DEVELOPMENT AND EVALUATION OF A HEALTH EDUCATION MODULE FOR THE PREVENTION OF RESPIRATORY TRACT INFECTIONS AMONG PRIVATE HAJJ AND UMRAH PILGRIMS

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by

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LIST OF SYMBOLS

$1 - \beta$	Power
α	Level of significance
n	Sample
$\dot{\eta}2$	Partial Eta Squared
<	Less than
>	More than
%	Percentage
σ	Standard deviation
Δ	Estimated difference from population mean
ε	Epsilon
y	Dependent variable
e	Residual
H_O	Null hypothesis
H_A	Alternate hypothesis
df	Degree of freedom

LIST OF ABBREVIATIONS

ANOVA	Analysis of variance
ARI	Acute Respiratory Infection
CDC	Centers for Disease Control and Prevention
CFA	Confirmatory Factor Analysis
CI	Confidence Interval
DF	Degree of freedom
EFA	Exploratory Factor Analysis
e.g	example gratia or for example
HBM	Health Belief Model
HAdV	Human Adenovirus
Hajj HEM	Hajj Health Education Module
IF	Immunofluorescence
IRT	Item response theory
ILI	Influenza-like illness
LRTI	Lower Respiratory Tract Infection
KAP	Knowledge, Attitude and Practice
PCR	Polymerase chain reaction
PIV	Parainfluenza virus
RNA	Ribonucleic acid
RSV	Respiratory Syncytial Virus
RT-PCR	Reverse transcription-polymerase chain reaction
RTI	Respiratory tract infection
SARI	Severe Acute Respiratory Infection
SD	Standard deviation
SRMR	Standardized Root Mean Square Residual
TLI	Tucker Lewis Index
URTI	Upper Respiratory Tract Infection
VTM	Viral transport medium
WHO	World Health Organization
USM	Universiti Sains Malaysia

PEMBANGUNAN DAN PENILAIAN MODUL PENDIDIKAN KESIHATAN KE ARAH PENCEGAHAN JANGKITAN SALURAN PERNAFASAN DALAM KALANGAN JEMAAH HAJI DAN UMRAH SWASTA

ABSTRAK

Ibadah haji biasanya dikaitkan dengan kejadian jangkitan saluran pernafasan dalam kalangan jemaah. Pengambilan vaksin dan lain-lain tingkahlaku pencegahan sangat rendah dalam kalangan jemaah di seluruh dunia. Walaubagaimanapun, pada masa ini tiada teori kesihatan berdasarkan modul pendidikan kesihatan yang disahkan untuk memberi panduan kepada jemaah tentang cara bagaimana untuk meningkatkan kepatuhan kepada amalan-amalan pencegahan ini dan meningkatkan ilmu mereka terhadap jangkitan saluran pernafasan, sikap dan amalan pencegahan ke arah strategi pencegahan. Objektif umum kajian ini adalah untuk mengembangkan dan menilai keberkesanan modul pendidikan kesihatan dalam mencegah jangkitan saluran pernafasan dalam kalangan jemaah Haji dari Malaysia. Kajian ini dijalankan dalam beberapa fasa yang terdiri daripada fasa pembinaan dan validasi soalselidik, pembinaan dan validasi modul kesihatan untuk pencegahan jangkitan saluran pernafasan, fasa pencirian garis dasar jemaah, fasa intervensi dan fasa penilaian. Pada fasa pertama kajian, kajian keratin rentas telah diadakan untuk tujuan pembinaan dan validasi alat pengukuran menggunakan kandungan, konstruk (teori respon item, analisis faktor eksploratori dan analisis faktor pengesahan) validasi dan kebolehpercayaan. Fasa ini diikuti oleh pembinaan dan validasi modul pendidikan kesihatan yang baharu melalui aplikasi telefon pintar. Bagi fasa intervensi dan penilaian, kajian quasi-eksperimental telah digunakan manakala data untuk intervensi

