they are inherited in the family or result from a spontaneous mutation. This significantly influences the reproductive planning, allowing healthcare providers to inform the available prenatal options for future pregnancy to prevent recurrence of the genetic condition.

Another factor that facilitated the use of WES is its ability to provide a good diagnostic yield. When performing WES with their patients in their practice, half of the participants agreed that it would provide a good diagnostic yield. This finding is consistent with research conducted by Srivastava et al., who noted WES could facilitate early diagnosis, benefiting patients through targeted therapies. Based on a meta-analysis evaluating the clinical utility of WES for clinical presentations such as intellectual disability (ID), developmental delays (DD), and multiple congenital anomalies (MCAs), it showed a diagnostic yield of around 36%. Acquiring a molecular diagnosis in almost one-third of cases is regarded as a substantial advance. This encouraging yield gives rise to a consensus statement that warrants WES as a preferred genetic test for paediatric and adult cases that are encompassed by these categories. Previously, chromosomal microarray (CMA) was the first-tier clinical diagnostic test as proposed by Miller et al.. Notably, in 2021, an updated guideline on diagnosing patients molecularly with ID, DD and MCAs through CMA to the new recommendations by the American College of Medical Genetics and Genomics (ACMG), which strongly suggest next-generation sequencing as the first-tier test.

The study participants also mentioned that the diagnostic yield of WES depends on circumstances, the patient selection or suspected condition being targeted, and is also influenced by the clinicians' indication for ordering the test. Truong et al. reported that the indications for genetic testing within primary care physicians and paediatricians are sometimes uncertain. For instance, developmental delay as a probable indication for genetic testing is usually not recognised, even though there is a high possibility of obtaining a diagnosis. Having a clearer understanding of the anticipated diagnostic yield for varying clinical phenotypes could be beneficial, ensuring that patients with a likely genetic aetiology are offered testing. and to set expectations regarding the expected likelihood of reaching a genetic diagnosis. This outlines the significance of clinicians 'expertise in WES, which will determine the outcome of diagnostic yield.

Challenges Faced in Using WES

The theme perceived barriers of WES in investigating paediatric genetic conditions, illustrated that all participants emphasised the financial implications as a major challenge to its use. After introducing the cost of WES to patients from average or low-income families and explaining that they have to pay out of their pocket, most of them would refuse to undergo the test or would be unable to afford such a high amount.

This finding is consistent with previous research by Kapol et al., which highlighted that the accessibility towards WES causes an increase in expenditure, and the introduction of WES did not lead to a reduction in medical costs by avoiding unnecessary medical investigations or treatment procedures [10]. They believe that

if there is a reduction in WES cost henceforth, it would not pose an economic burden to the healthcare system in Thailand. In addition, Bertier et al. also described that the economic cost of WES remained a key barrier for clinical implementation. The parallel findings between these studies suggest that the exorbitant cost of WES imposes a financial burden on patients, as of yet limiting their accessibility to the test.

Another perceived barrier of WES was the interpretation challenges, as described by all of the participants. There are four outcomes of WES results, namely: pathogenic, likely pathogenic, benign, or variants of uncertain significance (VUS). The interpretation for variants is based on the ACMG guidelines for the classification of sequence variants [11]. When the results report a VUS, it poses challenges to clinicians to interpret the variant identified through WES and also explain it to the patient or the patient's parents. This finding is consistent with a study by Xue et al., who reported the dilemma in the interpretation of VUS, making it difficult in the interpretation process and constituting a bottleneck in clinical applications [12]. Another study conducted by Vaseghi et al. portrayed that even with the attempt made to standardise the classification of variants, in certain cases, it is unclear and still ambiguous regarding their pathogenicity, and at times, their interpretation fails to assist clinicians in ascertaining clinical correlation through WES results [13]. The coherence of results between the studies indicates that the current challenges faced when obtaining a VUS result through WES cannot be used to guide the clinical management of patients and require further research on the variant identified to assess its significance to the patient's condition.

