Correspondence

DOI: 10.5582/irdr.2024.01009

The epidemiology and healthcare burden of rare diseases requiring hospitalisation among adult patients in Langkawi, Malaysia: Insights from a pilot study

Ngah Kuan Chow[1,*], Norazila Abdul Ghani[2], Nursyahmina Zamri[1], Mohammad Nurhuzairie Anuar[1]

[1] Department of Pharmacy, Hospital Sultanah Maliha, Ministry of Health Malaysia, Langkawi, Kedah, Malaysia;
[2] Department of Pharmacy, Hospital Jitra, Ministry of Health Malaysia, Kedah, Malaysia.

SUMMARY In Malaysia, rare diseases affect fewer than 1 in 4,000 people. As of 2020, 491 rare diseases have been recorded in Malaysia, but with limited epidemiological data. As the first study in Malaysia, this retrospective cohort study examined the epidemiology and admission-related healthcare costs for adult rare disease patients in Langkawi. Among the 38 patients, rheumatological rare diseases topped the list (39.5%). The annual admission rate for rare diseases was 0.9%. Langkawi patients had lengthy hospital stays (9.7 days) and a 7.9% mortality rate. 23.7% of patients defaulted to follow-up, and 7.9% were referred to a tertiary hospital due to inadequate equipment or speciality care. Admission costs were Malaysian Ringgits (MYR) 244,598.63 (~US Dollars (USD) 51,280), with 80.2% from medication. The average healthcare resource utilisation was MYR 6,436.81/patient/year (~USD 1,350/patient/year).

Keywords rare disease, hospitalisations, healthcare costs, epidemiology, access to treatment

1. Introduction

Rare diseases in Malaysia are defined as conditions affecting fewer than 1 in 4000 people. As of August 2020, the Malaysian Rare Disease List has recorded 491 rare diseases (*1*). However, comprehensive data on their geographical and ethnic distributions within the country is lacking.

Rare diseases come with a substantial economic burden, with costs per patient per year (PPPY) being approximately ten times higher than mass-market diseases (US Dollars (USD) 266,000 PPPY versus USD 26,000 PPPY) (*2*). Orphan drugs are medicinal products designed to treat, prevent or diagnose rare diseases. Access to orphan drugs is limited, especially in Malaysia, where treatments like enzyme replacement therapy can cost more than Malaysian Ringgits (MYR) 700,000 (~USD 152,500) annually (*3*). However, funding constraints, particularly in district hospitals such as Hospital Sultanah Maliha in Langkawi, make it challenging to provide orphan drugs.

Geographical barriers further complicate access to treatment for rare diseases, especially in Langkawi, an island only accessible by air or sea. There is only one hospital in Langkawi, limiting treatment options for rare disease patients. The island's economy mainly relies on tourism, making it difficult for patients to allocate extra funds for healthcare-related travel outside Langkawi (*4*).

This retrospective cohort study aimed to describe the epidemiology and admission-related healthcare costs of managing adult patients with rare diseases in Langkawi from the perspective of the Ministry of Health (MOH) Malaysia, given that Hospital Sultanah Maliha is a public hospital under MOH Malaysia.

The patients recruited in this study from September 2021 to March 2023 were 13 years old and above, including those newly diagnosed with rare diseases during their current admission but not yet receiving treatment and those previously diagnosed and on treatment. Patients admitted for reasons unrelated to their rare diseases (*e.g.*, elective admission for arteriovenous fistula creation) were excluded.

The cost evaluation conducted in this study pertains to the year 2023. A micro-costing approach was employed, allowing for the quantification of each cost component associated with the treatment. From the provider's perspective, treatment costs were gathered using a 'bottom-up' approach. All costs were denominated in MYR as of 2023. The average hospitalisation cost per patient was calculated by dividing the total hospitalisation costs of all patients by total number of patients. Detailed information about the items in each cost category can be found in the Supplemental Table S1 (*http://www.irdrjournal.com/action/getSupplementalData.php?ID=200*).

This study has been granted ethical approval by MREC MOH Malaysia (NMRR ID-23-00353-BDS).

