DEMOGRAPHY AND CLINICAL CHARACTERISTICS OF PATIENTS WITH MELIOIDOSIS IN HOSPITAL TAIPING, MALAYSIA

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INTRODUCTION

• Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*, an environmental bacterium found in soil and water in tropical regions.

*Burkholderia pseudomallei* are motile aerobic, non-spore forming gram negative bacilli.
Whitemore Disease

Burma/Myanmar 1912

Malaysia, Singapore 1913

Vietnam 1925

Indonesia 1929

(Whitmore A & Krishnaswami CS, 2012)
(Zueter AR et al., 2016)
History of Melioidosis

1913
- Fletcher & Stanton recognized the disease in laboratory animals at the Institute for Medical Research in Kuala Lumpur, Malaysia

1917
- Stanton at first described infection in a human from Kuala Lumpur

(Stanton AT & Fletcher W, 1932)
(Puthucheary SD, 2009)
OBJECTIVES of the STUDY

- **GENERAL OBJECTIVES:** To study the definitive cases of Melioidosis that had been admitted in any department of Hospital Taiping in the year of 2016 & 2017.

- **SPECIFIC OBJECTIVES:**
  - To determine the association between demographic characteristics & outcome of the patient with Melioidosis admitted in any department of Hospital Taiping in the year of 2016 & 2017.
  - To evaluate the association between clinical spectrum & outcome of the patient with Melioidosis admitted in any department of Hospital Taiping in the year of 2016 & 2017.
### Methodology

<table>
<thead>
<tr>
<th><strong>Study Design</strong></th>
<th>Cross sectional, Retrospective study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study Location</strong></td>
<td>Hospital Taiping, Perak, Malaysia</td>
</tr>
<tr>
<td><strong>Study Duration</strong></td>
<td>August 2017 to September 2018</td>
</tr>
<tr>
<td><strong>Study Population</strong></td>
<td>Definitive case of Melioidosis admitted in any department of Hospital Taiping in the year of 2016 &amp; 2017</td>
</tr>
<tr>
<td><strong>Source of Data</strong></td>
<td>Patient’s medical records of Hospital Taiping.</td>
</tr>
<tr>
<td><strong>Sample Size</strong></td>
<td>43 &amp; 54 patients were diagnosed as definitive case of Melioidosis in Hospital Taiping in the year of 2016 &amp; 2017 respectively. Therefore our sample size is 97.</td>
</tr>
<tr>
<td><strong>Data Collection</strong></td>
<td>Data was collected in a formulated data sheet</td>
</tr>
</tbody>
</table>
Study Subject Enrolment

Inclusion Criteria

- A confirmed diagnosed patient of Melioidosis based on case definition.

Case Definition of Melioidosis

- Positive culture of Gram negative bacillus, *Burkholderia pseudomallei* from blood, other fluid (pus, wound swab, urine, CSF) or sputum sample

  And or

- Fourfold or greater rise in *Burkholderia pseudomallei* antibody by indirect immunofluorescence antibody test (IFAT)

  And or

- *Burkholderia pseudomallei*-specific PCR positive from any biological sample
Study Subject Enrolment

Exclusion Criteria

- Clinical setting consistent with Melioidosis but

- Negative culture of *Burkholderia pseudomallei* from blood, other fluid (pus, wound swab, urine, CSF) or sputum sample

- Less than fourfold rise in titre in *Burkholderia pseudomallei* antibody by IFAT.
Data Collection Tool

Descriptive Demography
- Age
- Gender
- Place of Living
- Department admitted
- Hospital Stay

Clinical Spectrum
- Clinical Presentation
- Diagnosis

Study End Points
- Good Outcome
- Morbidity
- Mortality
The Study Endpoint

Good Outcome

- Resolution of all clinical features
- Repeat culture of *Burkholderia pseudomallei* from samples are negative
- Antibody titer of *Burkholderia pseudomallei* decreasing to normal (titer <1:80)

Bad Outcome

- The study subjects who developed complications
  And or
- The study subjects shifted to ICU for the complications of Melioidosis.
  And or
- Death of study subjects

Results of the consequence Melioidosis infection in the study subjects that can be measured objectively and will be described in terms of complete recovery, morbidity and mortality.
<table>
<thead>
<tr>
<th></th>
<th>Quantitative</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Descriptive</strong></td>
<td><strong>statistic</strong></td>
<td>Frequency, Percentage, Median</td>
</tr>
<tr>
<td><strong>Inferential</strong></td>
<td><strong>statistic</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Pearson’s Chi square</strong></td>
<td>To determine the association of two categorical or qualitative variables</td>
</tr>
</tbody>
</table>
Ethical approval was obtained from University Research Ethics Committee of QUIP.