sebelum dan selepas dianalisa dalam kalangan 52 dan 50 jemaah Haji/Umrah dalam kumpulan intervensi atau kawalan. Kumpulan intervensi telah diberikan modul pendidikan kesihatan ke arah pencegahan jangkitan saluran pernafasan semasa Haji dan Umrah dalam bentuk aplikasi telefon pintar yang berpandukan model kepercayaan kesihatan. Kumpulan kawalan menerima aplikasi telefon pintar dalam panduan Haji dan Umrah biasa daripada syarikat Haji dan Umrah yang berlainan. Data dikumpulkan menggunakan soalselidik yang sama iaitu yang telah digunakan semasa pengumpulan data sebelum dan selepas. Ukuran ANOVA ulangan rekabentuk campuran telah digunakan untuk menilai kesan ke atas kumpulan, masa dan masa interaksi ke atas pembolehubah bersandar. Terdapat pembaikan signifikan dalam skor pengetahuan dan kesan utama dalam kumpulan intervensi berbanding dengan kumpulan kawalan, berdasarkan masa ($p = 0.005$, $\eta p2 = 0.075$). Terdapat juga pembaikan yang sama dalam skor sikap dan kesan utama berdasarkan masa ($p = 0.035$, $\eta p2 = 0.044$). Terdapat perubahan signifikan dalam skor amalan dan kesan utama berdasarkan masa ($p = <0.001$, $\eta p2 = 0.155$) dan interaksi kumpulan dengan masa ($p = 0.042$, $\eta p2 = 0.041$). Kejadian TRI dalam kumpulan intervensi adalah lebih rendah berbanding dengan kumpulan kawalan. Modul intervensi pendidikan kesihatan yang dibangunkan adalah berkesan dalam memperbaiki pengetahuan, sikap dan amalan ke arah pencegahan TRI dalam kalangan jemaah Haji dari Malaysia. Kajian lanjut juga diperlukan untuk mengetahui penghalang dan motivasi untuk menghubungkan jurang pengetahuan mengenai pengambilan vaksin yang mandatory dan yang disyorkan bersama-sama dengan lain-lain komponen dalam modul. Oleh sebab itu, agensi Haji perlu mengadakan pendidikan kesihatan sebelum keberangkatan jemaah untuk memberi persediaan pencegahan jangkitan saluran pernafasan biasa atau pada masa wabak jangkitan sewaktu Haji atau Umrah.

DEVELOPMENT AND EVALUATION OF HEALTH EDUCATION MODULE FOR THE PREVENTION OF RESPIRATORY TRACT INFECTIONS AMONG PRIVATE HAJJ AND UMRAH PILGRIMS

ABSTRACT

Hajj pilgrimage is usually associated with a regular occurrence of respiratory tract infection among pilgrims. Vaccination uptake and other preventive behaviours have generally been low among pilgrims across the globe. Despite this, there is presently no validated health theory-based health education module in Malaysia to guide the pilgrims on how to boost compliance with these preventive practices and increase their knowledge towards respiratory tract infection, preventive attitudes and practices towards prevention strategies. The general objective of this study is to develop and evaluate the effectiveness of health education modules against respiratory tract infections among Hajj pilgrims from Malaysia. This study was carried out in phases comprising of development and validation of questionnaire phase, development and validation of health education module for respiratory tract infection prevention phase, baseline characterization of pilgrims' phase, intervention phase and evaluation phase. At the first phase of the study, a cross-sectional study was conducted for the development and validation of a measurement tool using the content, construct (items response theory, exploratory factor analysis and confirmatory factor analysis) validation and reliability. This phase is followed by the development and validation of new health education module via a smartphone application. For the intervention and the evaluation phase, a quasi-experimental study was utilized, where pre-post intervention data were analysed among 52 and 50 Hajj/Umrah pilgrims in the intervention or control group respectively. The intervention group was given health

education module on the prevention of respiratory tract infections during Hajj and Umrah in the form of a smartphone application which was strictly guided by the health belief model. The control group received a smartphone application on normal Hajj and Umrah guidance from a different Hajj/Umrah travel company. Follow-up data were collected using the same questionnaire that was used during the pre-test data collection. Mixed design repeated measure ANOVA was used to analyse the effect of group, time, and group-time interaction on the dependent variables. There was a significant improvement in knowledge score and the main effect in the intervention group compared to the control group, based on time ($p = 0.005$, $\eta p2 = 0.075$). Likewise, there was significant improvement in attitude score and main effect based on time ($p = 0.035$, $\eta p2 = 0.044$). Similarly, there was a significant change in practice score and also main effect based on time ($p = <0.001$, $\eta p2 = 0.155$) and interaction of group with time ($p = 0.042$, $\eta p2 = 0.041$). Similarly, the occurrence of RTI in the intervention group is lower when compared to the control group. The new health educational intervention module developed was effective in improving the knowledge, attitude and practices toward prevention of RTI among Hajj pilgrims from Malaysia. Further studies are also needed to investigate the barriers and motivators to link the knowledge gap about the uptake of mandatory and recommended vaccine as well as the other components of the module. Therefore, Hajj agencies need to conduct health education before departure of pilgrims to prepare them against the common respiratory infections or in the event of outbreaks of infection during Hajj/Umrah.