Other barriers faced in utilising WES were the limited accessibility to the test. Half of the participants mentioned that they have difficulty, such that only some tertiary hospitals, for instance, Hospital TABTAR, have access to WES. In Malaysia, WES services are not widely provided in commercial laboratories; therefore, most of the WES samples are outsourced to overseas laboratories.

According to the Ministry of Health (2024), WES at this current stage is not available in MOH facilities, which has led to some district hospitals not having access to WES. This finding aligns with a study conducted by Awad et al., who noted that scarcity of access to genomic sequencing facilities in developing countries leads to outsourcing as the sole available choice to utilise this test. Outsourcing them may lead to low-quality services, such that the improper handling of samples, transportation, and lengthy service waiting period contribute towards it. Outsourcing may also be an expensive and lengthy process that could require a few months. The consistency across both studies implies there are clinicians who were unable to access WES services due to limited-resource settings, constraining the ordering of the test for their patients.

Proposed Solutions to Implement WES as a Diagnostic Tool

In the final theme, proposed strategies for WES implementation as an investigative tool in Malaysian hospitals, ten participants suggested funding from the hospital, government, and non-government organisations. The financial assistance would be prioritised for patients who are unable to afford the test. On the availability and funding of clinical genomic sequencing internationally, Phillips et al. have conducted case studies of three countries with differing funding of WES and genome sequencing for suspected genetic diseases. In the UK, it is one of the countries with national government-based funding for next-generation sequencing, and other countries that do provide these are Belgium, Denmark, the Netherlands, and Australia [14]. For Canada, public funding of tests is supplied at the provincial level, following approval, depending on meeting specific criteria. In the USA, it has variable private and public insurer coverage for WES and genome sequencing. This finding highlights the difference between Malaysia's healthcare policy and healthcare policies in other countries, such as the UK, USA, and Canada, whereby patients in Malaysia would have to self-pay for WES, unlike the countries mentioned above. With the availability of financial assistance, more patients would be able to undergo the test.

Another recommended strategy for WES implementation, educating healthcare providers, policymakers, and the public, which nine participants mentioned. Creating awareness among clinicians about WES on how to order the test, when to order the test, and for what indications, which can be achieved through courses, talks, seminars, or even an attachment at a genetic clinic. Unlike previous research conducted by Seaby et al., which identified that many clinicians are unacquainted with this swiftly evolving genomic sequencing, evidently a need for training clinicians in genomics to improve their genomic literacy [15]. This difference highlighted in this study is the need to also educate policymakers and the public about WES as a significant diagnostic tool in diagnosing paediatric genetic conditions. Only through increased awareness and understanding of WES among clinicians, policymakers, and the public can its implementation be more effective.

Other proposed strategies mentioned by two participants were having more local laboratories in Malaysia that provide WES services. This would improve the accessibility of clinicians for this test and also shorten the turnaround time for the results, as there is no need to transport samples overseas. This aligns with previous research by Flynn, who reported that for WES implementation to be viable, the need to build local laboratories is necessary [16]. The agreement between the studies suggests that with the availability of more local laboratories, more clinicians would be able to access the test, and the cost of WES could be reduced, as there are no overseas transportation fees.

Further recommended strategies on WES implementation suggested by half of the participants were having a dedicated in-house genetic team and a multidisciplinary team. If clinicians are having difficulties with a complex genetic case, requiring more information on a genetic condition, or facing interpretation challenges, an established in-house genetic team and a multidisciplinary team would be readily available for communication and provide them guidance. This is in line with findings from previous research by Valencia et al., highlighting the need for a team of clinical molecular and medical geneticists, paediatric subspecialists, and genetic counsellors to assist in interpreting WES data [17]. Taylor et al. also emphasised the importance of establishing a genomic medicine multidisciplinary team (GM-MDT) in Oxford, which encourages engagement across specialities and eases the delivery of results to clinicians in charge [18-25].

The consistency across the studies indicates that clinicians working together with an in-house genetic team and a multidisciplinary team would help them in result interpretation, which is regarded as a key barrier in utilising WES [26-35].

