ORIGINAL ARTICLE

The epidemiology of chronic myeloid leukaemia in southern Sarawak, Borneo Island

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ABSTRACT

Objectives: There are very few published chronic myeloid leukaemia (CML) epidemiology studies in South-East Asia and no representative from Malaysia.

Methods: This is a cross-sectional study of adult CML patients (citizen) in a single but representative centre in southern Sarawak.

Results: Total 79 patients (Malay 39%, Chinese 30.4%, Iban 17.7%, Bidayuh 12.7%) were identified from the databases. Median age at diagnosis was younger, 40, compared to developed countries due to population structure. M:F ratio was higher, 2.6:1 compared to other countries 1.3-1.7:1. Majority presented at chronic phase (89.5%), low/intermediate risk score (80%) and started imatinib (96%) as first line tyrosine kinase inhibitor (TKI), which 40% of them switched to other TKI due to intolerance (17%) and failure (including disease progression)/not achieving major molecular response (83%). Quantitative polymerase chain reaction (qPCR) assessment after three months of TKI treatment had higher positive predictive value to predict Imatinib failure, 75%, than qPCR assessment after six months of TKI treatment, 58%. Presenting phase, symptoms, signs and laboratory data were like most countries. Estimated prevalence and incidence of CML in southern Sarawak was 69.2/1,000,000 population at the Year 2016 (similar to most developing countries) and 8.0/1,000,000 population per year at the Year 2011-2016 (similar to most countries), respectively. The incidence increased with age and was lowest among Iban, 12.8 and highest among Chinese, 19.5, which was 4x higher than Chinese in China. The prevalence of different *BCR-ABL1* transcript type was like other Asia countries

Conclusion: Significant epidemiological differences on M:F ratio and ethnic groups compared to other countries warrant further study.

KEY WORdS:
CML, BCR-ABL1, tyrosine kinase inhibitor, epidemiology, Malaysia, Asia

INTRODUCTION

Chronic myeloid leukaemia (CML) is a myeloproliferative neoplasm that originated in an abnormal pluripotent bone marrow (BM) stem cell and is consistently associated with the *BCR-ABL1* fusion gene located in the Philadelphia (Ph) chromosome.[1] Philadelphia chromosome is the derivative chromosome 22 resulting from the translocation between the long arm of chromosomes 9 and 22, designated as t(9;22)(q34.12;q11.23). On chromosome 9, the *v-abl Abelson murine leukaemia viral oncogene homolog 1* (*ABL1)* gene breaks, usually at the intron between exon 1a and exon a2 or between exon a2 and exon a3. On chromosome 22, the *breakpoint cluster region* (*BCR*) gene breaks, usually at a region called major breakpoint cluster region (M-BCR), i.e., the intron between exon e13 and e14 or exon e14 and e15, which after translocation fused with *ABL1* gene (at the exon a2 or exon a3) and remaining part from chromosome 9, resulting in a fusion gene, *BCR-ABL1* (e13a2, e13a3, e14a2 or e14a3), which produce 210 kilodalton protein, designated as $p210^{BCR\text{-}ABL1}$. Much less found in CML, when *BCR* gene breaks at minor breakpoint cluster region (m-BCR) or micro breakpoint cluster region (μ-BCR), it would result in a fusion gene, *BCR-ABL1* (e1a2 or e1a3) or *BCR-ABL1* (e19a2 or e19a3), which produce 190 or 230 kilodalton protein, designated as $p190^{BCR\text{-}ABL1}$ or $p230^{BCR\text{-}ABL1}$, respectively.[2] These proteins were an abnormal kinase, Tyrosine Kinase, that apparently was the stimulant for the proliferation of myeloid cells to produce CML.