CHAPTER 1

INTRODUCTION

1.1 Background of the study

The Holy pilgrimage to Mecca, in Saudi Arabia is among the five cardinal pillars of worship upon every financially and physically able Muslim individual. The Hajj is among the largest mass gathering in the world. Annually, an estimated 2-3 million Muslim pilgrims from different countries across the globe including thousands from Malaysia participate in the Holy pilgrimage of Hajj in the Kingdom of Saudi Arabia (U.S. Department of State, 2019). Hajj and Umrah pilgrimages are associated with a high density of crowding, presence of comorbidities among the pilgrims and adverse climatic condition which posed a potential risk for confined outbreaks. This can also result in the spread of infectious agents to different parts of the world upon pilgrims return the return of the pilgrims to their various countries.

The cities of Makkah and Madinah have a higher prevalence and annual risk of acquiring infections of respiratory viruses when compared with the national average. This could be due to the crowding at the Grand mosque during circumambulation and at the Mount Arafat (Choudhry *et al.*, 2006; Rashid *et al.*, 2008c). Saudi Arabia, as the sole host of the world largest religious mass gathering, has been the centre of the emerging Middle East respiratory syndrome coronavirus (MERS-CoV) (Zaki *et al.*, 2012). MERS-CoV infection has been reported in other parts of the Arabian Gulf region since it was first identified in the Kingdom of Saudi Arabia in 2012 (Bermingham *et al.*, 2012). However, respiratory tract infections are the most prevalent illnesses spread throughout the Hajj pilgrimage (Memish *et al.*, 2015). The most commonly acquired respiratory viruses during Hajj pilgrimage are

human rhinovirus, followed by human coronaviruses and influenza A virus (Hoang and Gautret, 2018). *Haemophilus influenzae, Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Haemophilus parainfluenzae* and *Moraxella catarrhalis* were the common bacteria isolated by culture (Razavi *et al.*, 2014; Zuraina *et al.*, 2018). These public health issues are enormous challenges to both participating and the host countries especially regarding infectious diseases such as respiratory tract infections (Memish *et al.*, 2014c).

Therefore, pilgrims coming from all country particularly those having a pre-existing medical condition (e.g. chronic lung disease, diabetes immunodeficiency, chronic kidney disease etc) are at increased risk and more susceptible to develop severe respiratory tract infection (RTI) during Hajj pilgrimage particularly MERS-CoV if they are exposed to the virus. Other risk factors of contracting respiratory infections could be due to direct contact with infected pilgrims, cigarette smoking, intermittent use of facemasks and a decline to use alcohol-based hand disinfection (Gautret *et al.*, 2016). Pilgrims are encouraged to consult health officials before travelling to review the risks and evaluate whether embarking on the pilgrimage is advisable (World Health Organization, 2017b).

It has been reported that the annual morbidity rate of respiratory viruses ranges from 3-10% of adults (Al-Romaihi *et al.*, 2019). Consequently, more severe RTIs such as pneumonia are the major cause of hospitalization during the Hajj or Umrah (Hoang and Gautret, 2018; Madani *et al.*, 2006). However, mild infections are seldom reported; there is a growing indication that severe RTI can occur particularly among older adults and those with the presence of comorbidities (Ferkol and Schraufnagel, 2014). Over 90% of pilgrims suffered from at least a specified respiratory symptom

and the risk of respiratory infections due to mainly viruses increases several folds during Hajj (Benkouiten *et al.*, 2014b).

The transmission and dissemination of respiratory viruses during the Hajj period could result in the worldwide spread, which has already been reported among the US pilgrims (Barasheed *et al.*, 2014b). High occurrence of respiratory illnesses was reported among returning Malaysian Hajj pilgrims even though they practice some preventive measures. All these preventive strategies which, include the use of face masks, hand hygiene and vaccination must be done concurrently to decrease the respiratory illness effectively (Hashim *et al.*, 2016).

