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ORIGINAL ARTICLE

Rare Diseases in Malaysia: Mapping the Landscape and Building a Framework for Comprehensive Care Support

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ABSTRAK

Penyakit jarang jumpa merupakan isu kesihatan sedunia yang semakin mendapat perhatian, yang dianggarkan menjejaskan 5.9% daripada populasi dunia, dengan lebih daripada 8,000 jenis penyakit yang telah dikenal pasti dan bilangannya semakin meningkat. Di Malaysia, penyakit jarang jumpa ditakrifkan sebagai penyakit yang menjejaskan kurang daripada seorang bagi setiap 4,000 penduduk. Pesakit yang menghidap penyakit jarang jumpa ini terpaksa mengharungi pelbagai cabaran, termasuk tahap kesedaran yang rendah di kalangan penyedia perkhidmatan kesihatan, kelewatan diagnosis, liputan perkhidmatan kesihatan yang tidak mencukupi serta akses yang terhad kepada ubat orfan. Artikel ini mencadangkan satu rangka kerja bagi menangani isu-isu tersebut dengan meningkatkan tahap kesedaran dalam kalangan masyarakat dan profesional kesihatan, mewujudkan pendaftaran kebangsaan untuk penyakit jarang jumpa, menggalakkan kerjasama antara organisasi tempatan dan antarabangsa, serta menubuhkan skim pembiayaan. Langkah-langkah ini bertujuan menggalakkan diagnosis awal, memastikan akses rawatan yang adil dan penjagaan pesakit secara menyeluruh. Dengan menangani jurang dalam pengurusan dan rawatan, usaha dapat diperkukuh ke arah membangunkan satu rangka kerja pengurusan yang lebih komprehensif dan efektif.

Kata kunci: *Kebolehcapaian; perkhidmatan kesihatan; polisi kebangsaan*

ABSTRACT

Rare diseases (RDs) represent an emerging global health issue affecting an estimated 5.9% of the world's population, with over 8,000 conditions identified and counting. In Malaysia, RDs are defined as diseases affecting fewer than one in 4,000 people. These patients face significant barriers, which include limited awareness among healthcare providers, delayed diagnoses, insufficient healthcare coverage and restricted access to orphan drugs. This article proposes a framework to tackle the issues mentioned by enhancing public and professional awareness, establishing national RD registries, encouraging local and international collaborations, and creating dedicated funding schemes. These points aim to improve early

diagnosis, equitable access to treatment, and overall patient care. By addressing these management and treatment gaps, we can work towards a more comprehensive and effective RD management framework.
Keywords: Accessibility; health service; national policy

INTRODUCTION

Rare diseases (RDs) are often overlooked, although it is emerging as a global health issue. The definition varies from one region to another. In the United States (US), the Orphan Drug Act, a law passed by Congress in the 1980s, followed by the Rare Disease Act in 2002, defines a RD if fewer than 200,000 individuals in the US are affected (Abozaid et al. 2022). The World Health Organisation (WHO) states that RDs are when less than 65 per 100,000 people of a population is affected. The European Union (EU) defines it as conditions that affect less than 50 per 100,000 people (Nguengang Wakap et al. 2020).

Globally, up to 8000 conditions have been identified as RDs, of which 80% have a genetic cause and more than half affect the pediatric population (Chung et al. 2022). A conservative estimate suggests that the global prevalence of RDs stands between 3.5 to 5.9% of the global population, which equates to 263 – 446 million people (Nguengang Wakap et al. 2020). Considering the time invested by caregivers, the impact of RDs may extend to 1.0 to 1.4 billion individuals (Groft & Posada De La Paz 2017). The prevalence of RDs in the United States is estimated to affect 15.5 million people (Yang et al. 2022). In Southeast Asia, some estimates suggest that approximately 9% of the population (~45 million people) may suffer from a RD (Shafie et al. 2016).