The first Tyrosine Kinase Inhibitor (TKI), Imatinib (Glivec® or Gleevec®, Novartis Pharmaceuticals Corporation), was approved by the United State Food and Drug Administration at 2001.[3] The invent of TKI has changed the paradigm of CML treatment and revolutionised the direction of oncology. Secondary (Nilotinib, Tasigna®, Novartis Pharmaceuticals Corporation; Dasatinib, Sprycel®, Bristol-Myers Squibb) and third generation TKI (Bosutinib, Bosulif®, Pfizer Inc.; Ponatinib, Iclusig®, ARIAD Pharmaceuticals, Inc.) are now available for clinical use. In Malaysia, Imatinib was available starting around 2000 under trial. Later, majority of patients from hospital in Ministry of Health (MOH), Ministry of Higher Education (MOHE) or private sector received Imatinib free of charge via Glivec International Patient Assistance Program (GIPAP), which officially started in 2003 and managed by Max Foundation (MF), a non-profit cancer organisation (personal communication with Dr Ong Tee Chuan). Very minority self-purchased Imatinib, which the cost per month was around two times of the 2014 median monthly household income.[4] Imatinib supply for patients in MOH hospitals experienced smooth transition on 29th Nov 2007 from GIPAP to Malaysia Patient Assistance Program (MYPAP), which meant Malaysia's

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government purchased and supplied Imatinib to patients free of charge. Starting 1st November 2016, GIPAP in MOHE hospitals and private sectors was terminated (personal communication with MF, Malaysia). Hence, most of the patients received Imatinib from GIPAP previously and newly diagnosed patients were referred to MOH hospital to get Imatinib supply under MYPAP. After registered in Malaysia, Nilotinib entered into MOH formulary, which means medications are supplied to the patient free of charge, as a second and first line starting 2011 and 2014, respectively (personal communication with Novartis Pharmaceuticals Corporation). At the time of writing, Dasatinib was not accepted in MOH formulary, while Bosutinib and Ponatinib were not registered in Malaysia. Dasatinib direct import program, free of charge supply was first applied by Malaysia in 2011 and still opened until the time of writing. Bosutinib compassionate use program (CUP) for Malaysia was available for new case application from 2013 until the end of June 2015 and the existing patients still received CUP supply at the time of writing. Ponatinib CUP is available via MF, Malaysia starting 2016 till the time of writing, but the number of access to this drug fixes, which meant it is only available when there was existing patient left the program (personal communication with Bristol-Myers Squibb, Pfizer (Malaysia) Sendirian Berhad and MF). Because of the above scenario of TKI in Malaysia, at the time of writing, the majority of CML patients in Malaysia and almost all CML patients in Sarawak receive TKI treatment in MOH hospitals.

To our knowledge, there are limited epidemiological data of the CML patients in West Malaysia[5-7] and none from East Malaysia, which has different ethnicity distribution and less accessible to advance laboratory facility compared to West Malaysia. Sarawak, "Land of Hornbill", has a population of 2.35 million citizens according to census of 2010[8], with 27 ethnic groups,[9] of which the major ethnic groups are the Iban (the biggest group of Dayak, i.e. Sarawak natives), Malays, Chinese, and other Dayaks like Bidayuh, Orang Ulu and Melanau as well as several other minor ethnic groups, each boasting a distinctive culture, language and lifestyle. Our study aimed to study the epidemiology of CML patients seen by Adult Haematologist in Sarawak General Hospital (SGH) and compared it to the other areas.

MATERIALS AND METHODS

This is a cross-sectional study conducted at SGH after receiving approval from Medical Research and Ethics Committee, MOH (Identification No.: NMRR-16-1969-32122). The study period was from 9th Jan to 6th Mar 2017. The study population was CML patients seen by the Adult Haematologist in SGH. The disease status of patients was taken as per 6th Mar 2017.

The list of CML patients was generated after compiling all the CML patients ever attending Medical Daycare and Haematology Clinic from the database at Medical Daycare (created since 2011) and Haematology Clinic (created since 2013), SGH, respectively. The medical records of all the patients were traced according to hospital procedure and reviewed. Laboratory data was gathered from formal peripheral blood reports, handwritten documentation for older records and available SGH's laboratory archives.

Relevant institutions were contacted to acquire information that was missing in the record. Required information was extracted using a standard prepared proforma, which gathered data on patient demographics, symptoms, signs and investigation results during the presentation, treatment and disease monitoring. If documentation of symptoms during the presentation was not found or inadequate, a face to face interview using prepared patient questionnaires would be conducted after getting a signed consent if the patients had follow-up appointment during data collection period. If not, a phone interview using the prepared patient questionnaire would be conducted after getting a verbal consent. If the distance in cm of the spleen below costal margin was unavailable, the reported distance based on ultrasound or CT scan reports will be recorded.