Health education can be explained as a systematic way by which people or groups acquire knowledge to behave in a way favourable to the improvement, sustaining or restoration of health (Saha *et al.*, 2005). Various modules can be used for health education in promoting awareness for the pilgrims such as lectures, discussions, symposia, posters, public address, radio and television messages depending on the gender, age, educational qualification, background and type of employment (Nishtar *et al.*, 2004). Health education can help a society figure out its needs, include in its problem-solving capabilities and gather its resources to improve, promote, implement and assess strategies to develop its health status (Hou, 2014). Health education through an internet-based intervention to prevent the transmission of influenza showed trends in change of behaviour effectively (Little *et al.*, 2015).

The Saudi Health ministry usually undertakes the planning and design of programs to educate the pilgrims such as infection control practices (e.g., use of face mask) to reduce the incidence of severe Hajj-related illness (Almutairi *et al.*, 2018; Memish, 2002). This scheme of the seasonal layout plan is coordinated with numerous

international organizations such as the European Centre for Disease Prevention and Control (ECDC), World Health Organization (WHO) and the United States Centre for Disease Control and Prevention (CDC), who issued guidelines for control of respiratory diseases, especially MERS-CoV during Hajj and Umrah (Almutairi *et al.*, 2018). Participating countries should ensure proper and adequate preparation of pilgrims before embarking on Hajj pilgrimage. This is very critical before departure to Saudi Arabia due to collectivism required from all participating country to tackle the health challenges. Healthcare professionals, statutory bodies and collaborative community efforts are essential to maintain well-coordinated Hajj rites.

1.2 Problem statement

The prevalence of respiratory symptoms during Hajj has continued to rise over the recent years among pilgrims from Malaysia. In 2010 Hajj season, the prevalence of respiratory symptoms was reported at 40.1% among Malaysian Hajj pilgrims (Deris *et al.*, 2010b). In a similar study conducted during the 2013 Hajj season among Malaysian pilgrims, a prevalence rate of 78.2% was reported for influenza-like illnesses infection (Hashim *et al.*, 2016). In comparison to the prevalence of pre and post-Hajj RTI infection, it rose from 7.4% among the Hajj samples before departure to 45.4% among the Hajj samples after return in a study conducted at the time of 2013 Hajj pilgrimage (Memish *et al.*, 2015). These rising trends pose serious concern and public health challenge for pilgrims.

Hajj pilgrims usually experience shared shelter, air pollution and lack of proper hygiene as well as extreme and inevitable overcrowding which facilitates the transmission of respiratory tract infection which can be spread to pilgrim's country of origin upon return. These factors also facilitate the smooth spread of respiratory

infections worldwide after Hajj pilgrims return to their based countries (Barasheed *et al.*, 2016). These conditions can result in both upper and lower respiratory tract infections among the pilgrims leading to a significant increase in morbidity and hospitalization, with pneumonia being the greatest cause of severe septicaemia and shock in patients hospitalized to intensive care units (ICUs) (Al-Tawfiq *et al.*, 2013; Memish *et al.*, 2014a; Memish *et al.*, 2015). A possible high rate of morbidity and mortality are commonly associated with immunocompromised people and other high-risk population due to RTI during Hajj. These pilgrims challenged by severe medical conditions or greater-risk health status and participating in the pilgrimage are at considerable risk to their health and a great burden for the Saudi and their home country on return (Yezli *et al*., 2016).

Hajj pilgrimage is associated with several rites that are physically demanding and strenuous which could suppress the immunity of pilgrims, making the pilgrims vulnerable to infections (Alqahtani *et al.*, 2019). The interwoven aggregation of risk factors during Hajj such as intense crowding, change in lifestyle and dietary habit, air pollution, psychological stresses, fatigue, lack of sleep, limited facilities and time for personal hygiene facilitates the risk of acquiring of respiratory infections considerably (Benkouiten *et al.*, 2013; Haworth *et al.*, 2013).

Presently, there is a paucity of validated measurement tools for the assessment of knowledge, attitude and practice towards prevention and control of respiratory infections among Hajj and Umrah pilgrims. So far, there are few studies that specifically reported the knowledge, attitude and practice of various respiratory tract infections preventive behaviours by Hajj pilgrims (Alhomoud and Alhomoud, 2017; Alqahtani *et al.*, 2016b; Alqahtani *et al.*, 2016c; Dumyati *et al.*, 2018; Gautret *et al.*,

2013a; Gautret *et al.*, 2009; Sridhar *et al.*, 2015). However, none of these studies was documented to have employed a questionnaire that was appropriately developed and validated.