The study protocol was approved by the Medical Research & Ethics Committee (MREC) of the Ministry of Health (MOH), Malaysia via the National Medical Research Register (NMRR). [NMRR ID: 17-1322-36608]

Data collected were solely for research purposes. Their information was remained strictly confidential.
Ethical Consideration

Dr Umadevi A. Muthukumaru
Hospital Taiping

Dato' / Tuan / Puan,

SURAT KELULUSAN ETIKA:

NMMR-17-1322-36658 (ER)

No Protocol : NA

1. The Socio-demographic, Clinical and Laboratory Characteristics of Melioidosis in Hospital Taiping, Malaysia: Year 2016

Lokasi Kajian: HOSPITAL TAIPING

Dengan hormatnya perkara di atas adalah dirujuk.

2. Jawatankuasa Etika & Penyelidikan Perubatan (JEPP), Kementerian Kesihatan Malaysia (KKM) tiada halangan, dari segi etika, ke atas pelaksanaan kajian tersebut. JEPP mengambil masuk bahawa kajian tersebut hanya melibatkan pengumpulan data melalui:

I. Data Sekunder

3. Segala rekaan dan data subjek adalah SUAM dan hanya digunakan untuk tujuan kajian ini dan semua isi serta prosedur mengenai data confidentiality mestilah dipatuhi.

4. Kenberian daripada Pegawai Kesihatan Daerah / Pengurusan Hospital dan Kesel-Kesel dysfunctional kajian atau pengawal yang bertanggungjawab disetop lokasi kajian di mana kajian akan dilakukan mestilah diperoleh sebelum kajian dijalankan. Dato' / Dr / Tuan / Puan perlu asur dan mematuhi keputusan tersebut. Sila rujuk kepada surat perundangan Kementerian Kesihatan Negara mengenai penyelidikan di Institut dan fasiliti Kementerian Kesihatan Malaysia (Pindaan 01/2015) serta lampiran Appendix 5 untuk tempat surat menunjuk kebenaran tersebut.


   i. Continuing Review Form selepas-lawatnya dalam tempoh 1 bulan (30 hari) sebelum tamat tempoh kelulusan ini bagi memperbaharui kelulusan etika.
   ii. Study Final Report pada penghujung kajian.

Reference Number: RCF/05/010/2017-3

27th October 2017

Title of the Project: The Socio-demographic, Clinical and Laboratory Characteristics of Melioidosis in Hospital Taiping, Malaysia in the year of 2016.

Principal Investigator: Assoc. Prof. Dr. Mohd. Shahril Hanif Kassim,
Department of Medicine,
Faculty of Medicine.

The proposal has been reviewed by the Research Ethics Committee of the faculty of Medicine, Quest International University Perak. After careful consideration of all points from Research Ethics view point, the Committee has approved the above research project.

The standard conditions of this approval are:

a) The ethical aspects of the project will be reviewed from time to time.
   b) The conduct of the project should be in accordance with proposal submitted as well as the granted ethical approval.
   c) The timeframe should be informed in writing if there are any changes in the project.

Thank you,

[Signature]

Assoc. Prof. Dr. Shahril Hanif Kassim
Chairman
Research Ethics Committee
Faculty of Medicine
Quest International University Perak
RESULTS & OBSERVATIONS
Distribution of Study Population by Age & Gender

<table>
<thead>
<tr>
<th>Age Group</th>
<th>n</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40 yrs</td>
<td>14</td>
<td>14.4%</td>
</tr>
<tr>
<td>40-60 yrs</td>
<td>49</td>
<td>50.5%</td>
</tr>
<tr>
<td>&gt; 60 yrs</td>
<td>34</td>
<td>35.1%</td>
</tr>
</tbody>
</table>

Mean Age ± SE 54.86 ± 1.365
Patient’s Distribution by Race & Department

- Malay: 78%
- Indian: 13%
- Chinese: 9%

Mean Hospital Stay ± SE: 13.19 ± 1.463
Range (Min-Max): 1 – 84 days
Geographical Distribution of Study Population

