KNOWLEDGE, ATTITUDE, AND PRACTICE (KAP) QUESTIONNAIRE ON MELIOIDOSIS: DEVELOPMENT AND VALIDATION AND ASSOCIATED FACTORS AMONG FIELD AGRICULTURAL FARMERS IN KELANTAN, MALAYSIA

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by

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In the name of ALLAH, the Most Beneficent and the Most Merciful. Salutations upon His messenger Muhammad S.A.W (peace be upon him), his family, and his companions. Alhamdulillah, I am deeply grateful to Allah SWT for granting me the opportunity of completing this research.

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LIST OF SYMBOLS

%	percent
=	equal to
≥	more than and equal to
≤	Less than and equal to
>	more than
<	less than
α	alpha
β	beta
p	p-value
r	Pearson correlation coefficient
R^2	coefficient of determination
χ^2	chi square
n	number of observations

LIST OF ABBREVIATIONS

AMEE	Association for Medical Education in Europe
AVE	Average variance extracted
B. pseudomallei	*Burkholderia pseudomallei*
CDC	Communicable Disease Center
CFA	Confirmatory Factor Analysis
CFI	Comparative fit index
CI	Confidence Interval
CR	Composite reliability
CVI	Content Validity Index
DoA	Department of Agriculture
FVI	Face Validity Index
I-CVI	Item- level content validity index
I-FVI	Item- level face validity index
IQR	Interquartile range
KADA	Kemubu Agricultural and Development Authority
KAP	Knowledge, attitude and practice
KMO	Kaiser-Meyer-Olkin
MI	Modification indices
ML	Maximum likelihood
MLR	Robust maximum likelihood estimator
MOH	Ministry of Health
NHMS	National Health Morbidity Survey
PAF	Principal Axis Factoring
RMSEA	Root mean square error of approximation
SAGE	Strategic Advisory Group Experts
S-CVI	Scale-level content validity index
SD	Standard deviation
S-FVI	Scale-level face validity index
SPSS	Statistical package for social sciences
SRMR	Standardised root mean square residual
TLI	Tucker-Lewis index
WHO	World Health Organization

LIST OF APPENDICES

SOAL SELIDIK PENGETAHUAN, SIKAP, DAN AMALAN (KAP) MENGENAI MELIOIDOSIS: PEMBANGUNAN DAN PENGESAHAN SERTA FAKTOR-FAKTOR YANG BERKAITAN DALAM KALANGAN PETANI LAPANGAN DI KELANTAN, MALAYSIA

ABSTRAK

Latar Belakang: Melioidosis, disebabkan oleh bakteria *Burkholderia pseudomallei*, merupakan kebimbangan kesihatan awam yang signifikan di Malaysia. Ini terutamanya dalam kalangan petani di lapangan yang menghadapi peningkatan risiko pendedahan disebabkan oleh aktiviti pekerjaan mereka. Walau bagaimanapun, terdapat kekurangan soal selidik yang disahkan untuk menilai pengetahuan, sikap, dan amalan (KAP) mengenai melioidosis serta kajian berkaitan faktor yang berkaitan KAP dalam kalangan petani.

Objektif: Kajian ini bertujuan untuk membangunkan dan mengesahkan soal selidik baru yang menilai KAP terhadap melioidosis dalam kalangan petani lapangan di Kelantan, Malaysia. Ia juga bertujuan untuk menentukan skor KAP dan faktor-faktor yang berkaitan dengannya.

Kaedah Kajian: Kajian ini dijalankan bermula Mei 2023 sehingga Mac 2024. Ia dilakukan dalam dua fasa. Dalam Fasa 1, soal selidik KAP dibangunkan dan disahkan melalui proses yang ketat melibatkan kajian gelintaran kesusasteraan, pengesahan kandungan, pengesahan muka, teori respons item (IRT), analisis penerokaan faktor (EFA), dan analisis pengesahan faktor (CFA). Soal selidik tersebut melibatkan 432 orang petani lapangan di Kelantan (222 untuk EFA, 210 untuk CFA). Dalam Fasa 2, satu kajian rentas-seksional dijalankan dalam kalangan 392 petani untuk menilai skor KAP mereka dan mengenal pasti faktor-faktor yang

berkaitan menggunakan soal selidik yang disahkan. Analisis IRT, EFA dan CFA menggunakan R software manakala analisis untuk faktor berkaitan KAP menggunakan SPSS versi 26.

Keputusan: Soal selidik KAP melioidosis yang baru dibangunkan, dinamakan M-KAP, terdiri daripada 65 item yang menunjukkan kebolehpercayaan kandungan yang sangat baik (S-CVI/Ave:0.97 untuk pengetahuan, 0.96 untuk sikap, 0.99 untuk amalan) dan kebolehpercayaan muka yang baik (S-FVI/Ave:0.997 untuk pengetahuan, 0.95 untuk sikap, 1.0 untuk amalan). IRT, EFA, dan CFA mengesahkan kebolehpercayaan dan keabsahan konstruk soal selidik dengan analisis menunjukkan julat kesukaran dan diskriminasi yang berpatutan dalam IRT, konsistensi dalaman yang boleh dipercayai dengan nilai alfa Cronbach 0.7 dan ke atas dalam EFA, dan kebolehpercayaan komposit yang memuaskan, seperti yang ditunjukkan oleh nilai rho Raykov yang melebihi 0.70 dalam CFA. Dalam Fasa 2, skor purata keselurahan untuk pengetahuan, sikap, dan amalan masing-masing adalah 36.4%, 62.6% and 77.6%. Faktor yang secara signifikan berkaitan dengan skor pengetahuan yang lebih tinggi adalah jantina wanita (laras β =3.84, p=0.013), dan individu dengan kenalan rapat yang menghidapi melioidosis (laras β =7.20, p=0.008). Walau bagaimanapun, mereka yang bekerja dengan tanaman bukan padi (laras β=-6.17, p<0.001), adalah faktor signifikan berkait dengan skor pengetahuan yang lebih rendah. Perokok berkaitan dengan sikap yang lebih rendah (laras β =-1.69, p=0.008) dan petani dengan tanaman bukan padi (laras β=1.67, p=0.007) mempunyai skor sikap yang lebih tinggi. Tahap pendidikan yang lebih tinggi (laras β =-1.56, p=0.011) dan mempunyai pelbagai tugas pekerjaan (laras β=-1.58, p<0.001) berkaitan dengan skor amalan yang lebih rendah.