Some studies have been conducted on educational interventions on respiratory tract infection prevention among Hajj pilgrims from different countries (Aelami *et al.*, 2015; Alamri *et al.*, 2018; Turkestani *et al.*, 2013). However, none of the health educational intervention was based on any health behaviour theory. Furthermore, most of the previous studies had only studied primary outcomes like knowledge, attitude and practice, not going beyond, to assess the secondary outcomes like detection of influenza viruses objectively. Similarly, none of these interventions were delivered via an accessible mobile-based application specifically for RTI among pilgrims. Smartphone and cyber-based technologies have been regarded as a suitable and feasible means to deliver intervention modules in several studies. Smartphone phone-based delivery, such as short message service (SMS), has been used broadly and successfully in the literature to sustain portable and widespread interventions (Buhi *et al.*, 2013). Web-based services, such as email and website portals, have also been used greatly and with accomplishment (Brouwer *et al.*, 2011). The capacity to digitally distribute material grants multiple benefits to health care researchers and end-users alike: prominently, personalization of resources, enhanced scalability, and affordable costs. Hence it is hypothesized that a health educational module that proffers evidence-based data concerning risk factors associated with RTI prevention strategies may have the added advantage of decreasing the uncertainty for other health situations with a distinct improvement in general well-being (Hartin *et al.*, 2016).

1.3 Significance of the study

This research will be useful in the field of public health as it developed a novel and innovative approach to health education intervention. The Hajj health education module from this study could be adopted and incorporated into the routine Hajj and Umrah preparations for self-learning by Malaysian pilgrims to complement the currently used strategies. This study would help reduce the burden of the incidence of RTIs, together with their complications among Hajj and Umrah pilgrims. This study will also create awareness of preventive measures for the reduction of the symptoms of RTI. Knowing the baseline characteristics of the pilgrims will assist in the future planning and organization of Hajj and Umrah. Other researchers in future studies could also adopt the validated questionnaire developed from this research.

1.4 Research questions

The research questions of this study were:

1. Is the measurement tool for determining the knowledge, attitude and practice of Malaysian Hajj and Umrah pilgrims towards respiratory tract infections prevention valid and reliable?

2. What is the baseline socio-demographic characteristics and KAP of Malaysian Hajj and Umrah pilgrims for respiratory tract infections?

3. What is the effect of a health education intervention on the knowledge, attitude and practice for respiratory tract infection prevention and control during Hajj and Umrah pilgrimage?

4. What is the effect of a health education intervention on the proportion of respiratory like illnesses and vaccine-preventable infections on Hajj and Umrah

pilgrims from Malaysia?

5. Is smartphone app effective for delivering health education modules to Hajj pilgrims?

1.5 Objectives of the study

(a) General objective

The general objective of this study was to develop and evaluate the effectiveness of health education modules against respiratory tract infections among Hajj pilgrims from Malaysia.

(b) Specific objectives

Phase 1: Development and validation of measurement tools

i. To develop and validate the questionnaire on knowledge, attitude and practice of Respiratory traction infection prevention and control among Hajj pilgrims

Phase 2: Baseline characterization

i. To determine the socio-demographic characteristics (such as age, gender, marital status, ethnicity, level of education and monthly income), occupational history (working experience, training and preventive measures) and medical history of Malaysian Hajj pilgrims

ii. To determine the knowledge of Malaysian Hajj pilgrims towards respiratory tract infection and its prevention in terms of risk factors, the benefit of prevention and problems associated with the disease

iii. To determine the attitude of Malaysian Hajj pilgrims towards RTI about the disease, its severity, health-seeking behaviour, common treatment and prevention

iv. To determine their practice based on the current recommendation

Phase 3: Development and validation of educational module for respiratory tract infection

i. To develop a health education module towards respiratory tract infection prevention and validation of the education module

ii. To validate the health education modules towards respiratory tract infection prevention and validation of the education module

Phase 4: Intervention study

i. To compare the effectiveness of the education modules on the knowledge, attitude and practice of Malaysian Hajj pilgrims towards respiratory tract infection by comparing the pre and post- hajj test knowledge, attitude and practice

ii. To compare the proportion of occurrence RTI symptoms between intervention and control group based on ILI symptoms.

1.6 Research hypotheses

H1: The measurement tool and health educational module are valid and reliable

H2: There is variation in knowledge, attitude and belief among the Malaysian Hajj pilgrims regarding respiratory tract infections.

H3: There will be a significant difference in the knowledge, attitude and belief score between pre-test and post-test among the Malaysian Hajj pilgrims

H4: Health education package will improve the knowledge, attitude and practice of respiratory tract infection control among Malaysian Hajj pilgrims.