The Malaysian Rare Disease Society (MRDS) defines a disease affecting less than one per 4000 people as a RD. Recently, the National Rare Disease Committee of the Ministry of Health Malaysia updated its list of conditions to include 492 diseases affecting various systems. Examples of RDs include Marfan syndrome, osteogenesis imperfecta and Mucopolysaccharidosis type II. A systemic review by Shafie et al. (2020) estimated that 1,249 patients with RDs were treated at public hospitals in Malaysia in 2020, though this may likely be an underestimate.

Despite the term rare or orphan disease, the prevalence within communities is substantial as a whole, and yet they do not garner the same attention and care as other common medical conditions (Groft et al. 2021). This disparity creates several challenges for patients, caregivers, healthcare providers and policymakers. Developing countries such as Malaysia face diverse issues as opposed to developed countries. Thus, this article attempts to elaborate the current landscape of RDs in Malaysia by focusing on the barriers faced in addressing these diseases. This article also proposes a framework to enhance care and support for individual living with RDs.

Barriers to Treatment

(i) Gaps in awareness and knowledge among healthcare providers

One of the main barriers in this region is a lack of awareness among not only the general population, but also the healthcare professionals (Shafie et al. 2020). Li et al. (2021) had reported that only 5.3% of physicians had a moderate level of awareness about orphan diseases, with over 80% encountering an RD diagnosis less than three times. In addition, self-perceived knowledge of RDs among healthcare providers may be discordant to their actual knowledge in assessments (Sinan et al. 2023). Perhaps, awareness on RDs can be instilled from the start of their education, as only 13% of medical students knew the definition of RDs and the availability of genetic testing in one study (Hristova-Atanasova et al. 2023).

The lack of comprehension and expertise about RDs contributes to two major issues. Firstly, there may be difficulty in recognising

uncommon diseases, leading to missed diagnosis, underreporting and failure to treat RDs. It is not uncommon for the diagnosis of rare conditions to be delayed by 4–5 years from the onset of symptoms (Marwaha et al. 2022). Secondly, poor understanding may contribute to misinformation, where healthcare professionals may incorrectly assume a patient with RD would not have access to genetic testing or treatment options in this region. Only 6% of healthcare providers in Malaysia were aware of companies providing gene profiling services locally (Amini et al. 2014).

(ii) Diagnostic challenges

Delay in diagnosis is another key barrier in managing RDs. In Europe, the average time to diagnosis was 4.7 years, with an average of five months between the first symptom and initial medical consult, followed by 4.3 years until diagnosis (Faye et al. 2024). This finding is echoed in an analysis carried out in Spain, where the mean time to diagnosis is approximately 6.18 years (Benito-Lozano et al. 2022). RD patients often consult several physicians before receiving a diagnosis, with one study reporting and average of 6 physicians per patient before encountering an expert (Willmen et al. 2023). While there is no clear data of the mean time to diagnosis of a RD in Asia, considering the challenges faced, it is likely that diagnosis times are similarly prolonged, if at all a diagnosis is eventually obtained.

RDs frequently pose as diagnostic dilemmas due to the lack of availability of confirmatory diagnostic tests locally. While a number of tests pertaining to autoantibodies and enzyme levels are offered at diagnostic laboratories like the Institute for Medical Research Malaysia, Premier Integrated Labs, Innoquest Pathology and Lablink Medical Laboratories, many molecular and genomic tests need to be outsourced to centers overseas. Sending samples abroad to facilities offering these tests like the Mayo Clinic Laboratories (US) or 3 billion (South Korea) incur significant costs and would be inaccessible to those of lower socioeconomic status.

(iii) Healthcare coverage

Malaysia is striving towards providing universal health coverage, whereby the majority of Malaysians are entitled to free healthcare (Chua & Cheah 2012). Malaysia's healthcare financing is dependent on contributions from the general population via taxes, the Employees Provident Fund, Social Security Organisation, out-of-pocket payments and insurance premiums (Yu et al. 2008). Healthcare delivery is carried out by government and private sectors. The former is heavily subsidised by the government through the Ministry of Health, while the latter is provided to anyone who can afford to pay for their services through their own savings or insurance (Jamal et al. 2023).