Three baseline prognostic-scoring systems (prior to any treatment) – Sokal score,[10] Hasford score[11] and European Treatment and Outcome Study (EUTOS) score[12] - were used to predict response to TKI and outcome because there was no single scoring system that was proven superior to others.

Definition of disease phase - chronic phase (CP), accelerated phase (AP) and blast crisis (BC) - followed World Health Organization classification 2008.[1] Categorisation of treatment response followed the European LeukemiaNet (ELN) guideline 2013.[13]

The Statistical Package for Social Science (SPSS) 24 software was used for entering and cleaning data and for relevant statistical analysis. With the use of descriptive statistics, patient demographics, clinical characteristics, treatment modalities and disease monitoring was analysed.

RESULTS

A total of 79 patients was identified from the databases. All referred medical records over the follow-up period were handwritten.

Demography

The age at CML diagnosis and gender of our cohort was shown in Figure 1 (a). The median (range) age at diagnosis in our cohort was 40 (10-71) years.

The prevalence of CML among different ethnic groups was roughly corresponded to population distribution of the five divisions, Malay 39% (population 18%), Chinese 30.4% (population 13%), Iban 17.7% (population 10%) and Bidayuh 12.7% (population 8%).

CML Phase and Presenting Symptoms, Signs and Prognostic Risk Scores

Out of 76 patients who had documentation on presenting full blood picture (FBP) and BM finding, 89.5%, 6.6% and 3.9% presented in CP, AP and BC, respectively. The available data on presenting symptoms, signs and prognostic risk scores of the cohort were shown in Table I. Despite the different formula, all three prognostic scoring methods showed about 20% of patients had a high-risk disease at presentation.

Table I: Presenting symptoms, signs (hepatosplenomegaly) and prognostic scores of Chronic Myeloid Leukaemia patients seen by Adult Haematologist at Sarawak General Hospital

	Frequency (n)	Percentage (%)
Symptoms (N = 73)		
Asymptomatic	11	15.1
Loss of weight	33	45.2
Abdominal swelling/mass	25	34.2
Fever	17	23.3
Lethargy	17	23.3
Loss of appetite	15	20.5
Flu-like symptoms[1]	12	16.4
Abdominal discomfort	10	13.7
Headache, dizziness	7	9.6
Bleeding symptoms[2]	6	8.2
Night Sweats	4	5.5
Blurred vision	3	4.1
Feeling unwell	2	2.7
Enlarged lymph nodes	3	4.1
Auditory symptoms[3]	2	2.7
Palpitations	1	1.3
Priapism	1	1.3
Signs (N = 60)		
Palpable Spleen	40	66.7
Spleen not Palpable	20	33.3
Palpable Liver	18	30.0
Sokal risk score (N = 51)		
Low <0.8	18	35.3
Intermediate 0.8-1.2	24	47.1
High >1.2	9	17.6
Hasford risk score (N = 49)		
Low ≤780	21	42.9
Intermediate 781-1480	19	38.8
High >1480	9	18.4
EUTOS risk score (N = 50)		
Low ≤87	41	82.0
High >87	9	18.0

[1] Flu symptoms include dry cough, chills, runny nose and myalgia.
[2] Bleeding symptoms were rectal bleeding, occasional nosebleeds, gum bleeding after tooth extraction and retinal bleeding leading to blurred vision respectively.
[3] Auditory symptoms include acute sensorineural deafness or tinnitus.

Laboratory Data

The available data on the presenting laboratory findings (normal value was based on West Malaysia population),[14] cytogenetics and molecular study was shown in Table II. There was a patient, only hand-written note available, had normal presenting cytogenetic and no fluorescence in-situ hybridisation (FISH) result due to inadequate sample. After one and a half year waiting for the cytogenetic and FISH result, this patient was finally started on TKI after polymerase chain reaction (PCR) send to Singapore showed the presence of *BCR-ABL1* and later cytogenetic showed the presence of Ph chromosome. We felt the normal presenting cytogenetic was a false negative result. We still report the normal presenting cytogenetic because that was the only documentation available. The additional presenting cytogenetic abnormality in two patients was a loss of Y chromosome and extra der(22)t(9;22).