Kesimpulan: Soal selidik KAP melioidosis yang baru dibangunkan sah dan boleh dipercayai untuk menilai pengetahuan, sikap, dan amalan terhadap melioidosis dalam kalangan petani di Kelantan. Faktor signifikan berkaitan KAP terhadap melioidosis adalah jantina, jenis tanaman, sejarah melioidosis dalam kalangan kenalan rapat, status merokok, tahap pendidikan, dan tugasan dikebun.

Keywords:

Melioidosis, KAP, *Bulkholderia Pseudomallei*, Petani , Faktor signifikan

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ABSTRACT

Background: Melioidosis, caused by the bacterium *Burkholderia pseudomallei*, is a significant public health concern in Malaysia, particularly among field agricultural farmers who face a heightened risk of exposure due to their occupational activities. Despite its importance, there is a lack of validated questionnaires to assess the knowledge, attitude, and practices (KAP) regarding melioidosis and study its associated factors among this high-risk population.

Objectives: This study aimed to develop and validate a new questionnaire assessing KAP towards melioidosis among fields agricultural farmers in Kelantan, Malaysia. Additionally, it was aimed to determine the KAP scores and associated factors among them.

Methods: This two-phase study was conducted between May 2023 and March 2024. In Phase 1, a KAP questionnaire was developed and validated through rigorous processes involving literature review, content validation, face validation, item response theory (IRT), exploratory factor analysis (EFA), and confirmatory factor analysis (CFA). The questionnaire was administered to 432 field agricultural farmers in Kelantan (222 for EFA, 210 for CFA). In Phase 2, a cross-sectional study was conducted among 392 farmers to assess their KAP scores and identify associated factors using the validated questionnaire. In the first phase, data were analysed using

R software, while in the second phase, the analysis was conducted using SPSS version 26.

Results: The proposed melioidosis KAP questionnaire named M-KAP, which consisted of 62 items has demonstrated excellent content validity (S-CVI/Ave: 0.97 for knowledge, 0.96 for attitude, 0.99 for practice) and face validity (S-FVI/Ave: 0.99 for knowledge, 0.95 for attitude, 1.0 for practice). IRT, EFA and CFA confirmed the construct validity and reliability of the questionnaire with analysis revealed an acceptable range of difficulty and discrimination in IRT, reliable internal consistency with Cronbach's alpha values of 0.7 and above in EFA, and satisfactory composite reliability, as indicated by Raykov's rho values exceeding 0.70 in CFA. In Phase 2, the total mean percentage for knowledge, attitude and practice were 36.4%, 62.6% and 77.6% respectively. Factors significantly associated with higher knowledge scores were female gender (adjusted β= 3.84, p=0.013), and individuals with affected close contacts (adjusted β= 7.20, p=0.008). However, those working with non-paddy crops (adjusted β= -6.17, p<0.001) associated with lower knowledge of melioidosis. Smoker associated with lower attitude (adjusted β= -1.69, p=0.008) and non-paddy crop workers (adjusted β= 1.67, p=0.007) associated high higher attitude score. Higher education level (adjusted β= -1.56, p=0.011) and having multiple job scopes (adjusted β= -1.58, p<0.001), were associated with lower practice scores.

Conclusion: The newly developed KAP questionnaire on melioidosis is valid and reliable for assessing knowledge, attitude, and practice towards melioidosis among farmers in Kelantan. Significant factors related to KAP towards melioidosis

are gender, type of crops, history of melioidosis among close contacts, smoking status, education level, and tasks in the farm.

Keywords:

Melioidosis, KAP, *Bulkholderia Pseudomallei*, Farmer , Associated factor

CHAPTER 1

INTRODUCTION

1.1 Overview of melioidosis

Melioidosis, characterized by a high fatality rate ranging from 10% to 50% in the absence of early detection and appropriate treatment, is an infectious disease caused by the saprophytic bacterium *B. pseudomallei* (Birnie et al., 2019). This pathogen, with the capacity to induce disease in a diverse array of animals, was first discovered in 1911 by British pathologist Alfred Whitmore in Rangoon, Myanmar, marking a pivotal moment in the understanding of this elusive bacterium (Whitmore, 1913).

The biothreat potential of *B. pseudomallei* has garnered significant attention, leading the US Centers for Disease Control and Prevention (CDC) to classify both *B. pseudomallei* and its close relative *B. mallei*, the latter having been used as a biological weapon in World War I, as tier 1 select agents. This classification designates tier 1 select agents as posing "the greatest risk of deliberate misuse with the most significant potential for mass casualties or devastating effects on the economy, critical infrastructure, or public confidence" (CDC, 2012).

The acquisition of melioidosis occurs through exposure to the causative agent via various routes, including broken skin (ulcer, minor injury), inhalation, or ingestion (Gassiep, Armstrong & Norton, 2020). The extent of exposure is influenced by occupational factors, as evidenced by an increased risk observed in certain occupations such as paddy farmers and laboratory staff (Benoit *et al.*, 2015; Ong *et al.*, 2017) Furthermore, environmental factors, particularly those associated

with the rainy season, play a role in amplifying the risk of exposure (Limmathurotsakul *et al*., 2013).

The disease manifests in various clinical presentations, ranging from subclinical and apparent infections to latent, acute, or chronic forms, often marked by recurrent infections. The spectrum of clinical manifestations is wide, encompassing local skin infections, pneumonia, intra-abdominal abscesses (e.g., spleen, liver, prostate), and fulminant sepsis. Additionally, less common yet significant manifestations include infections of the musculoskeletal system and the central nervous system (Birnie *et al*., 2019). Figure 1.1 below lists out the clinical manifestation of melioidosis.