However, this does not include most forms of genomic testing, implants and certain medications which are costly. The majority of the population may not be able to afford tests, such as chromosomal microarray analysis and whole genome sequencing, which may amount to USD 1,485 and USD 3,434 respectively (Runheim et al. 2023). According to the Department of Statistics Malaysia, the mean average household income in 2023 across its states ranged from USD 1,115/month to USD 3,750/month. This disparity in income, particularly in rural areas away from the nation's capital of Kuala Lumpur, have been reported in studies in the past (Thangiah et al. 2020). Eventually, this leads to a cascade effect, where misdiagnosis results in inappropriate care, progressive deterioration of symptoms and delay in definitive treatment.

Separate funding is provided by the Ministry of Health to the genetic clinic at Kuala Lumpur General Hospital. In 2016, approximately USD 3.2 million was allocated, with a steady increment of 7-10% annually (Shafie et al. 2020). In the recent national budget tabled for 2025, about USD 5.7 million has been earmarked for use in RD. However, while there are few available therapeutic options for the large number of RD that exists, treatment with enzyme replacement therapy like idursulfase and avalglucosidase alfa for Mucopolysaccharidosis type II and Pompe's

disease, respectively, would cost upwards of USD 200,000 per patient annually. The high cost of medications alone would deplete funds rapidly, leaving no reserves for important screening tests.

(iv) Treatment access

The scarcity of orphan drugs and its high cost pose an additional challenge. Due to their low prevalence, RDs are of low health priority nationally and will fall behind in appropriate funding and care. There is a lack of incentive and economic gain for pharmaceutical companies to research and develop treatments for a small patient base (Katakowski & López 2025). Inevitably, manufacturers set a high selling price to recoup their research investments, leading to its inaccessibility. Furthermore, logistical issues such as specialised storage and distribution for small batches of drugs adds to the cost and burden (Yoo 2024).

In addition, there is reluctance among those at risk to undergo advanced tests like genetic testing due to insurance discrimination. Companies view genetic test results as an important factor in underwriting (Prince et al. 2021). Some patients insurance coverage have been cancelled or void, due to genetic conditions detected during adulthood, on the pretense that it is a pre-existing condition. As a result, affected patients are denied for the healthcare coverage they need, particularly when they require expensive drugs for treatment.

Locally, there are limited specialised facilities and experts to treat RDs. In 2020, only five hospitals offer RD services, with 13 RD specialists on duty (Shafie et al. 2020). Unfortunately, the centers offering genetic and metabolic services are in Peninsular Malaysia, near major urban centers, leaving East Malaysia underserved. This complicates access to screening and treatment, particularly rural areas. Moreover, the lack of a national patient registry makes it difficult to quantify RD prevalence, making it difficult to estimate its impact. Without the availability of data, it would be difficult to formulate a strategy or create policies to assist. Figure 1 depicts the barriers to treatment and integrated management strategies to strengthen the support for RD.