Study Limitations

This research study had several limitations. Firstly, the study participants were part of the study population for Malaysia; however, the cohorts were selected from the same tertiary hospital. The findings may not reflect all paediatricians' or paediatrician medical officers' perceptions of WES from other tertiary teaching hospitals in Malaysia. The perceptions of WES may differ for other clinicians in other Malaysian tertiary hospitals or outside tertiary institutions, for instance, district hospitals. In the proposed total of participants, which was previously 14, it was limited to only 12 participants due to time constraints and the unavailability of certain selected participants. Nevertheless, the primary researcher noticed during the data analysis, there was a repetition of themes and codes, as no new insights from additional participants were elicited, indicating data saturation [36,37]. Moreover, during some of the interviews conducted by the primary researcher, there was an acknowledgement that his background and knowledge may have shaped how the participants responded to the interview questions, even though efforts were made to reduce the influence of the interviewer [38-53].

Conclusions

This study delved into Malaysian paediatricians and medical officers' perception of WES within their current practice, focusing on the facilitators, barriers, and strategies for WES implementation as an investigative tool for paediatric genetic conditions. The findings revealed four themes: perception of WES, perceived facilitators of WES, perceived barriers of WES, and proposed strategies for WES implementation. These qualitative insights address the initial research questions. In the perception of WES, paediatricians and medical officers mentioned the concept of precision medicine and recognized the importance of WES as a diagnostic tool in the paediatric setting. The facilitators of WES that were explored from this study were good diagnostic yield and assisted in family planning and prenatal counselling. The barriers perceived in utilizing WES included limited accessibility to the test, interpretation challenges, and the financial implications. Proposed strategies of WES implementation included funding from the hospital, government, and non-government organisations, educating healthcare providers, policymakers, and the public about WES, having more local laboratories providing WES services, and having a dedicated in-house genetic team and multidisciplinary team to assist. This study expands our understanding of how WES is an investigative tool in paediatric settings from the Malaysian paediatricians and medical officers' point of view. Exploring their perceptions utilizing WES in their current practice could validate or refute existing theories. It informs the current status and the degree of progress still required for WES implementation in Hospital TABTAR. Healthcare providers, policymakers, and laboratories could be informed of the diagnostic utility of WES in paediatric clinical medicine. The findings suggest a need for a policy to support the implementation of WES in Malaysian hospitals. This study offers new evidence of WES utility in Malaysian paediatric settings, representing the Southeast Asian population.

Future Recommendations

Future research could explore more diverse participants, such as clinicians from different specialties, who were not covered in this current study. There could be research collaborations across multiple Malaysian tertiary teaching hospitals or private hospitals that offer WES services, allowing for a broader understanding of WES as an investigation tool in different healthcare settings.

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Conflict of Interest Statement

The author declare no conflicts of interest.

Data Availability Statement

The data cannot be shared because of privacy and ethical concerns.

Ethics Statement

Approval (JEP-2024-1158) to conduct this research study was obtained from the Research Ethics Committee, the National University of Malaysia (RECUKM). Written consent was acquired from all participants to participate in the study.

Appendix 1

Semi-Structured Interview Guide

Demographic Data to be Obtained.

1. Role: Medical Officer / Specialist / Consultant
2. Subspecialty (if any)
3. Years of medical practice

Questions with Prompts

1. In your own words, describe what you understand by the concept of 'precision medicine'.
2. In your own words, describe what you understand by the whole exome sequencing (WES).
3. In your opinion, what is whole exome sequencing (WES) used for?
4. What are the types of samples that can be taken for WES?
5. In your own words, why do you think whole exome sequencing (WES) is important?
6. In your opinion, how does WES help/assist in investigating paediatric genetic conditions?
7. In your opinion, what are the challenges of using WES in investigating paediatric genetic conditions?
8. What suggestions do you have for implementing whole exome sequencing (WES) as a tool in investigating paediatric genetic conditions at Malaysian hospitals?

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