H5: There is a significant difference in the proportion of influenza-like illness symptoms and respiratory infection between intervention and control group

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

2.1.1 The Hajj

The Hajj is among the five pillars of Islam and one of the biggest annual religious mass gatherings in the world involving pilgrimage to the Holy land of Makkah in Saudi Arabia. This religious rite is obligatory on every financially and able-bodied Muslim to perform it at least once in a lifetime. On the other hand, Umrah also known as Lesser Hajj can be performed at any time of the year and is not obligatory on Muslims, however; is a highly significant religious practice. This pilgrimage attracts millions of worshippers for Umrah and about 2-3 million people from various countries across the globe converge for the yearly Hajj rituals.

Hajj rituals usually commenced with the absolute intention of performing an act of worship with the visit to the Holy Kaaba in Makkah on the first day where the pilgrims perform the circumambulations (Tawaf) round the Grand mosque for seven times. This is later followed by an overnight stay in Mina, which is some 6km away from Makkah. On the next morning, pilgrims from all over the world regardless of gender depart to Mount Arafat on what is known as the Day of Arafat which is equivalent to the 9th day of Dhu al-Hijjah of the Hijrah calendar to pray for forgiveness from Allah. Mount Arafat is located about 21.9 km southeast of Makkah where pilgrims will remain there until sunset of the same day. After the rituals at Arafat, the pilgrims will make a return with another overnight stopover at Muzdaliffah. During return back to Mina, the pilgrim halt to collect pebbles at Jamarat to perform the symbolic stoning of the pillars that are effigies of satan. To round up the obligatory

requirements, each pilgrim sacrifices an animal as gratitude to Allah for an accepted Hajj and then shaves the hair on his head. After a farewell Tawaf, pilgrim takes off his ihram and then leaves Mecca.

The Malaysian Hajj Fund (Lembaga Tabung Haji [LTH]) is an institution saddled with the responsibility of managing the Malaysian pilgrims during Hajj. They are the regulators and service provider for Hajj and Umrah. They also served as the muassasah for Hajj services that are subsidized to a certain extent by the LTH and the private Hajj package done by tour and travel companies. The LTH grant permission to Hajj tour companies to offer private hajj packages as an option for pilgrims who do not want to utilize the muassasah package. The official figures for Malaysian Hajj quota stand at 30,200 pilgrims based on current population of Malaysian muslims. Tabung Haji Malaysia rendered welfare services to pilgrims during Hajj such as accommodation, medical services, and information to the pilgrims. Tabung Haji Malaysia also render pre-Hajj services including Hajj registration, Hajj orientation courses and travel plans. Malaysian pilgrims spend about 40 days in the holy land throughout the pilgrimage. Usually, some of the pilgrims travel first to Madinah where they spend some days in the city for visits and tour of the city while some travel to Makkah first. As the Hajj rituals approach, they depart to Makkah to comply with the Hajj obligations. Upon completion of the rituals of the Hajj, pilgrims are lodged at a transit camp called Madinatul-Hujjaj in Jeddah before finally returning home through Jeddah airport.

2.2 Respiratory tract infections (RTIs)

RTI is defined as any infectious disease of the upper and lower respiratory tract. RTIs are one of the most common illnesses ranging from mild flu to potentially

most severe and life-threatening disease such as pneumonia treated by health care practitioners. RTI can broadly be categorized as upper respiratory tract infections (URTI) and lower respiratory tract infections (LRTI). These infections are commonly caused by viruses and bacteria are also responsible for these infections. Co-infection of virus and bacteria are also reported. However, a large proportion of these infections are viral.

2.2.1 Aetiologic agent

The aetiologic agents of RTI are complicated due to multiple organism isolated in clinical cases. Several pathogens including viruses, bacteria, and fungi are capable of infecting the respiratory tract. In some instance, the identification of the causative pathogen is quite tricky in most clinical studies. Viruses are implicated in most of the cases of RTI reported with fewer cases of bacterial infections reported (Berry *et al.*, 2015). It is essential to understand the significance of aetiological agents in routine diagnosis, treatment and research preferences, particularly in the fields of public health (Self *et al.*, 2015). Among the common viral agents include influenza virus, respiratory syncytial virus, parainfluenza virus, rhinovirus and human adenovirus.