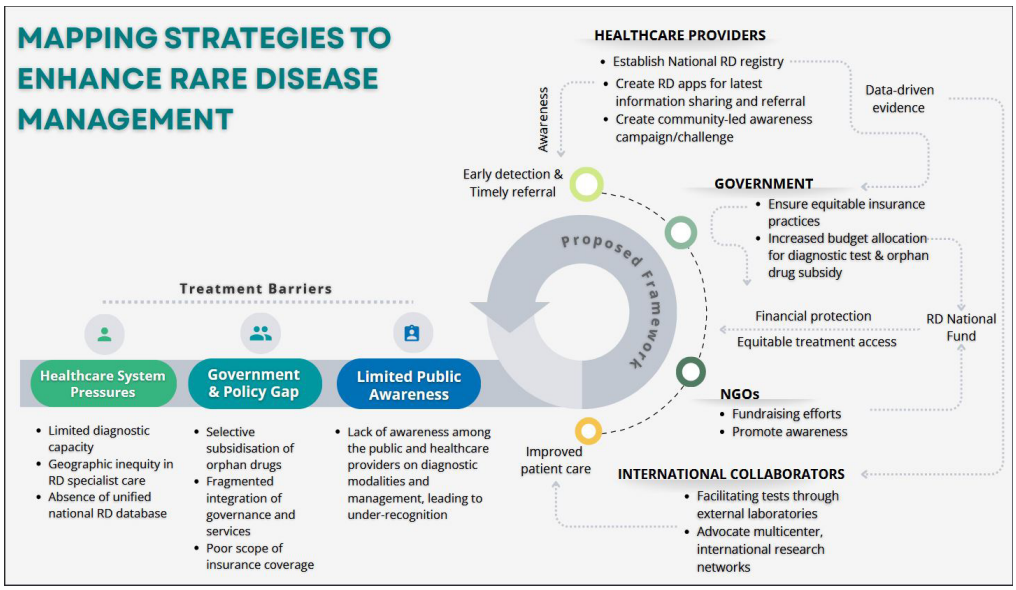

FIGURE 1: Barriers to treatment and an integrated framework for enhanced support for rare diseases. *Created by the authors using Canva (Canva Pty Ltd., Sydney, Australia)*

Proposed Framework

(i) Raising public awareness

Public awareness of RDs is important for several reasons. By educating the general population on RDs, it could encourage them to present earlier to healthcare facilities to seek treatment, leading to earlier diagnosis and prompt treatment. Greater understanding would also reduce stigma and alleviate any potential bias that may affect employment opportunities of those afflicted. (Velvin et al. 2023) In addition, there would be increased participation in non-profit organisations through volunteer work and financial support if people are aware about the physical and social barriers faced by RD patients.

Social media plays an influential role in promoting causes and spreading information. As many as 2.9 billion people utilise social media platforms in 2022. Commonly used platforms include YouTube, Instagram, WeChat and X (Kanchan & Gaidhane 2023). The average person spends 3.57 (SD ±2.87) hours on mobile devices daily, including 3.32 (SD ±1.42) hours per day on social networks (Saman et al. 2020). Influencers have a profound effect on followers, young and old, which may bring about positive or negative health effects (Powell & Pring 2024). Content creators have in the past promoted unhealthy food items, supplements and spread misinformation on medical related topics, especially during the COVID-19 pandemic. Despite not being experts in these fields, their followers continue to support and adhere to the suggestions, even ignoring health warnings.

Therefore, their impact cannot be disregarded and incentives should be provided to channel their influence positively. Campaigns like the ice bucket challenge is a good case study, whereby prominent personalities helped raise up to USD 115 million for the amyotrophic lateral sclerosis (ALS) association worldwide as well as disease awareness. (Sohn 2017). A spike in search volume on Stiff Person Syndrome when the news of Celine Dion's diagnosis was announced highlights their impact (Elsalti et al. 2023). Collaborating with local influencers who are passionate to help could boost RD awareness. To bridge the gap, allocations can be directed to campaigns and road shows to reach out to those who are less tech-savvy.

(ii) Enhancing local collaboration

Medical registries are an important component in public health surveillance, providing data on disease prevalence, demographics and management to guide policy making decisions. (Richesson & Vehik 2010) While it may require manpower to update and maintain the registry, they are essential for cost-benefit analysis and understanding the population impact of treatments (AHRQ Methods for Effective Health Care 2014; Pop et al. 2019). At present, there is no local registry for RD in Malaysia, making resource allocation challenging and often based on underestimated numbers. The use of existing census on orphan drug use from resources like the Malaysian Statistics on Medicine will not reflect the true prevalence of RD as it documents only those actively receiving treatment.