The presence of BCR-ABL1 and other gene abnormality was detected in two patients. The first patient had both M-BCR and m-BCR and ETV-ABL1, which was detected by multiplex PCR containing 28 common translocations in acute leukaemia. The concomitant presence of BCR-ABL1 and ETV-ABL1 in CML is very rare.15 Cytogenetic revealed Ph chromosome, but no FISH test was done. The other patient had b3a2 and JAK2V617F mutation, which was detected later after diagnosis because of the persistent thrombocytosis despite good BCR-ABL1 molecular response with TKI. We decided to include the JAK2V617F mutation as the presenting molecular abnormality because we felt the abnormality would present during the presentation (platelet count during the presentation was 944 x 109/L) and this was a rare case.

Treatment, Disease Response, Outcomes

All patients were started on TKI (Imatinib, n=69, Nilotinib, n=3) except six patients, who defaulted treatment after diagnosis or followed up elsewhere, and one patient, a 52-year-old lady presented in AP and progressed to BC within few months, was put on palliative treatment. All patients, except one who was in Malaysia Stop TKI Trial (National Medical Research Registry Identifier: NMRR-13-1186-15491, ClinicalTrials.gov Identifier: NCT02381379), were put on indefinite TKI treatment unless patient refused, defaulted or had medication intolerance.

After excluding patients who defaulted or follow-up at other centre, 24 out of 60 (40%) patients, who were initial on Imatinib, were switched to Nilotinib due to disease progression to AP or BC (n=11), Imatinib failure (n=8), not

Table II: Laboratory findings at first presentation of Chronic Myeloid Leukaemia Patients seen by Adult Haematologist at Sarawak General Hospital

Haematological findings	Frequency (n)	Percentage (%)
Haemoglobin, g/dL		
Males (N = 50)		
<7.0	7	14.0
7.0-13.4	40	80.0
13.5-17.4*	3	6.0
>17.4	0	0
Females (N = 18)		
<7.0	1	5.6
7.0-11.5	13	72.2
11.6-15.1*	4	22.2
>15.1	0	0
Total white cell count $x10^9$/L (N = 73)		
<4.08	0	0
4.08-11.37*	1	1.4
11.38-50.00	15	20.5
50.01-100.00	13	17.8
100.01-300.00	34	46.6
300.01-500.00	8	11.0
>500	2	2.7
Platelet count $x10^9$/L (N = 71)		
<142	5	7.0
142-399*	16	22.5
400-1,000	41	57.7
>1,000	9	12.7
Absolute eosinophil count $x10^9$/L (N = 60)		
<0.5	5	8.3
0.5-1.4	12	20.0
1.5-2.9	8	13.3
3.0-5.0	10	16.7
>5.0	25	41.7
Absolute basophil count $x10^9$/L (N = 60)		
<0.2	6	10.0
≥0.2	54	90.0
PB blasts (%) (N = 66)		
<5	55	83.3
5-9.9	6	9.1
10-19.9	4	6.1
≥20	1	1.5
BM blasts (%) (N = 54)		
<5	47	87.0
5-9.9	7	13.0
10-19.9	0	0
≥20	0	0
Cytogenetics (N = 65)		
Ph chromosome	40	61.5
Ph chromosome & other abnormality	2	3.1
Ph chromosome negative Suboptimal	1	1.5
samples; no/short spread	22	33.8
FISH Studies (N = 11)		
Positive FISH	10	90.9
Inadequate FISH sample	1	9.1
Molecular Studies (N = 59)		
BCR-ABL1 present	49	89.1
M-BCR	44	89.7
b3a2	27	61.4
b2a2	9	20.5
b3a2 & b2a2	1	4.1
unknown	7	15.9
M-BCR & M-BCR	4	0.8
Unknown	3	0.6
BCR-ABL1 & other abnormality	2	3.6
Suboptimal samples	4	7.3