(a) Respiratory viruses

Influenza viruses are negative-sense, single-stranded viruses with multiple segmentation of ribonucleic acid (RNA) and are taxonomically classified as Group V [(-)ssRNA] family of *Orthomyxoviridae* and Genera called Influenza A virus (McDonald *et al.*, 2016). Influenza viruses are broadly classified into three major classifications as influenza A, B, and C. Influenza A is regarded as the major one among them such as H1N1 (Vesikari and Esposito, 2017). The influenza A virion is

highly pleomorphic, manifesting both rounded and filamentous particles in appearance with a diameter of about 100nm and longer (Elton *et al.*, 2013).

Influenza-like illnesses (ILIs) are also known as flu-like syndrome/symptoms and most cases of ILIs influenza virus is not the usual aetiological agent, but they are caused by other viruses such as coronaviruses, rhinoviruses, human respiratory syncytial virus, adenoviruses, and human parainfluenza viruses. Over the recent years, some novel human respiratory viruses have been documented; these include the human metapneumovirus (hMPV), bocavirus (Van den Hoogen *et al.*, 2001), four new human coronaviruses including Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), human coronavirus NL63 (HCoV-NL63), HCoV-HKU1 and Middle East Respiratory Syndrome coronavirus (MERS-CoV) (Berry *et al.*, 2015). In rare instances, some fundamental aetiologic agents of ILI include bacteria such as *Chlamydia pneumoniae, Legionella, Streptococcus pneumoniae* and *Mycoplasma pneumoniae* (Khan *et al.*, 2015).

The Respiratory syncytial virus (RSV) belongs to the family *Paramyxoviridae* and the subfamily *Pneumovirinae* (Farnon *et al.*, 2013). Respiratory syncytial virus (RSV) is responsible for seasonal outbreaks and a significant cause of acute respiratory infection (ARI) with its global burden estimated at 33·8 million new episodes (Bloom-Feshbach *et al.*, 2013). Human adenovirus (HAdV) is a member of the family *Adenoviridae* and genus *Mastadenovirus*. *Adenoviruses* are a typical viral agent that can result in opportunistic infections with notable morbidity and mortality in immunocompromised individuals (Podgorski, 2016). The bulk of HAdV respiratory infections happen in children under the age of five (Taylor *et al.*, 2017).

Human rhinoviruses are the predominant cause of viral respiratory illness during the spring, summer, and fall months, after influenza and RSV during winter. Its peak incidence is recorded in early fall and a smaller peak in the spring (Jacobs *et al.*, 2013). Human parainfluenza viruses (PIVs) are a predominant community-acquired respiratory pathogen that affects all ethnic, socioeconomic, demographic or geographic groups (Fiave, 2014).

(b) Bacteria

The most common bacterial causes of respiratory tract infections reported during Hajj pilgrimage from various studies are *Haemophilus influenzae, Klebsiella pneumoniae, Streptococcus pneumoniae, Staphylococcus aureus, Streptococcus pyogenes, Legionella pneumophilia, Klebsiella pneumoniae, Moraxella catarrhalis, Haemophilus parainfluenzae* and *Mycoplasma pneumoniae* while pneumonia caused by *Mycobacterium tuberculosis* is the common infection that leads to hospitalization (Aelami *et al.*, 2015; Al-Abdallat *et al.*, 2017; Zuraina *et al.*, 2018).

(c) Fungi

Fungal infections of the respiratory tract are mostly not clearly understood, and the actual burden is elusive (Fauci and Morens, 2012). Fungi may occur in body sites without eliciting disease, or they may be a true pathogen, resulting in a wide variety of clinical syndromes (Mostaghim *et al.*, 2019). Fungal respiratory infections are becoming increasing attention among immunosuppressed individuals (Lamoth and Alexander, 2014). In general, one of the most prevalent pathogenic fungi producing respiratory tract disorders is *Aspergillus* species resulting in invasive pulmonary infections (Rick *et al.*, 2016). However, over the last decade, there is the emergence of some filamentous fungi, such as *Scedosporium, Fusarium, Penicillium*, melanized moulds, and basidiomycetes as causing well-characterized respiratory ailments. The

term “respiratory mycosis” now encompasses not only invasive illness but also uncommon entities such as fungal ball, severe asthma with fungal sensitization (SAFS), fungus-associated chronic cough (FACC), allergic bronchopulmonary mycosis (ABPM), and allergic fungal rhinosinusitis (AFRS) (Chowdhary *et al.*, 2014; Ogawa *et al.*, 2009; Singh *et al.*, 2013).

