Short Communications

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Cost of Treatment for Myelofibrosis Patients in Ministry of Health Hospitals in Sarawak, Malaysia

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Abstract

Objective: Primary myelofibrosis is a rare type of myeloproliferative neoplasm with an annual incidence rate of 0.47 per 100,000. A retrospective, observational study was conducted to determine the disease evolution and costs of treatment for myelofibrosis (MF) patients managed in 4 Ministry of Health (MOH) hospitals in Sarawak, Malaysia. **Methods:** The estimation of treatment cost was a planned analysis of the Real World Evidence (RWE) study which included retrospective chart review of adult MF patients treated in Sarawak General, Sibu, Bintulu and Miri Hospitals. The study was approved by Sarawak General Hospital HRRC and MREC. The current study was conducted to estimate the cost of out-patient visits, hospitalisation, transfusion and medication from the perspective of MOH. Out-patient visits and hospitalisation costs were calculated using current unit costs for full fee-paying charges of MOH hospitals. Transfusion costs were estimated for packed cell and platelet transfusions. Medication costs were calculated using drug prices from IQVIA database for MOH hospital sub-sector in 2021. Unit costs were standardised to index year of 2021. **Result:** Data from 63 patients was available for analysis. Mean annual health resource utilisation (HRU) was 6.13 clinic visits, 9.47 days of hospitalisation and 1.61 transfusions per patient per year. Mean HRU cost was RM23,320 (USD5,217) per patient per year, comprised of RM19,122 (USD4,278) in drug costs, RM3,030 (USD678) for hospitalisation, RM799 (USD178) for transfusions and RM368 (USD82) for outpatient cost. **Conclusion:** The present analysis suggests that medication and hospitalisation were the main drivers of costs for MF treatment in Sarawak MOH hospitals. This study provides the first RWE estimate of the cost of MF in Malaysia and may provide insight into unmet clinical needs and a guide for further health economic research into the treatment of MF.

Keywords: Primary myelofibrosis- medical care costs- healthcare resource utilization- Malaysia

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Introduction

Myeloproliferative neoplasms are a group of clonal haematological disorders that arise from the transformation of a multipotent haematopoietic stem cell (Skoda, 2007). Primary myelofibrosis (MF) is one of three distinct clinical sub sets of Philadelphia-negative, BCR/ABL-negative MPNs (Cools et al., 2003). It is a rare disease with an estimated average annual incidence rate of 0.47 per 100,000 population, though the data underpinning the estimate was heterogenous (Titmarsh, 2014).

Sarawak, is the country's largest state with a population of almost 3 million and is comprised of 26 ethnic groups (Department of Statistics Malaysia, 2022; Minority Rights Group International, 2018). Studies on MPNs are scarce in Malaysia and to our knowledge, there is only one published study reporting the epidemiology and clinical characteristics of MPNs in Malaysia and no past studies on the cost of treatment for the disease (Yap et al., 2018).

Hence, the aim of the present study was to estimate the health resource utilisation (HRU) and direct medical cost of MF treatment in Sarawak Ministry of Health (MOH) hospitals.

Materials and Methods

The Sarawak Myelofibrosis Experience (SaMy) Real World Evidence (RWE) study was a non-interventional, retrospective observational study of MF in Sarawak. The study performed retrospective record review of adult MF patients diagnosed from January 2001 to 31 December 2021 and managed in Sarawak MOH hospitals (Sarawak General, Miri, Sibu and Bintulu hospital). The study was approved by Sarawak General Hospital HRRC and MREC. The study included all primary and secondary MF cases that met WHO diagnostic criteria. More details on the methodology of the SaMy study is presented elsewhere (Tang et al., 2022).

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Health resources included in the analysis were drugs, hospitalisation, out-patient visits and transfusions. Health resource utilisation (HRU) costs were calculated from the perspective of MOH and standardised to index year of 2021. Costs were calculated in annualised terms to account for variations in treatment duration between patients. Analyses were conducted using RStudio statistical software. All costs are reported in Malaysian Ringgit (RM) which had an exchange rate of USD1=RM4.47 on 17 August 2022.