Therefore, a collaborative effort between each hospital is important to collect RD data and update the registries, enabling future funding requests based on demand. Mobile health applications have also been used in healthcare assessment in several conditions, such as epilepsy (Choi et al. 2021). Creating an application specifically for RD patients, will allow data collection for registry purposes, dissemination of important information on available funding assistance and related support groups for the RD of interest. Using existing mobile health platforms like MySejahtera and repurposing it would save costs (Farhani et al. 2024). However, ensuring data privacy and preventing security breaches will be challenging, in addition to integrating the system with local hospital records (Conduah et al. 2025).

Once a registry is in place, resources can be distributed to address the needs of the patients effectively. If the numbers are low, it may be more cost-efficient to consolidate pathology services to save costs (Lone et al. 2025). For

private laboratories, services to test for RDs could be integrated, where the tests offered do not overlap and could therefore be processed or outsourced in bulk, bringing expenses down. Additionally, setting a cost cap could prevent inflation by service providers. Another method would be to subsidise tests performed in these private centers, avoiding the cost of importing specialised laboratory equipment to cater to local needs.

Besides that, a mechanism should be implemented whereby centers under the Ministry of Health can refer out cases to university hospitals under the Ministry of Higher Education for RDs, and vice versa at no added costs. Despite being government bodies, cooperation between both government entities is limited, resulting in suboptimal management of patients when a certain specialty is not offered at their center. One of the main barriers to co-management is the added costs involved as university hospitals have added charges compared to the universal healthcare offered in government hospitals (Mustapa et al. 2004).

(iii) Greater international collaboration

Seeing that several factors cannot be addressed locally, greater collaboration with regional and international counterparts would have a positive impact on RD management. Diagnostic tests unavailable domestically can now be outsourced easily to other countries. Advancement in techniques continue to bring down costs and increase reliability of tests. A good example is the use of dried blood spots for measurement of biomarkers and genetic testing, which requires considerably less volume, is easy to collect, requires less storage space and transported in room temperature (Mcclendon-Weary et al. 2020). However, the transportation of clinical samples would still be subjected to the standard operating procedures outlined by the Institute for Medical Research. In addition to providing a declaration for dangerous goods, specimens would require import permits from the local government and export permits from the Disease Control Division, Ministry of Health, or the Kuala Lumpur International Airport Health Office. Reducing logistical barriers will help in driving the overall costs down significantly.

Continued research is essential to progress in terms of disease management, improving outcomes and quality of life of RD patients. Special interest groups like the International Rare Diseases Research Consortium brings researchers and institutions together to develop new tests and treatment modalities (Boycott et al. 2017). Incentives and allocation to support research in translational medicine, encourages analysis of preclinical data to be applied in future clinical practice (Murdock et al. 2024).

(iv) Establishing a national fund for rare diseases

The availability of funds poses as a major barrier to diagnosis and treatment of RD. Creating a dedicated national fund would support advanced testing and timely administration of orphan drugs. It is important to note that the existing budget tabled for use for RD is not accessible to university hospitals, where no additional funding is given for this purpose. To boost funds, we can adopt policies already in effect in other countries. For example, Australia's Life Saving Drugs Program, established since 1995 to cover the cost of few essential medicines to treat RD, with periodic reviews of orphan drug efficacy and financial impact biennially (Ng et al. 2024).

Singapore established a charity fund that combines community donations with government-matching contributions (1-to-3 ratio), where every SGD 1 donated by the public would receive a contribution of SGD 3 from the government. As of 2022, a total of SGD 143 million was reported in the RD fund, which covers for 7 medications in treating 5 diseases. However, applications for other unlisted RD will be rejected (Ng et al. 2024). In the United Kingdom, the National Health Service is publicly funded, but approval for orphan drugs depends on the cost-benefit analysis by the National Institute for Health and Care Excellence. The Highly Specialised Technologies Programme

allows a limit of £ 300,000 per Quality-Adjusted Life Year (QALY) for treatment with orphan drugs with high costs (Mccabe et al. 2008). The Innovative Medicines Fund has an annual grant of £340 million that can be used for drugs with uncertain clinical cost-effectiveness. This allows early administration of promising therapies for all conditions including RDs (Angelis et al. 2023).