*based on the published normal range of West Malaysian population[14].
BM, bone marrow; FISH, fluorescence in-situ hybridization; M-BCR, major breakpoint cluster region; m-BCR, minor breakpoint cluster region; PB, peripheral blood; Ph, Philadelphia chromosome

Table III: Prevalence of types of BCR-ABL1 transcript in various countries

	N, (%)						
	M-BCR	**b3a2**	**b2a2**	**b3a2 & b2a2**	**m-BCR**	**µ-BCR**	**Others**
Sarawak, Malaysia	44/48 (96)	27/37 (73)	9/37 (24)	1/37 (3)	0	0	M-bcr & m-bcr: 4/48 (8)
Korea[25]	538/548 (98)	364/538 (68)	174/538 (32)	2/538 (0.4)	2/548 (0.4)	4/548 (0.7)	b1a1: 1/548 (0.2) b2a3: 1/548 (0.2)
Thailand[26]		-/136 (73)	-/136 (27)				
Serbian[27]	135/136 (99)	100/135 (74)	34/135 (25)	1/135 (0.7)	1/136 (0.7)	0	0
Mexico[28,29]		-/654 (44)	-/654 (49)	-/654 (7)	24/250 (10)		
Iran[30]	64/75 (85)	47/64 (73)	15/64 (23)	2/64 (3)	1/75 (1)	3/75 (4)	b3a3/b2a3: 7/75 (9)

M-BCR, major breakpoint cluster region; m-BCR, minor breakpoint cluster region; µ-BCR, micro breakpoint cluster region

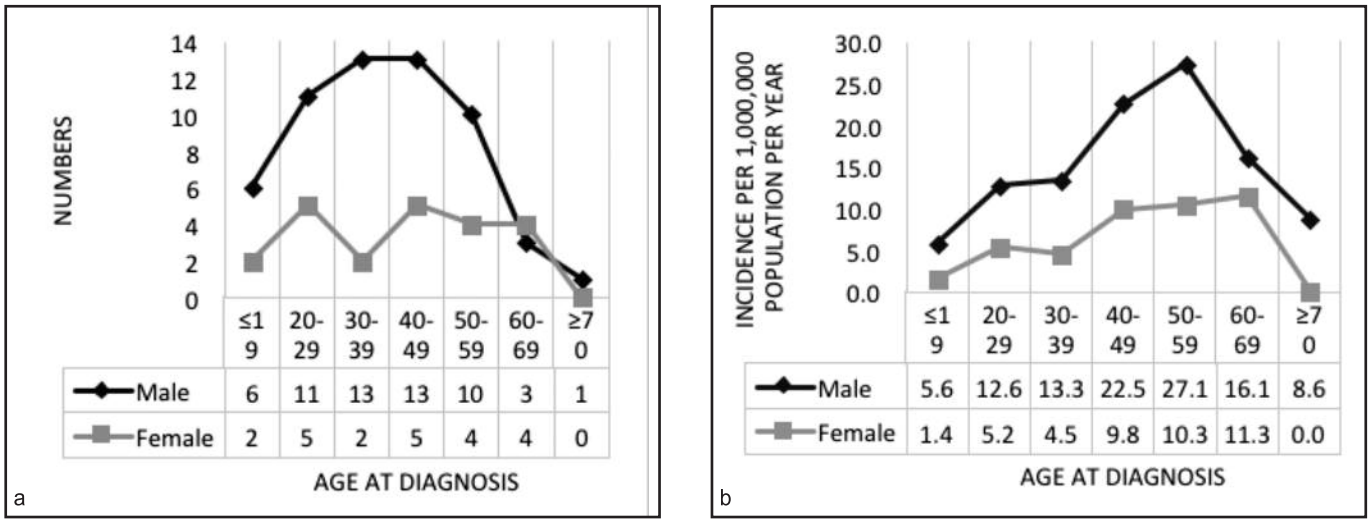

Fig. 1: (a) number of Chronic Myeloid Leukaemia patients seen by Adult Haematologist[1] at Sarawak General Hospital according to gender and age at diagnosis[2], (b) estimated incidence of Chronic Myeloid Leukaemia patients according to gender and age group in 2011 – 2016 based on population census 2010 (assuming the ratio of population in the five divisions of Sarawak was constant across gender and age group).