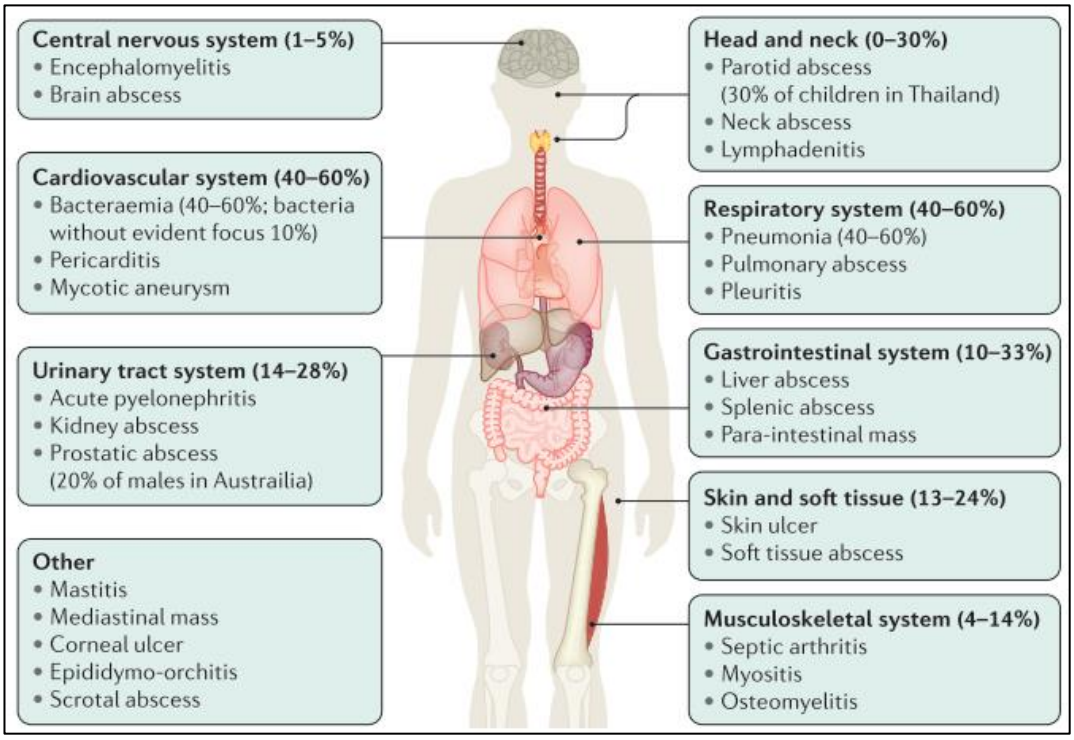

Figure 1.1: Clinical manifestation of melioidosis (Source: Wiersinga *et al.*, 2018)

1.2 Global burden of melioidosis

Estimations of the global burden of melioidosis, as predicted by Limmathurotsakul *et al.* in 2016, reveal alarming figures. In 2015 alone, it was projected that there were 165,000 melioidosis cases among the three billion people living in areas likely to contain *B. pseudomallei*, with an estimated mortality of 89,000 globally. Economically, the burden was substantial, with an estimated 4.6 million Disability-Adjusted Life Years (DALYs) in 2015, surpassing the burden of diseases such as measles and ranking higher than leptospirosis and dengue infection, both considered high-priority diseases by international health organizations (Birnie *et al.*, 2019).

It is projected that the global burden of melioidosis would increase as a result of population and pathogen movements, which will increase the chance of its formation in new places. There are a variety of factors that contributing to this potential spread, including shifts in land use, an increase in the amount of anthrosol, and a considerable rise in the prevalence of diabetes mellitus internationally.

1.3 Melioidosis in Malaysia

Melioidosis has been documented in Malaysia since the year 1913. Fletcher identified the disease in laboratory animals at the Institute for Medical Research in Kuala Lumpur, Malaysia, in 1913, and Stanton described the infection in a human patient from Kuala Lumpur in 1917 (Stanton *et al*., 1924). Malaysia is recognized as an endemic hot spot for this disease. The prevalence of melioidosis in Malaysia is a significant public health concern, with over 1,000 cases reported annually (Nathan *et al.*, 2018). In endemic regions, melioidosis is a major cause of fatal community-

acquired bacteraemia and pneumonia in adults (Chaowagul *et al.*, 1989; Limmathurotsakul *et al.*, 2016). The disease was reported all over the country with different number of occurrence (Ministry of Health, 2022). The number of reported diseases could be under reporting as it's only notified by administration since 2015 (Ministry of Health, 2019). However, six states that had been recognized with higher melioidosis occurrence are Kelantan, Pahang, Johor, Kedah, Sabah and Sarawak. The prevalence of melioidosis in Pahang, Kedah and Sarawak were 6.1, 16.35 and 12.3 in 100,000 population respectively (How *et al.*, 2005; Hassan *et al.*, 2010a; Mohan *et al.*, 2017).

Melioidosis research in Kelantan reveals a connection between land usage and disease occurrence (Adib *et al.*, 2021). Figure 1.2 below shows the disease distribution in this state. More than 60% of cases were documented in Kota Bharu and Bachok districts, which have a larger population density and significant agricultural activity, resulting in increased soil exposure as melioidosis is known to be spread mostly through the environment (Nathan *et al.*, 2018).