Outpatient visits, hospitalisation and transfusions cost

HRU costs were calculated as a product of the annualised rate resource utilisation and the unit cost of resource, as shown in the formula below:

HRU cost=annualised rate of HRU x unit cost of health resource

As shown in the formula below, the annualised rate of HRU was calculated by dividing the quantity of HRU encounters (e.g. visits, days, etc) by the total duration for each patient. The duration was calculated from the date of diagnosis (index date) to the end date of data collection, defined as either (1) the date of death or (2) date of data collection for the SaMy study.

$$Annualised\ rate\ of\ HRU = \frac{Quantity_{HRU}}{End\ date - Index\ date}$$

Unit cost

The unit costs for out-patient visits and hospitalisation costs were calculated by applying current charges for full fee-paying patients to MOH hospitals (Hospital Putrajaya, 2022; Hospital Selayang, 2022). Transfusion costs were estimated for packed cells, platelet, cross matching and transfusion equipment (Shafie et al., 2021). All HRU unit costs were standardised to index year of 2021.

Medication costs

Medication costs were calculated as the product of the duration of therapy and the daily cost of drugs. Treatment duration was calculated from the date of treatment initiation until discontinuation. Daily cost of treatment was calculated as the product of the assumed daily dose of MF drug, based on the authors' clinical experiences, and the drug unit costs which were obtained from the Sarawak General Hospital pharmacy and IQVIA data for MOH hospital sub-sector in 2021. For drugs that are not used daily, the equivalent daily cost was calculated based on the normal treatment regimen (e.g. 4000 iu per week would be equivalent to 571.43 iu per day).

Results

The data of 63 MF patients identified through the SaMy study were used for the HRU analysis reported in this analysis. The study cohort had a mean age of 59 years and 50.8% were female as shown in Table 1. Most of the study cohort were diagnosed with primary MF (74.6%) with JAK2V617F mutation (82.5%) and had high risk disease assessed by DIPSS+ score (54%). 47.6% of patients were categorised as transfusion dependent. More details of patient characteristics and health outcomes from the SaMy study is published in (Tang et al., 2022).

The mean cost of HRU for the entire cohort was RM23,320 (USD5,217) per patient per year, of which RM19,122 (82%, USD4,278) was for drugs while RM3,030 (13%, USD678) was incurred for 9.47 days of hospitalisation, RM799 (3%, USD178) for 1.61 transfusions and RM368 (2%, USD82) for 6.13 out-patient visits. Of the 1.61 transfusions per year, 1.35 (84%) were for packed cells and 0.26 (16%) were with platelets

Table 1. Baseline Characteristics

Characteristic	Statistic (N=63)
Age (mean, SD)	59.0 years (11.06)
Female (n, %)	32 (50.8%)
Primary MF (n, %)	47 (74.6%)
Mutation status (n, %)	
JAK2V617F	52 (82.5%)
CALR	6 (9.5%)
Negative	5 (7.9%)
Spleen size (mean)	62 cm
DIPSS+ risk group (n, %)	
Low	2 (3.2%)
Intermediate-1	8 (12.7%)
Intermediate-2	19 (30.2%)
High	34 (54.0%)
Transfusion dependent (n, %)	30 (47.6)

SD, standard deviation

Table 2. Drug Treatment Patterns, Annualised Duration (Days Per Year) and Costs (RM Per Patient Per Year)

Drug regimen	All lines of treatment			1st line treatment			2nd line treatment			3rd line treatment			4th line treatment	
	Duration	Cost	N	Duration	Cost	N	Duration	Cost	N	Duration	Cost	N	Duration	Cost
All drugs	238.5	19,122	61	253.4	7,142	43	226.5	30,258	18	200.8	30,039	2	365	51,878
HU	255.2	1,276	41	261.5	1,307	4	243.5	1,218	1	52	260	0		
HU comb	283.2	6,055	3	267.7	7,148	2	324	2,773	0			0		
INF	197.1	4,454	8	206.1	4,658	9	185.6	4,194	5	203.4	4,597	0		
Rux	279.6	70,687	4	304.5	76,990	18	261.3	66,511	5	302	76,358	1	365	92,287
Rux comb	365	100,536	0			0			2	365	100,536	0		
Other Rx	196.9	2,589	5	214.2	1,913	10	180.9	2,825	5	94	1,019	1	365	11,468

USD1,RM4.47; Patients on non-drug treatment (e.g. transplant) were excluded from the analysis of drug costs

at a cost of RM561.37 (USD125.59) and RM238.12 (USD53.27) per patient per year, respectively.