From 3 States

1

4

92
## Geographical Distribution of Study Population

<table>
<thead>
<tr>
<th>DISTRICT</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kerian</td>
<td>38</td>
<td>39.2</td>
</tr>
<tr>
<td>Larut Dan Matang</td>
<td>33</td>
<td>34.0</td>
</tr>
<tr>
<td>Kuala Kangsar</td>
<td>10</td>
<td>10.3</td>
</tr>
<tr>
<td>Selama</td>
<td>5</td>
<td>5.2</td>
</tr>
<tr>
<td>Hulu Perak</td>
<td>4</td>
<td>4.1</td>
</tr>
<tr>
<td>Hilir Perak</td>
<td>2</td>
<td>2.1</td>
</tr>
<tr>
<td>Bandar Baharu</td>
<td>4</td>
<td>4.1</td>
</tr>
<tr>
<td>Seberang Perai Selatan</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

From 8 Districts:
Geographical Distribution of Study Population

Top 5 among 22 Towns

Bagan Serai: 16
Kamunting: 13
Parit Buntar: 9
Taiping: 7
Kuala Kangsar: 6
<table>
<thead>
<tr>
<th>CLINICAL PRESENTATION</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>86</td>
<td>88.7</td>
</tr>
<tr>
<td>Cough</td>
<td>46</td>
<td>47.4</td>
</tr>
<tr>
<td>Shortness of Breath</td>
<td>31</td>
<td>32</td>
</tr>
<tr>
<td>Skin &amp; Soft tissue Infection</td>
<td>29</td>
<td>29.9</td>
</tr>
<tr>
<td>Headache</td>
<td>15</td>
<td>15.5</td>
</tr>
<tr>
<td>Vomiting</td>
<td>14</td>
<td>14.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CLINICAL PRESENTATION</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea</td>
<td>8</td>
<td>18.6</td>
</tr>
<tr>
<td>Joint Pain &amp; Swelling</td>
<td>7</td>
<td>7.2</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5</td>
<td>5.2</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>5</td>
<td>5.2</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>3</td>
<td>3.1</td>
</tr>
<tr>
<td>Dysuria</td>
<td>2</td>
<td>2.1</td>
</tr>
</tbody>
</table>
## Distribution of Study Population by Diagnosis

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>45</td>
<td>46.4</td>
</tr>
<tr>
<td>Septicaemia</td>
<td>77</td>
<td>79.4</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>43</td>
<td>44.3</td>
</tr>
<tr>
<td>Abscess</td>
<td>15</td>
<td>15.5</td>
</tr>
<tr>
<td>Septic Arthritis</td>
<td>8</td>
<td>8.2</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>7</td>
<td>7.2</td>
</tr>
<tr>
<td>Carbuncle</td>
<td>4</td>
<td>4.1</td>
</tr>
<tr>
<td>Ulceration</td>
<td>4</td>
<td>4.1</td>
</tr>
</tbody>
</table>
## Outcome of the Study Population

<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good Outcome</td>
<td>23</td>
<td>23.7</td>
</tr>
<tr>
<td>Morbidity</td>
<td>24</td>
<td>24.7</td>
</tr>
<tr>
<td>Mortality</td>
<td>50</td>
<td>51.5</td>
</tr>
</tbody>
</table>
# Association between Patient’s Age & the Outcome

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Good Outcome</th>
<th>Morbidity</th>
<th>Mortality</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n  %</td>
<td>n  %</td>
<td>n  %</td>
<td></td>
</tr>
<tr>
<td>&lt; 40</td>
<td>9 64.3</td>
<td>2 14.3</td>
<td>3 21.4</td>
<td>0.001**</td>
</tr>
<tr>
<td>40 – 60</td>
<td>5 10.2</td>
<td>14 28.6</td>
<td>30 61.2</td>
<td></td>
</tr>
<tr>
<td>&gt; 60</td>
<td>9 26.5</td>
<td>8 23.5</td>
<td>17 50.0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>Good Outcome</th>
<th>Morbidity</th>
<th>Mortality</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n  %</td>
<td>n  %</td>
<td>n  %</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>15 22.4</td>
<td>15 22.4</td>
<td>37 55.2</td>
<td>0.05*</td>
</tr>
<tr>
<td>Female</td>
<td>8 26.7</td>
<td>9 30.0</td>
<td>13 43.3</td>
<td></td>
</tr>
</tbody>
</table>

Data were analysed using Pearson Chi-Square ($\chi^2$) Test

* Significance at 1% level; ** Significance at 5% level
# Association Between Race & Outcome