2. Access to treatment

Rheumatological rare diseases top the rare disease list (39.5%), mostly suffering from systemic lupus erythematosus (SLE) (n = 11). The sociodemographic data and types of rare diseases of the patients are in Table 1. Among the 38 patients studied, 18 (47.4%) were newly diagnosed with a rare disease upon admission, while the others had a median of 1.5 years post-diagnosis. The annual admission rate for rare diseases in Langkawi was 0.9% (61 out of 6,773 admissions), with a higher rate among females at 1.7% (58 out of 3,369 admissions). Moreover, 13 (34.2%) patients experienced readmissions, a figure comparable to the 32% readmission rate in the USA (*5*). The readmission rate can be as many as five admissions within a year. Langkawi patients had longer hospital stays (9.7 days) compared to the other countries (6.1 days in Hong Kong and 6.3 days in the USA) (*5,6*), and it was double the duration among patients who required antimicrobial therapy (24 versus. 12 days, p = 0.001).

On the other hand, 9 (23.7%) patients had defaulted follow-up. These defaulted patients were significantly younger, with an average age of 31 compared to 44 (95% CI: 1.15 to 23.91; p = 0.033). Meanwhile, the mortality rate is double that reported in the literature (n = 3, 7.9% versus 3.9% in the USA) (*5*). 7.9% of patients were referred to a tertiary hospital due to inadequate equipment or speciality care. The rest of the patients (84.2%) were discharged home. A majority of the patients (n = 31, 81.6%) were receiving immunosuppressant treatment for their rare diseases, with corticosteroids (n = 25, 65.8%) being the most prescribed. With the high percentage of immunosuppression, 23 (60.5%) patients had to be treated with antimicrobials for infections. The other treatment modalities received by the patients include blood product transfusion, oxygen supplementation, and haemodialysis.

Table 1. Sociodemographic data and type of rare diseases of the study participants

Variables	n (%)
Sex	
Male	3 (7.9)
Female	35 (92.1)
Ethnic	
Malay	36 (94.7)
Chinese	2 (5.3)
Age group (years)	
13 - 29	10 (26.3)
30 - 49	17 (44.8)
50 - 64	7 (18.4)
≥ 65	4 (10.5)
Marital status	
Unmarried	10 (26.3)
Married with no children	4 (10.5)
Married with children	23 (60.6)
Divorced / Widowed	1 (2.6)
Employment status	
Employed	14 (36.8)
Unemployed	14 (36.8)
Not in labour force	10 (26.3)
Place of stay (distance from hospital)	
Kuah (6 km)	13 (34.1)
Ulu Melaka (10 km)	8 (21.1)
Padang Matsirat (11 km)	4 (10.5)
Kedawang (13 km)	8 (21.1)
Bohor (13 km)	2 (5.3)
Ayer Hangat (20 km)	3 (7.9)
Type of rare diseases	
Rheumatological (MCTD, rheumatoid meningitis, scleroderma, SLE)	15 (39.5)
Haematological (AIHA, Evans syndrome, HbH disease, PNH)	10 (26.3)
Neuromuscular (GBS, NMOSD, NORES)	7 (18.4)
Endocrine (primary adrenal insufficiency)	4 (10.5)
Dermatological (pemphigous vulgaris)	1 (2.6)
Renal (minimal change disease)	1 (2.6)

AIHA: autoimmune haemolytic anaemia; GBS: Guillain-Barré syndrome; MCTD: mixed connective tissue disorder; NMOSD: neuromyelitis optica spectrum disorder; NORES: new-onset refractory status epilepticus; PNH: paroxysmal nocturnal haemoglobinuria; SLE: systemic lupus erythematosus.

Table 2. Estimated costs (MYR) of rare disease management in Langkawi

Type of costs	Costs in MYR (USD)	Percentage of total costs (%)
Medication	196,161.63 (41,124)	80.20
Hospitalisation	29,600.00 (6,205)	12.10
Laboratory tests	12,891.00 (2,703)	5.27
Imaging and radiology	2,791.00 (585)	1.14
Blood products	2,700.00 (566)	1.10
Surgery and procedure	455.00 (95)	0.19
Total costs	244,598.63 (51,280)	100.00

3. Costs

The total admission costs of the recruited rare disease patients were MYR 244,598.63 (~USD 51,280), of which 80.2% were medication costs (Table 2). The total medication costs in this study (MYR 196,161.63 or ~USD 41,124) constituted 11% of the total medication costs for adult inpatients (all diseases) in the hospital during the study period (MYR 1,783,013.57 or ~USD 373,798). The treatments received by the patients include immunosuppressants, antimicrobials, fluid management, and other medications, in which immunosuppressants were the most expensive category of medication costs. On average, a rare disease patient in Langkawi pays

MYR 333.20 (~USD 70) per hospital admission, which only represents 5.2% of the annual hospitalisation cost per patient related to rare diseases borne by the hospital (MYR 6,436.81 or ~USD 1,350).