The most used first-line therapy, as shown in Table 2 was hydroxyurea (HU), where 44/61 patients (72%) were treated with HU or HU combination therapy followed by interferon 8/61 (13%). For patients on second-line therapy, 18/43 (42%) switched to ruxolitinib and 9/43 (21%) were switched to interferon.

Table 2 also reports the duration and cost of drugs by line of therapy. The mean annualised drug cost shows an increasing trend by line of therapy from RM7,142 per patient per year for first-line therapy to approximately RM30,000 in second- and third-line respectively, and RM51,878 for fourth-line therapy. However, there are only two patients in the cohort who are on fourth-line therapy. Mean duration of treatment was 253.5 days in a year for first-line treatment to 200.8 days for third-line treatment.

Discussion

The present analysis found that similar to other studies, medication and hospitalisation were the main drivers of costs of MF treatment in Sarawak MOH hospitals. A study from Canada of 1,031 MF patients in the Ontario provincial health database reported treatment cost of C$25,863 per patient per year, with hospitalisation and medication accounting for 66.5% and 18.6% of treatment costs, respectively (Bankar et al., 2020). Similarly, an analysis of US data reported MF-related medical costs of US$38,383 in the first 6 months post-MF diagnosis, of which inpatient stay and pharmacy costs contributed to 45.5% and 32.2% of total costs (Copher et al., 2022). However, it should be noted that hospitalisation costs in our study was likely to be underestimated as we did not include the cost of ICU or procedures during admission. Therefore, hospitalisation would probably account for more than 13% of MF treatment cost in MOH if these costs were included, and consequently medication costs would comprise less than 82% that was reported in our results.

Other studies have also reported high cost of drugs as a proportion of overall treatment cost from the MOH perspective. An analysis of the treatment cost for early breast cancer in MOH reported that drug costs constitute 98.2% to 99.3% of treatment cost for IV and SC administered cancer treatment (Lee et al., 2016).

Medication costs are lowest in first-line therapy and increase in subsequent lines, driven by drug costs and longer mean duration of treatment on ruxolitinib compared to non-targeted drugs in the same line of treatment. As MF is a life-threatening disease, prolonging treatment duration with ruxolitinib may translate into prolonged survival compared to patients on non-targeted treatments, as was reported in the ERNEST registry study from Europe that found a significantly longer median overall survival in patients treated with ruxolitinib compared with those who received HU (6.7 vs 5.1 years; P = .001) (Guglielmelli et al., 2022). The corresponding SaMy study reporting the demographics and clinical outcomes found that the use of ruxolitinib in myelofibrosis patients showed a better overall 5-year survival compared to the no ruxolitinib arm, although the difference was not statistically significant (p=0.34) (Tang et al., 2022).

The present analysis has a few limitations. Firstly, since the HRU analysis was based on the data collected in the SaMy study, the data available is inherently constrained by the availability and quality of data that could be extracted from medical records. Specifically in this study, data on ICU admissions, emergency department visits and procedures and investigations performed (apart from transfusions) were not available. Therefore, the HRU cost results from this study are likely to underestimate the actual HRU cost for MF treatment in MOH. Similarly, the calculation of drug costs was based on assumed doses as data on actual dosing was not available. Lastly, the entire analysis was conducted on a small sample of patients (N=63).

There has been a lack of published research in MF in Malaysia. To our knowledge there has only been one recent study on the epidemiology and clinical characteristics of MPN in Malaysia (Yap et al., 2018), and no previous published research on HRU or cost of MF treatment in Malaysia or the region. We hope that despite its shortcomings, the present analysis of HRU for MF in Sarawak can provide insight for future studies into the cost of MF treatment. In particular, studies from a wider sample of centres and more detailed data on real-world drug dosing, investigations and procedures for treatment of MF or cost estimated using MalaysianDRG case mix would provide a more representative estimate of the cost of MF treatment in Malaysia (Medical Development Division, 2020)

Author Contribution Statement

All authors designed the study, analysed and interpreted the data, and read and approved the final manuscript

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Approval

The research was not conducted as part of a student thesis or approved by a scientific body.

Ethical approval

The present analysis was a sub-analysis of the SaMy RWE study which was approved by Sarawak General Hospital HRRC and Malaysia Medical Research and Ethics Committee (NMRR-20-2285-56865).

Availability of data

Not applicable as the study utilised data from the SaMy retrospective, observational study.

Conflict of interest

The authors declare they have no conflict of interests.

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