[1]Adult Haematologists in Ministry of Health see patients age of 12 or above, unless patients were diagnosed at age less than 12 and Paediatricians continue to follow-up the patients after age of 12 or certain cases, for example like Acute Lymphoblastic Leukaemia age 12-15, were treated by Paediatricians after arrangement between Adult Haematologists and Paediatricians. Imatinib and Nilotinib was not recommended in children aged under one and 18, respectively due to lack of data.

[2]Age at diagnosis <12 (N = 3) and 12-17 (N = 3).

achieving major molecular response (MMR) (n=1) and Imatinib intolerance (n=4). Five of these patients were eventually switched to third or fourth TKI, Dasatinib, Bosutinib or Ponatinib. The first patient was diagnosed as a paediatric patient with failed CCyR after 16 months on her first TKI, detected E255K mutation, and now continues to exhibit borderline molecular response with Dasatinib as her fourth TKI. The second and third patient with Y253H mutation achieved optimal response (<10%) within three months of Dasatinib and continued to improve. The fifth, detect E459K mutation and achieved molecular response (<1.0%) within six months of Bosutinib and continued to improve. The fifth patient with D276G and T315I mutation was just switched to Ponatinib during the time of data cleaning.

After excluding patients who died (n=4, three due to disease progression, one due to comorbid and old age of 71), follow-up at other centre (n=9) or defaulted (n=6), the median follow-up of the 60 patients alive and on follow-up was 51 months (range 5-273 months). Out of 62 patients with more than 1-year follow-up, 22.6% had PCR *BCR-ABL1/ABL1* level of 0.01% at International Scale (IS) or better, 27.4% had MMR, 24.2% had complete cytogenetic response or PCR less than 1% IS, 19.3% with only complete haematological response (CHR) (disease progression to AP while on Imatinib (n = 1), Imatinib failure (n = 8), non-compliance (n = 2) and post-transplant (n = 1)), 3.2% progressed to AP and defaulted and 3.2% progressed to BC and died.

Only one patient had undergone sibling-matched allogenic stem cell transplant in this cohort and, at the time of writing, on Nilotinib under follow-up at SGH. This patient was diagnosed at other MOH hospital with CML CP at the age of 15 and started on Imatinib 400mg OD. However, disease rapidly progressed to BC three months after the diagnosis. Cytogenetic after disease progression did not reveal other clonal abnormality besides Ph chromosome. Mutation analysis did not detect an abnormality.

There were 17 and 35 patients had qPCR results after three and six months of Imatinib treatment, respectively. The positive predictive value to predict Imatinib failure (including disease progression into AP/BC) using worse than optimal qPCR response after three months of Imatinib treatment was higher, 75%, compared to six months of Imatinib treatment, 58%.

DISCUSSION

The limitation of this study was the completeness of data. Patients who were diagnosed and died before 2012 and admitted to the ward but never seen in Medical Daycare or Haematology Clinic were not captured in this study. However, the number of patients with above situation was very low.

Local laboratory data for patients who were diagnosed before 2006 was frequently not available because of the missing records and laboratory archive system. The available facilities for diagnosis of CML using cytogenetics and qualitative PCR (mainly Institute of Medical Research) and quantitative PCR (mainly Ampang Hospital) were in West Malaysia, which warrants the transportation of patient samples by air, posts a continuous challenge on the transportation of samples and dispatch of the report resulting in missing data. Presenting FISH study was only done when cytogenetic study yielded no or short spread. Qualitative PCR was available much later (about 10 years) than cytogenetic study. Quantitative PCR was available starting 2009 and its reporting according to IS starting March 2010 and followed new recommendation[16] beginning 15th January 2016. The frequency of qPCR allowed for patients increase from only six monthly to the addition of three months after initiating a TKI and whenever deemed necessary starting 26th February 2013 (personal communication with Dr Subramanian Yegappan).

We did not include paediatric population (<12 years old) in our cohort because of our concern on the different epidemiology between paediatric and adult population. Nonetheless, the number of paediatric CML patients in SGH was not many, less than 10, with only three patients ≥12 years old and still follow-up under Paediatric Oncologist (personal communication with Dr Ong Gek Bee).