4. Discussion

Our data revealed almost 50% of new diagnoses (18 out of 38 rare disease patients admitted) related to rare diseases per year in Langkawi. This exceptional finding prompted us to investigate and report this matter, as many cases may still be undiagnosed and warrant a more systematic screening system. Those geographically isolated patients might have limited understanding of their conditions and lack medicinal support, leading them to opt for traditional or alternative medicines without a proper diagnosis in the hospital.

To our knowledge, this study represents the first cost analysis of managing rare diseases in Malaysia after a comprehensive literature search using PubMed Central, PubMed/Medline, Cochrane Review, Springer Link, and Lippincott Williams & Wilkins journals. Our findings showed that the total economic burden of hospitalised patients with rare diseases at Hospital Sultanah Maliha approaches MYR 245,000 (~USD 53,000) over one and a half years, signifying a considerable strain on the hospital's resources. A financial study in Langkawi showed that 60.9% of the population earns a monthly income of MYR 3,500 (~USD 760) or less (*7*). This income instability could prevent patients from seeking further healthcare treatment outside Langkawi.

Following the founding of the National Framework for Rare Disease, the Malaysian MOH adopted the Patient Access Scheme (PASc) to broaden patient access to high-cost medicines (*8*). PASc is a collaborative initiative between pharmaceutical companies and the MOH Malaysia. This programme incorporates innovative pricing agreements to improve cost-effectiveness and ensure broader patient access to specific medications. Despite PASc use to procure orphan drugs, its potential impact is restricted to a small number of patients.

Most previous pharmacoeconomic studies on rare diseases evaluate all cost categories, including direct costs, indirect costs and mortality costs. However, our study focused exclusively on direct medical costs. While the current public healthcare system is still unable to cope with the rising demands of rare disease treatment costs, specific groups of patients, for example, those with more comorbidities, need to be prioritised via a systematic process of orphan drug supply.

Acknowledgements

We wish to thank the staff of the Medical Record Unit and Wan Nur Hafawati Wan Hussin of Revenue Unit, Hospital Sultanah Maliha, for their kind assistance. We also thank the Director-General of Health Malaysia for his permission to publish this article.

Funding: None.

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Pharmaceutical Services Programme Ministry of Health Malaysia. Malaysian Orphan Medicines Guideline. 2021. *https://pharmacy.moh.gov.my/sites/default/files/document-upload/malaysian-orphan-medicines-guideline-2020_0.pdf* (accessed April 26, 2024).
2. Cioffi G, Andreu P, Karam J, Child C, Chiesi G. Evaluation of the societal burden of rare diseases in the United States. Research Square. 2021; DOI: https://doi.org/10.21203/rs.3.rs-936611/v1
3. Shafie AA, Supian A, Hassali MAA, Ngu LH, Thong MK, Ayob H, Chaiyakunapruk N. Rare disease in Malaysia: Challenges and solutions. PLoS One. 2020; 15:e0230850.
4. Kayat K, Mohd Radzi R. Social tourism carrying capacity in Kampung Kilim, World Geopark, Langkawi. WIT Transactions on Ecology and the Environment. 2012; 166:93-102.
5. Navarrete-Opazo AA, Singh M, Tisdale A, Cutillo CM, Garrison SR. Can you hear us now? The impact of health-care utilization by rare disease patients in the United States. Genet Med. 2021; 23:2194-2201.
6. Chiu ATG, Chung CCY, Wong WHS, Lee SL, Chung BHY. Healthcare burden of rare diseases in Hong Kong - Adopting ORPHAcodes in ICD-10 based healthcare administrative datasets. Orphanet J Rare Dis. 2018; 13:147.
7. Hassan MF, Azwan Haris NA lail. Financial well-being in Langkawi tourism industry: An exploratory study. International Journal of Academic Research in Business and Social Sciences. 2022; 12:1174-1186.
8. Pharmacy Practice and Development Division Ministry of Health Malaysia. Guideline on Proposal Submission for Patient Access Scheme Implementation in Ministry of Health. 2018. *https://pharmacy.moh.gov.my/sites/default/files/document-upload/25.8.2020-guidelines-proposal-submission-patient-access-scheme-2018-dengan-no.-siri-kelulusan_0.pdf* (accessed April 26, 2024).

Received February 12, 2024; Revised April 27, 2024; Accepted May 14, 2024.

**Address correspondence to:*
Ngah Kuan Chow, Department of Pharmacy, Hospital Sultanah Maliha, Bukit Tekuh, Jalan Padang Mat Sirat, 07000 Langkawi, Kedah, Malaysia.
Email: kimi_nk_chow@yahoo.com