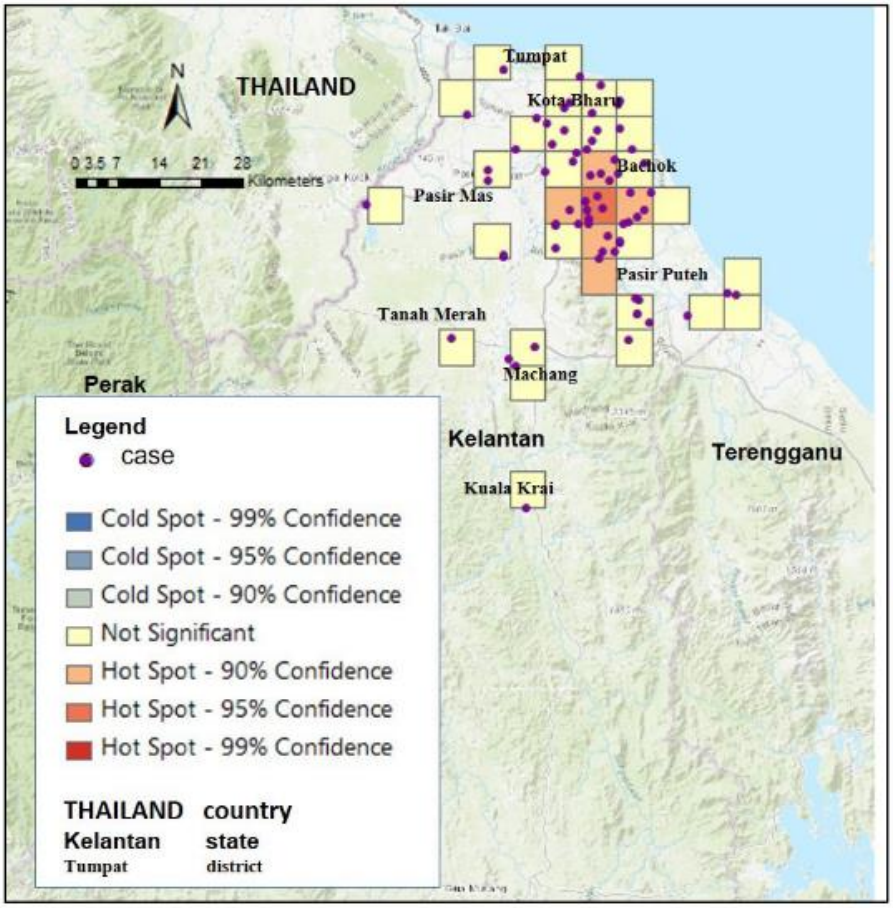

Figure 1.2: Melioidosis cases in Kelantan (Source: Adib *et al.*, 2021)

The identification of individuals at high risk of developing melioidosis is pivotal for preventive strategies. Considering that the causative agent resides in contaminated soil and water, individuals with frequent exposure to these environments, such as workers in agriculture, construction, military personnel, eco-tourists, and rescue personnel, are known to be at elevated risk. The specific occupation of farming, fishing, or forestry has been reported in a substantial percentage of cases, emphasizing the need for targeted interventions within these high-risk groups (Nathan *et al.*, 2018).

1.4 Knowledge, attitude and practice (KAP) of melioidosis

The epidemiological triad, comprising host, agent, and environment, serves as the foundational framework for understanding the dynamics of infectious diseases(Res *et al.*, 2023). In the context of melioidosis, within this triad, the intricate relationship between the host (human), the agent (*B. pseudomallei* causing melioidosis), and the environment forms the basis for assessing the risk, transmission, and impact of the disease and eventually the preventive measure that can be taken to prevent or at least reduce the disease occurrence. As melioidosis is endemic in Malaysia, investigating into the KAP of farmers becomes crucial.

Farmers, as the human hosts in the epidemiological triad, represent an important link in the transmission of melioidosis. Assessing their knowledge about the disease is fundamental for elucidating their awareness of risk factors, symptoms, and preventive measures. Understanding the cognitive landscape of farmers provides insights into their capacity to recognize and respond to potential threats posed by *B. pseudomallei* in their occupational and environmental settings.

In the other hand, *B. pseudomallei*, the infectious agent causing melioidosis, thrives in specific environmental conditions, particularly in soil and water. Farmers, by virtue of their occupation, encounter these environments regularly. Evaluating the attitudes of farmers towards melioidosis is pivotal for discerning their perceptions, beliefs, and feelings regarding the disease. Positive attitudes towards preventive measures and a clear understanding of the severity of melioidosis contribute to fostering a proactive strategy against its transmission.

Apart from that, the environment, encompassing the physical, social, and cultural surroundings, plays a pivotal role in the epidemiological triad. Farmers' practices in agriculture, irrigation, and hygiene directly impact their exposure to *B. pseudomallei*. Assessing the practices of farmers unveils the complex link between their daily activities and the risk of contracting melioidosis. It provides a lens through which interventions can be tailored to mitigate environmental factors contributing to disease transmission.

In conclusion, the epidemiological triad, consisting of host, agent, and environment, provides a comprehensive framework for understanding the dynamics of infectious diseases like melioidosis. In the case of melioidosis, the relationship between human hosts (farmers), the infectious agent (*B. pseudomallei*), and the environment underscores the importance of assessing farmers' knowledge, KAP to prevent disease occurrence.

Supplementary to that, melioidosis also demands a comprehensive One Health approach for effective prevention and control. This zoonotic disease affects humans and various animal species, with environmental factors playing a pivotal role in its transmission dynamics (Limmathurotsakul *et al.*, 2016). The One Health paradigm, which recognizes the interconnectedness of human, animal, and environmental health, is particularly relevant in addressing melioidosis, a disease caused by the environmental bacterium *B. pseudomallei*. Farmers, especially those engaged in agricultural activities in endemic regions, are at an elevated risk of exposure and play a crucial role in disease prevention and control efforts. Assessing their KAP can provide valuable insights to guide targeted educational campaigns and interventions(WHO, 2008).

Furthermore, their understanding of animal health and livestock management practices can influence zoonotic transmission dynamics, necessitating collaboration with veterinary services to control the disease in animal populations (Cascio *et al.*, 2011). Farmers' knowledge of environmental factors, such as soil and water conditions, and their agricultural practices can impact the survival and distribution of *B. pseudomallei*, influencing the risk of environmental contamination and subsequent exposure (Kaestli *et al.*, 2015). By incorporating farmers' KAP into One Health approach, multisectoral collaborations involving public health, veterinary, environmental, and agricultural authorities can be fostered, leading to the development of integrated interventions that holistically address the human, animal, and environmental dimensions of melioidosis prevention and control (Mariappan *et al.*, 2022).

Overall, by assessing farmers' KAP, stakeholders can gain valuable insights into the dynamics of melioidosis transmission and develop effective preventive strategies tailored to the specific needs of agricultural communities. This proactive approach is vital for reducing the burden of melioidosis and safeguarding public health in endemic regions like Malaysia.

1.5 Farmers and occupational health risk

Farmers are the backbone of the agricultural sector, embodying the knowledge, skills, and dedication required to ensure its success (Othieno, L., & Shinyekwa, 2011). Their contributions extend beyond food production to encompass economic, social, and cultural dimensions. Addressing SDG 2 – Zero Hunger, farmers are central to ensuring food security globally. Their efforts in cultivating crops and raising livestock are fundamental to meeting the nutritional needs of

populations. Sustainable agricultural practices play a crucial role in providing diverse and nutritious food, aligning with SDG 3 – Good Health and Well-being.