To our knowledge, there were only three publications on Malaysia's CML patients.[5-7] All three of them were from the same single MOHE hospital[5-7] and the same private hospital[5,6] in Kuala Lumpur and Selangor, West Malaysia. The finding in these articles could not confer the prevalence and incidence of CML in that area because there are other centres (two MOH hospitals and at least another one private centre at the time of writing), which follow-up majority of CML patients due to the reasons mentioned in Introduction. Whereas in our study, SGH is the only MOH hospital covers CML patients from five Divisions (Kuching, Samarahan, Serian, Sri Aman and Betong) with a population of 1.14 million citizen.[8] At the time of writing, there is only one private centre, which has CML patients on follow-up, but only with less than a handful, due to the reasons mentioned in Introduction. Hence, despite the above limitations, this study could give the overall epidemiology and real-world therapeutic outcome of CML patients in southern Sarawak, Malaysia, which was not reported before.

Chronic myeloid leukaemia is known to be commoner in the male. The sex difference in the incidence was suggested due to higher risk developing CML in male rather than a shorter latency from initiation to the diagnosis of CML and probably because the male has more target cells at risk to develop CML compared to female.[17] However, our cohort showed much higher M:F ratio, 2.6:1, compared to other Asia countries 1.5-1.7:1[18] and United State (Caucasian, African American and other races) 1.3-1.6:1.[19] We recalculated the ratio for patients diagnosed from 2011 onwards to eliminate the possible missing data, the ratio was still high, 2.7:1. This phenomenon warrants further epidemiological study inquiring into environmental influence like living area, dietary intake and occupational exposure. The median age at diagnosis of CML for a male was younger than female, 36.0 and 42.5, respectively. This finding was expected. However, the difference was not statistically significant likely due to small sample size.

The younger median age at diagnosis in our cohort, 40, was not of surprise, consistent with West Malaysia 44-48[6, 7] and other Asian countries, where the age at diagnosis is younger than Western or developed countries.[18,20,21] Iban group in our cohort showed even younger median age at diagnosis, 34, but we are aware of the limitation due to the small sample size. The younger age at diagnosis was likely because of the younger population in Sarawak and other Asian countries, as reflected by the incidence rate in Figure 1(b) after corrected by the number of population in that age group according to population census 2010.[8]

Based on our study and population census 2010,[8] the prevalence and incidence of CML in Sarawak was estimated at 69.2/1,000,000 population in 2016 and 8.0/1,000,000/year in 2011-2016, respectively. The prevalence is lower than European Union 200/1,000,00 population in 2012,[22] but higher than countries like Iran 29.8/1,000,000 population in 2006-2009. The incidence is similar to European 7-11/1,000,00 population in 2007-2011[23] and other Asia countries ranged 4-22/1,000,000 population,[18] but lower than the United State 17.5/1,000,000 population in 1975-2009.[24] The difference in prevalence was likely because of better survival in developed countries due to factors like availability of TKI treatment and better disease monitoring. The incidence of CML per 1,000,000 per year in 2011-2016 was different among the four ethnic groups, lowest among Iban 12.8 to the highest among Chinese 19.5. The incidence in our Chinese cohort was higher than Chinese in China, 3.9-5.5.[18] This difference among different ethnic groups and same ethnic among different region warrants further epidemiological study.

The prevalence of different *BCR-ABL1* transcript type in our cohort was most similar to Korean[25] and Thailand[26] compared to Serbian,[27] Mexican[28,29] and Iran,[30] as shown in Table III. The *BCR-ABL1* transcript type appeared did not affect the outcome in pre-TKI era,[31-35] but influenced the outcome when TKI is used[36-38] and related to different blood count parameters.[39,40] However, our cohort did not show difference, which might be due to small sample size.

In conclusion, our study provided the epidemiology and therapeutic outcomes of adult CML patients seen in a single centre, Borneo Sarawak, Malaysia with data in the Borneo natives that was not published before. Limitation in cytogenetic and molecular tests due to geographical reasons should be addressed in the future improvement in the care of patients with haematological tumours. There were significant epidemiological differences observed compared to another region, which warrants further study.

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