<table>
<thead>
<tr>
<th>Race</th>
<th>Good Outcome</th>
<th>Morbidity</th>
<th>Mortality</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>13 17.1</td>
<td>21 27.6</td>
<td>42 55.3</td>
<td>0.038*</td>
</tr>
<tr>
<td>Chinese</td>
<td>5 55.6</td>
<td>2 22.2</td>
<td>2 22.2</td>
<td>0.038*</td>
</tr>
<tr>
<td>Indian</td>
<td>5 41.7</td>
<td>1 8.3</td>
<td>6 50.0</td>
<td></td>
</tr>
</tbody>
</table>

Data were analysed using Pearson Chi-Square ($\chi^2$) Test

* Significance at 1% level; ** Significance at 5% level
## Association Between Diagnosis & Outcome

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Good Outcome</th>
<th>Morbidity</th>
<th>Mortality</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>5 11.1</td>
<td>9 20.0</td>
<td>31 68.9</td>
<td>0.004*</td>
</tr>
<tr>
<td>Septicaemia</td>
<td>12 15.6</td>
<td>18 23.4</td>
<td>47 61.0</td>
<td>0.000**</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>0 0.0</td>
<td>6 14.0</td>
<td>37 86.0</td>
<td>0.000**</td>
</tr>
<tr>
<td>Septic Arthritis</td>
<td>2 25.0</td>
<td>2 25.0</td>
<td>4 50.0</td>
<td>0.995</td>
</tr>
<tr>
<td>UTI / Genitourinary Infection</td>
<td>0 0.0</td>
<td>1 25.0</td>
<td>3 50.0</td>
<td>0.123</td>
</tr>
<tr>
<td>Skin &amp; soft tissue Infection</td>
<td>14 48.3</td>
<td>8 27.6</td>
<td>7 24.1</td>
<td>0.000**</td>
</tr>
</tbody>
</table>

Data were analysed using Pearson Chi-Square ($\chi^2$) Test

* Significance at 1% level; ** Significance at 5% level
Presently, Melioidosis is endemic in Malaysia (How SH et al., 2005 and Puthucheary SD et al., 1992), Thailand (Suputtamonkol Y, 1994), Singapore (Heng BH et al., 1998) and Australia (Currie BJ 2000).

In Perak it is already a notifiable disease.

Melioidosis is a disease involving all age groups but commonly occurs in the ages of 40 to 60 years and is related to farming (Guidelines for clinical and public health management of melioidosis in Pahang). [50.5% in our study]

The incidence of Melioidosis among male and female in Malaysia the M: F ratio was found to be 3.2:111 (Puthucheary SD, 2009). [Male (n=69%) & 55.2% mortality in our study]
Considering morbidity of Melioidosis among ethnic differences, studies show highest rate in Indians and then Chinese and then Malays (Puthucheary SD, 2002). [Malay:Indian:Chinese = 55.3:50:22.2% in our study]

The lung is the most frequently (50%) affected organ, presenting with fever, cough with purulent sputum with or without haemoptysis and fever because of pneumonia. (Chaowagul W et al., 1989). [n=46.4% & 68.9% mortality in our study]

In Pahang, the overall mortality rate was 54% (How SH et al., 2005 and Currie BJ 2000). [51.5% in our study]
Limitation of the Study

- Single centre study
- Following demographic characteristics were not documented –
  - Occupation
  - Source of infection
  - Socio-economic status
Suggestion for future Researcher

- Should consider multi-centre study with large sample size

- Should consider to document the following demographic characteristics in the study –
  - Occupation
  - Source of infection
  - Socio-economic status

- Should consider meta analysis
Implication of the Findings of the Present Study

Ministry / National Level
- Awareness program & provision of funding
- Guideline update, implication & monitoring

State / Hospital Level
- Arrangement of training among the doctors
- Establishment of Melioidosis ward in hospital

Physician Level
- Initiatives for appropriate treatment protocol
- Emphasize on early diagnosis & prevention of complications

Public Level
- Awareness about the source of infection
- Knowledge about the spectrum of disease
References


• Guidelines for clinical and public health management of melioidosis in Pahang.

• Guidelines for clinical and public health management of melioidosis in Sabah, 2014.


• Tan APA, Pui MH, Tan LKA. “Imaging patterns in melioidosis. Aust Radiol 1995; 39: 260-


Acknowledgement

1. Hospital Taiping authorities
2. CRC Hospital Taiping
3. Faculty of Medicine, QIUP
4. Dr Sandheep Sugathan, Senior Lecturer, Department of Public Health, UniKL, RCMP
5. Mr. Shanta Kumar A/L Chandrasekaran, FoM, QIUP
THANK YOU