However, farmers face unique occupational hazards and health risks due to their close interaction with the environment. They face health risks such as respiratory disorders and pesticide poisoning due to airborne contaminants during agricultural activities (Ye *et al.*, 2013). Apart from that, due to the specific nature of agricultural work, characterized by intense physical labour and repetitive movements, places farmers at a particular risk of developing musculoskeletal disorders(Mohini *et al.*, 2022). Moreover, agricultural work is characterized by inherent unpredictability, including factors such as weather variability, economic pressures, and changing farm practices, which can induce prolonged stress in farmers (Kureshi & Somsundaram, 2018). This unpredictability has been associated with increased levels of stress and mental health issues among farming populations, as they are exposed to a range of stressors, including financial stress, farming hassles, weather stress, and work overload (Kureshi & Somsundaram, 2018). Additionally, farmers are particularly vulnerable to melioidosis, a fatal infectious disease caused by *Burkholderia pseudomallei (B. pseudomallei),* due to their occupational exposure to the bacterium (Manivanh *et al.*, 2017).

1.6 Problem statement

Melioidosis, caused by B. pseudomallei, is associated with high mortality rates, which can reach up to 50% if not treated early. The estimated annual mortality from melioidosis is comparable to that of measles and higher than the mortality rates from leptospirosis and dengue. This raises public health concerns. A significant issue

contributing to this is the lack of awareness about the disease among both the public and healthcare providers, leading to underreporting, underdiagnosis, delayed treatment and increase mortality. Despite the severe health threat posed by melioidosis, there is scarcity of comprehensive studies measuring knowledge, attitudes and practices (KAP) regarding the disease, particularly among high-risk groups such as field agricultural farmers in Malaysia. Most previous research on melioidosis has focused on its aetiology, clinical presentation, risk factors, and outcomes, with limited attention to KAP among high-risk groups or healthcare workers.

Additionally, there is a lack of validated questionnaires, both locally and internationally, to assess Knowledge, Attitude, and Practice (KAP) regarding melioidosis among field agricultural farmers. The absence of such tools makes it challenging to properly evaluate KAP in this population, potentially hindering effective intervention and education efforts.

Farmers in melioidosis-endemic regions face significant risks due to their occupational exposure to soil and water sources. Agricultural activities like irrigation, ploughing, and land clearing can contribute to the spread and persistence of B. pseudomallei, increasing exposure risks for farmers and nearby communities (Kaestli *et al.,* 2015). Limited access to healthcare facilities in rural or remote endemic areas can delay diagnosis and appropriate treatment, leading to severe outcomes (Limmathurotsakul *et al.,* 2010).

Knowledge gaps and insufficient awareness about melioidosis, its transmission routes, and preventive measures hinder effective disease prevention and control efforts among farmers (Chansrichavala *et al.,* 2015). Despite educational

initiatives, some farmers may not adopt recommended preventive practices due to cultural beliefs, resource constraints, or lack of perceived risk (Suntornsut *et al.*, 2016).

1.7 Rationale of study

The findings discussed in the problem statement highlight the urgent need to develop and validate a Knowledge, Attitude, and Practice (KAP) questionnaire on melioidosis, particularly among field agricultural farmers. This is essential to address the significant health threat posed by the disease and its impact on public health and the agricultural sector. Studies on the socio-epidemiological context of melioidosis in Malaysia have shown that the disease is significantly related to gender (males), race, and occupation (farming, forestry, and fishing). These studies also emphasize the importance of considering the socio-ecological context, particularly land cover types, and their association with disease prevalence.

This study aims to provide a valid and reliable tool to assess the current KAP regarding melioidosis among field agricultural farmers. It will offer insights into the factors associated with knowledge, attitude, and practice among high-risk groups. Additionally, the newly developed and validated questionnaire will gather crucial information to guide policymakers in making more effective decisions regarding farmers' safe working environments. This tool can also be used in future studies to measure pre- and post-intervention changes, evaluating effectiveness.

Understanding KAP regarding melioidosis among field agricultural farmers is vital for developing targeted interventions and strategies for disease control and prevention. Comprehensive knowledge about melioidosis is fundamental for

preventing its transmission. Assessing farmers' awareness helps identify gaps in understanding the disease's causative agent, transmission dynamics, and preventive measures. Targeted educational interventions can then be designed to address these gaps, empowering farmers with the necessary information to adopt practices that reduce the risk of melioidosis. Moreover, understanding farmers' attitudes and practices allows for the development of strategies that align with their daily routines, promoting effective and sustainable disease control measures.

Furthermore, assessing the factors associated with farmers' KAP is crucial for disease prevention. By identifying specific agricultural practices, environmental conditions, and socio-demographic factors that influence KAP, interventions can be more effectively tailored to address the unique challenges faced by farmers. This proactive approach ensures that the interventions are relevant and practical, ultimately reducing the incidence and impact of melioidosis among agricultural communities.

1.8 Significance of the study

Knowledge, attitude, and practice are integral components of community engagement and health promotion initiatives. By assessing the KAP levels among farmers, health authorities can design culturally sensitive and context-specific awareness campaigns. Engaging with the farming community in a collaborative manner not only raises awareness but also fosters a sense of collective responsibility. Encouraging positive attitudes and promoting best practices become key elements in the broader health promotion agenda, creating a foundation for sustained community health and well-being.

Furthermore, the newly developed questionnaire about KAP of melioidosis can be used in future studies to measure pre- and post-changes and to assess the effectiveness of interventions. The questionnaire was designed to evaluate the level of knowledge, attitude, and practices related to melioidosis. The questionnaire can be a valuable tool for assessing the impact of educational interventions or public health programs on increasing knowledge and improving practices related to melioidosis. Previous study shows the high mortality rate associated with melioidosis is often attributed to a lack of awareness and inefficient diagnosis, making the assessment of knowledge and practices crucial for improving disease outcomes.

In conclusion, development of valid questionnaire for the assessment of KAP levels and associated factors among farmers concerning melioidosis is a fundamental step in crafting effective and tailored interventions. It aligns with the broader goals of disease prevention and control, facilitates the identification of high-risk factors, and forms the basis for community engagement and health promotion initiatives. By addressing these aspects comprehensively, public health efforts can effectively contribute to reducing the burden of melioidosis within farming communities.