In the US, most support for RDs comes from non-government organisations, as private insurance is the primary health coverage for most of the population (Drell et al. 2022). However, insurance claims for orphan drugs are restricted. As many as one third of applications for specialty drugs are rejected (Chambers et al. 2019). The Affordable Care Act has certain rules in place, protecting patients with RDs from insurance companies who may write-off or drop the patient's policies once they are diagnosed. Unfortunately, to qualify, there are several criteria to fulfil based on the applicant's socioeconomic background. With similar issues observed locally, engaging the public and patient advocacy groups to be involved in discussions with government leaders and representatives of insurance companies may reveal potential solutions to this impasse before legislative changes are made to protect patients (Shi et al. 2023)

(v) Strengthening non-profit organisations

Patient advocacy groups are invaluable in large aspects of RD care. Roughly one-third of organisations conduct their own research, through their own registry or utilising their biobank (Patterson et al. 2023). Increasing patient and caregiver involvement will spur research in the field and increase awareness in the RD community. Their use of various platforms, including social media, acts as a platform to disseminate information and communicate or educate each other regarding the latest developments in RDs (Morgan & Subbiah 2023). The MRDS has provided support to patient and caregivers since its inception, on top of liaising with various stakeholders in improving the plight of patients with RD. Other support groups, such as the Malaysia Lysosomal Diseases Association and Malaysian Metabolic Society also play a crucial role in defending patient rights, providing emotional support and arranging various community driven activities in collaboration with healthcare providers to promote awareness and acquire funds.

(vi) Increasing experts and specialised facilities

Incentives for physicians to specialise in RDs could improve healthcare delivery and reduce long waiting times. Government-funded scholarships and fellowship opportunities will encourage more to pursue the field. As genomic testing becomes more cost-effective, the need for support staff such as genetic counselors is growing, mainly to assist the geneticists on educating those in need, from initial testing to treatment (Ormond et al. 2024). While there are 7,000 counselors registered globally, with 267 in Japan alone, the numbers are far fewer in South East Asia (Aizawa et al. 2021). They also assist in flagging cases with test order errors, with one study demonstrating total savings of USD 972,000 over 57 months, simply from modifying 32% of the 3,441 genetic tests received through outsourcing (Haidle et al. 2017).

Additionally, establishing a dedicated specialist center catering for RDs would improve care delivery, where future referrals and tests can be carried out. The first medical facility to form a RD center in China, the West China Hospital of Sichuan University (WCHSU), has assisted 1,185 RD patients over four years on-site, and an online platform that has received 866 patient applications. The committee has also arranged 3 conferences, 80 public events and clinic visits at no charge (Gong & He 2021). Once established, a pathway can be created to streamline referrals from primary care centers to increase accessibility.

CONCLUSION

As the nation grows, the prevalence of RDs is expected to rise, making it essential to address any challenges as soon as possible. A lack of

awareness and knowledge among healthcare personnel, diagnostic challenges, gaps in healthcare coverage and poor treatment access are the major issues plaguing RD management locally. Overcoming these barriers requires a comprehensive approach, involving multiple domains, through the concerted efforts of patients, caregivers, healthcare professionals, industry partners and government leaders. By increasing funding, fostering local and international collaboration, advancing research and raising awareness, our nation moves closer towards a future with improved care and support for RD patients, changing the landscape of RD management in Malaysia. We hope this article acts as a call to action for those in positions to make positive changes, as well as spur interest in policy development and research on genetics and novel treatment modalities.

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