1.9 Research questions

1. Is the newly developed questionnaire valid and reliable to assess the KAP regarding melioidosis among the field agricultural farmers?
2. What is the proportion of field agricultural farmers in Kelantan with low, moderate, and high levels of knowledge, as well as negative, neutral, and positive attitudes, and poor, fair, and good practices related to melioidosis?
3. What are the factors that associated with KAP towards melioidosis among the field agricultural farmers in Kelantan?

1.10 Objectives

General objective

To develop a valid and reliable questionnaire on KAP melioidosis, and determine the score of knowledge, attitude and practice and its associated factor among field agricultural farmers.

Specific objectives

1. To develop a valid and reliable questionnaire to assess the KAP among the field agricultural farmer toward melioidosis.
2. To determine the proportion of field agricultural farmers in Kelantan who have low, moderate, and high levels of knowledge, as well as those with negative, neutral, and positive attitudes, and poor, fair, and good practices related to melioidosis.
3. To identify factors associated with the KAP of melioidosis among field agricultural farmers in Kelantan.

1.11 Research hypotheses

1. The newly developed questionnaire is valid and reliable to be used in the assessment of the KAP of melioidosis prevention among the field agricultural farmers.
2. There are significant associations between sociodemographic characteristics, comorbidities with KAP scores towards melioidosis among field agricultural farmers in Kelantan.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

Melioidosis, caused by the bacterium *B. pseudomallei*, remains a significant public health concern in endemic regions, including Malaysia. Understanding the KAP of at-risk populations, such as field agricultural farmers, is crucial for effective prevention and control strategies. However, comprehensive assessments of melioidosis KAP among high-risk groups are limited.

The development and validation of a specialized KAP questionnaire tailored to the context of melioidosis among field agricultural farmers in Kelantan represents a vital step towards addressing this gap. Such a tool enables the systematic evaluation of farmers' awareness, perceptions, and behaviors regarding Melioidosis, providing valuable insights into the factors influencing disease transmission and prevention measures.

This literature review aims to explore existing research on the development and validation of KAP questionnaires in similar public health contexts and to identify factors associated with melioidosis KAP among agricultural populations. By synthesizing relevant literature, this review seeks to establish a theoretical framework for the design and implementation of the melioidosis KAP questionnaire and subsequent research initiatives in Kelantan, Malaysia.

The literature search was conducted systematically across two academic databases: PubMed and Google Scholar. Utilizing the predefined keywords, including "KAP questionnaire development," "melioidosis awareness," "agricultural communities," "Kelantan," and variations of "factors associated with KAP," relevant

articles, books, and other scholarly sources were identified. The search results were evaluated based on their relevance to the research topic, with particular attention paid to abstracts and titles to ensure alignment with the objectives of the thesis. Upon identification of pertinent sources, the full text of relevant articles, books, and other scholarly materials was retrieved. These sources were then organized and managed using Mendeley software, facilitating efficient tracking and systematic review throughout the literature search process.

2.2 Melioidosis

2.2.1 Discovery of disease

Over a century ago, in 1911, melioidosis or Whitmore's disease was reported by British pathologist Alfred Whitmore in Rangoon, Myanmar. In his paper, the disease was well described regarding postmortem finding, characteristic of the newly discovered causative agent, and the possible mode of transmission and method to investigate this disease . At first, he thought the disease was glanders disease, but the suspicious aroused, as medical officer who received the notification said that glanders infection appeared improbable as from his investigation the man just had been released from the jail previously and had no close contact with horses. This doubt was strengthened by the finding of organism culture result which show rapidity, and luxuriance, of the growth and the appearance of the culture after 24 hour of growth which was unusual for *Burkholderia mallei* (causative agent of glanders disease). The striking different characteristic of this new discover bacterium is motile which compare to *Burkholderia Mallei* is non-motile (Whitmore, 1913).

From his observation upon 38 cases and experiment upon several guinea pig, it concluded that anybody could be infected with this new discovered disease, even though the cases were prominent among morphine injection person and the mode of transmission could be via ingestion of contaminated food and drink. The disease could present as acute (fever, pneumonia) or chronic (prolong fever, dysentery, wasting, join pain) form. Apart from lung, other important organ that involve were spleen, liver, and kidney. Agent could be cultured from blood and urine and the disease mortality was high (Whitmore, 1913). Latter research has proven his observational findings.

This new discovered bacterium initial name was Whitmore's bacillus or *Bacillus pseudomallei*, the organism's taxonomy was changed to *Bacillus whitmori, Malleomyces pseudomallei, Loefflerella whitmori,* and *Pfeifferella whitmori* until 1992, when *Pseudomonas pseudomallei* was reclassified into the genus Burkholderia. A new genus Burkholderia is proposed for the RNA homology group II of genus Pseudomonas base on the 16S rRNA sequences, DNA-DNA homology values, cellular lipid and fatty acid composition, and phenotypic characteristics. Together with *B. pseudomallei*, other 6 species under pseudomonas reclassified to new genus were *Burkholderia cepacia, Burkholderia mallei, Burkholderia caryophylli, Burkholderia gladioli, Burkholderia pickettii* and *Burkholderia solanacearum* (Yabuuchi *et al.*, 1992). The new discovered disease name melioidosis or Whitmore disease (after Captain Alfred Whitmore, who first described the disease). The term "melioidosis" was first used in 1921. Melioidosis is derived from the Greek melis meaning "a sickness of asses" with the suffixes -oid meaning "like to" and -osis meaning "a condition," that is, a condition similar to glanders.

Melioidosis also known with other various names such as Pseudoglanders, Nightcliff gardener's disease (Melioidosis is endemic in Nightcliff, a Darwin suburb in Australia.), paddy-field disease, and morphia injector's septicaemia (Infection Disease Epidemiology Section, 2015).

2.2.2 Epidemiology

The epidemiology of melioidosis is characterized by its global distribution, with endemicity in tropical areas, particularly in Southeast Asia and Northern Australia regions, with reported hot sport associated with agriculture-related activities and emerging hotspots contributing to the burden of the disease. Understanding the incidence, prevalence, and global distribution of melioidosis is crucial for effective surveillance, prevention, and control efforts.

The true incidence and prevalence of the disease remain unknown. Studies by Limmathurotsakul *et al*. (2016) has focused on the global burden of melioidosis, mapping documented human and animal cases, and the presence of environmental *B. pseudomallei* involving 22,338 geo-located records to estimate the global burden of the disease (Figure 2.1). It is estimated that there would be 165,000 melioidosis cases in 2015 among the three billion people living in the areas likely to contain *B. pseudomallei* (incidence rate of 5.0 per 100,000 people at risk per year). The estimated annually mortality is 89,000 cases. This global mortality estimation of melioidosis is comparable to measles (95,600 per year) and higher than for leptospirosis (50,000 per year) and dengue infection (9,100 – 12,500 per year) (Limmathurotsakul *et al.*, 2016).

Apart from that, burden of melioidosis also has been calculated in terms of DALYs (Disability-Adjusted Life Years). It is estimated that the global burden of

melioidosis in 2015 was 4.6 million DALYs or 84.3 per 100,000 people. The global burden of melioidosis, as expressed in DALYs, is greater than that of leptospirosis (2·90 million), dengue (2·86 million), schistosomiasis (2·63 million), lymphatic

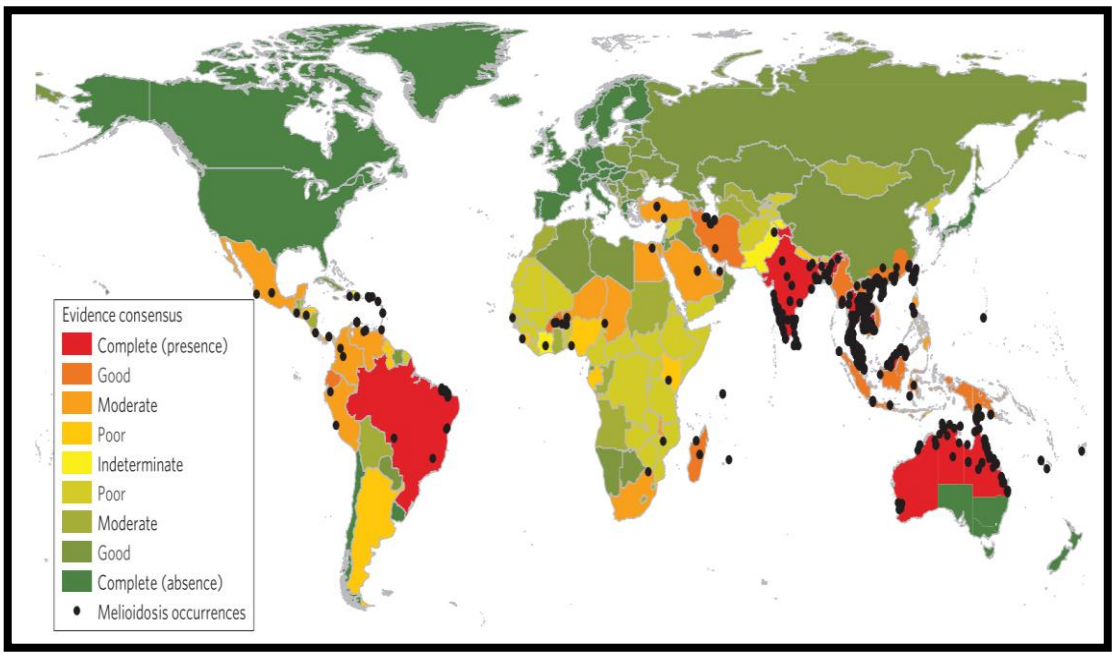

Figure 2.1: Global evidence consensus and geographic locations of occurrence data from 1910 to 2014, (Source : Limmathurotsakul *et al.*, 2016)

filariasis (1·24 million), and leishmaniasis (1·06 million) (Birnie *et al.*, 2019).

According to the two studies mentioned above, the burden of this disease is comparable to measles and greater than leptospirosis and dengue, which have been prioritised in prevention and control activities by many international health organisations. As a result, melioidosis must be recognised as a neglected tropical disease so that aggressive disease control and prevention measures can be implemented.

Since the disease is endemic in southeast Asia region, all countries in this region have reported of its occurrence (Wiersinga *et al.*, 2018; Guterres *et al.*, 2023)

In this region only Brunei, Singapore and Thailand included melioidosis in the national disease registry (Hinjoy *et al.*, 2018; Wiersinga *et al.*, 2018). Selvam *et al.* (2022) conducted a scoping review, analysing 26 studies across six countries in this region, namely Thailand, Cambodia, Myanmar, Vietnam, Malaysia, and Singapore, to ascertain the prevalence of melioidosis in the region. In Thailand, melioidosis prevalence has predominantly been investigated in the northeastern region. High prevalence rates were documented in Thailand (48.0%) and Cambodia (74.4%) among specific high-risk groups, including patients with septic arthritis and children with suppurative parotitis, respectively. Cambodian studies primarily focused on provinces such as Takeo, Kampong Cham, and Siem Reap. Myanmar's melioidosis prevalence ranged from 0.33% to 5.7% between 2004 and 2019, with Yangon being the focal point of most studies. Across Southeast Asia, melioidosis prevalence varied from 0.02% to 74.4%, as determined through various diagnostic methods including culture, antigen detection, and molecular assays utilizing blood, sputum, synovial fluid, and pus samples.

In Timor-Leste, despite the presence of antibodies against *B. pseudomallei* among 17% of East Timorese refugees as early as 1999, the lack of adequate laboratory infrastructure hindered the confirmation of bacteriological cases until 2022. Following the enhancement of the National Health Laboratory in 2020, there was a remarkable surge in sample processing, indicative of a substantial improvement in diagnostic capacity. Consequently, the laboratory's heightened functionality facilitated the identification of the initial three cases of culture-confirmed melioidosis in Timor-Leste (Guterres *et al.*, 2023). Similarly, in Laos, the prevalence of diagnosed cases of melioidosis correlates with the accessibility of laboratory resources (Dance *et al.*, 2018).

The history of melioidosis in Malaysia dates back to an outbreak in 1913 involving laboratory animals (Stanton & Fletcher, 1925). Later case among human was reported (Stanton, Flectcher & Kanagarayer, 1924). While there was a gap in documented cases possibly due to geopolitical unrest, interest resurged in the 1960s with environmental and serosurveillance studies (Nathan *et al.*, 2018). During the late 1980s and early 1990s, research on melioidosis initiated by Malaysian clinicians and microbiologists began to pick up pace, resulting in surge of publications, notably clinical reports and reviews. Over time, this research interest broadened to encompass molecular microbiology, genomics, and pathogenesis, facilitated by improved infrastructure, funding, and the presence of skilled local experts (Nathan *et al.*, 2018).

In Malaysia, disease was reported all over the countries with different occurrence (Hassan *et al.*, 2010b; Hii, Kee & Ahmad, 2016; Arushothy *et al.*, 2024) However, the true burden of it is unknown as melioidosis only register administratively. A non-exhaustive review of epidemiological data, clinical studies, risk factors, and mortality rates from available literature and case reports, revealed 6 major states with reported cases of melioidosis namely Kedah, Kelantan, Pahang, Johor, Sarawak and Sabah (Nathan *et al.*, 2018) .

Arushothy *et al.* (2024), employed the National Surveillance for Antibiotic Resistance (NSAR) as a surveillance tool to assess the burden of melioidosis in Malaysia. NSAR, an initiative launched by the Ministry of Health (MOH), serves to monitor and evaluate antibiotic resistance among various bacterial isolates in the country. This program, despite the widespread availability of 154 government hospitals throughout Malaysia, operates through a network of microbiology laboratories located in 43 hospitals across all 13 states, including Sabah and Sarawak

in Malaysian Borneo. This study constitutes a retrospective, cross-sectional analysis encompassing data spanning from 2014 to 2020, involving 17,840 cultured confirmed melioidosis case. The results of this investigation revealed that the mean incidence rate of melioidosis in states situated within Peninsular Malaysia was recorded at 3.39 per 100,000 population, whereas in Sabah and Sarawak, it stood at 3.52 per 100,000 population. Pahang exhibited the highest incidence rate at 11.33 per 100,000 population, followed by Melaka, Negeri Sembilan, Kedah, and Terengganu, ranging from 8.12 to 6.27 per 100,000 population. The average number of melioidosis cases reported annually in Kelantan range from 39 to 60 (Arushothy *et al.*, 2024).

Other than that, the burden of melioidosis has been evaluated using seropositivity database of The Institute for Medical Research (IMR) (Hii, Kee & Ahmad, 2016). The IMR serves as the primary laboratory for serodiagnosis of melioidosis in Malaysia. Serum samples from all suspected cases identified in local hospitals were sent to IMR for diagnostic evaluation. This cross-sectional study was conducted over a span of two years, from 2013 to 2014. The estimated occurrence of melioidosis per 100,000 individuals exhibited a greater incidence among males, with rates of 4.8 (2013) and 2.4 (2014), compared to females, with rates of 3.0 (2013) and 1.7 (2014). Geographically, the eastern coast demonstrated the highest incidence rates per 100,000 population in both years, registering 8.3/100,000 in 2013 and 4.5/100,000 in 2014 (Hii, Kee & Ahmad, 2016). This coastal region encompasses the states of Pahang, Terengganu, and Kelantan.

Two-thirds of the studies indicate high occurrence of melioidosis in the state of Kelantan. The absence of findings indicating a high incidence of melioidosis in Kelantan in the second study may be attributed to the non-participation of USM

Hospital in the program. Nonetheless, it is noteworthy that USM Hospital significantly contributes to the diagnosis and treatment of melioidosis cases.

Numerous studies concerning melioidosis in Kelantan have been published, covering various aspects of the disease. These studies encompass investigations into the occurrence and distribution of the disease (Adib et al., 2021), the development of novel diagnostic methods (Mohd Ali *et al.*, 2019; Wong Tzeling *et al.*, 2021; Oslan *et al.*, 2022), and the sensitivity and susceptibility of the causative agent to drugs (Mohamad *et al.*, 2018; Zamani *et al.*, 2020). Additionally, there is research focusing on the clinical epidemiology of the disease, which has revealed that environmental exposure is a significant factor, particularly given that most patients originate from rural and agricultural regions in Kelantan (Zueter *et al.*, 2016). Moreover, a study aimed at evaluating the sequence types of *B. pseudomallei* revealed significant findings. Among the 15 sequence types analysed, seven were identified as novel sequence types (STs), designated as ST1731 to ST1737. Additionally, eight previously reported STs, namely ST10, ST50, ST54, ST84, ST289, ST366, ST371, and ST414, were identified (Adib *et al.*, 2021). This discovery suggests a diverse and heterogeneous genetic composition of *B. pseudomallei* isolates within the Kelantan districts. The emergence of novel STs underscores the bacterium's capacity to generate new clones through a series of mutation processes, thereby persisting in the environment. The next section will be discussed on the characteristic of this bacterium.

Table 2.1: Summary of melioidosis burden studies

No.	Author	Level of burden	Finding	Comments
1.	Limmathurotsakul *et al.*, 2016	Global	An estimated 165,000 cases of melioidosis occurred among three billion people at risk, with an incidence rate of 5.0 per 100,000 per year, and 89,000 deaths globally.	The disease burden quantifies in incidence rate.
2.	Birnie *et al.*, 2019	Global	Melioidosis causes an estimated 84.3 DALYs per 100,000 globally, with the highest burden in Southeast Asia at 158.1 DALYs per 100,000.	The disease burden was quantified in DALYs
3.	Hii *et al.*, 2016	Malaysia	In 2013 and 2014, the estimated incidence of melioidosis per 100,000 population was highest in the east coast region, with rates of 8.3 and 4.5, respectively.	Estimation done by using seropositivity investigation in IMR
4.	Nathan *et al.*, 2018	Malaysia	6 major states with reported melioidosis are Kedah, Kelantan, Pahang, Johor, Sabah, and Sarawak	non exhaustive overview from available literature and case reports
5.	Arushothy *et al.*, 2024	Malaysia	The average annual melioidosis incidence was 3.41 per 100,000 population, with Pahang recording the highest at 11.33 per 100,000.	The study utilized data from 43 out of 154 available government hospitals.