2.2.2 Upper respiratory tract infections (URTIs):

Upper respiratory tract infections are acute, febrile infectious illness with cough, coryza, or sore throat, colds, tonsillitis, peritonsillar abscess, epiglottitis, laryngitis, tracheitis and hoarseness that are predominant in the community. Moreover, URTIs are one of the frequent reasons for appointments at health care centres, especially during the colder season and is also the most common acute illness found in a hospital setting. This infection has a broad range of clinical signs and symptoms that ranges from mild to self-limiting such as the common cold to a more perplexing and life-threatening disease, such as epiglottitis (Baz *et al.*, 2006). This infection involves the nose, trachea, pharynx, larynx, paranasal sinuses and bronchi (Bove *et al.*, 2006). The vast preponderance of URTIs quandaries is mild. Therefore further examination is usually required to identify the precise aetiology but is not a usual routine practically.

2.2.3 Lower respiratory tract infections (LRTI):

LRTI is regarded as the most common human infection all over the globe. It can be regarded as an acute illness which is manifested for 21 days or less, displaying primary symptoms such as cough. It is also characterized with the occurrence of at least one or more than one RTI symptoms such as wheezing, dyspnea, chest

discomfort/pain, sputum production and no alternative explanation such as sinusitis or asthma (Woodhead *et al.*, 2011). LRTIs are considered to be among the leading infection that results in morbidity and mortality across all age-groups globally, with an approximated 2.7 million deaths linked to them in the year 2013 (Khor *et al.*, 2012). LRTIs are a remarkable global health predicament and a significant basis of infections and mortality in several communities. LRTIs are the most common human infectious disease globally (Carroll, 2002). However, they result in significant morbidity and financial costs to the person and community. The incidence is higher in ageing patients of 60 years and above than people who are less than 50 years old. The most considerable number of LRTI cases are typical in people having a premorbid condition.

2.3 Case definition of respiratory infections

The World Health Organization (WHO) surveillance case definitions for influenza-like illness (ILI) is an acute respiratory infection with a measured fever of ≥ 38°C and cough, with onset within the last ten days. Severe acute respiratory infections (SARI) can be defined as an acute respiratory infection with a history of fever or measured fever of ≥ 38°C; and cough with onset within the last ten days and requires hospitalization. Respiratory infection is defined as having a history of fever or measured fever of 38°C, and cough (in some sites cough or shortness of breath). Acute respiratory tract infection (ARI) is defined as a sudden onset of symptoms. The ILI case definition is usually designed for practice in outpatient treatment centers and the SARI definition for inpatient hospital settings. The SARI definition aims to capture both the influenza-related cases of pneumonia and influenza-related exacerbations of chronic illnesses such as asthma or heart disease. The focus of ILI and SARI surveillance is on the proportion of laboratory-confirmed influenza-associated disease.

For the reasons of surveillance, laboratory confirmation can be achieved by any of the following

- Conventional or real-time reverse transcriptase-polymerase chain reaction (RT-PCR).
- Viral antigen detection by immunofluorescence or enzyme immunoassay methods (including commercially available bedside tests).
- Viral culture with a second identification step to identify influenza viruses (immunofluorescence, haemagglutination–inhibition, or RT-PCR).
- Four-fold rise in antibody titre in paired acute and convalescent sera.

Viral detection techniques for laboratory confirmation of influenza is best achieved within the first five days after onset of illness. A significant portion of influenza cases may present with SARI after this period. Therefore, SARI cases may be recognized and examined for influenza up to 10 days after illness start with a slight rise in the value per positive test (World Health Organization, 2017c).

2.4 Global Epidemiology of Respiratory tract infection

Mass gatherings across the globe attract huge crowds, creating high-risk conditions for the rapid spread of infectious diseases (McCloskey *et al.*, 2014; Memish *et al.*, 2014c). Religious and sporting mass gathering attracted thousands to millions of participants from all over the world and living in crowded conditions, exposing themselves and the local population to a range of respiratory viruses (Smallwood *et al.*, 2014). The converging of people temporally and spatially may lead to the emergence of infectious diseases due to enhanced transmission between attendees during such mass gatherings. The exceptionally high mortality and absence of specific

MERS-CoV treatments or vaccines will severely impact healthcare services of countries from which mass gatherings such as Hajj originate if a Korea-like outbreak occurs from returning pilgrims. The outbreak of meningococcal meningitis after the 2000/2001 Hajj pilgrimage demonstrated the peril of infectious diseases on global health security. The World Health Organization (WHO) issues operational support and strategic plans for public health preparedness to organizers of mass gatherings.

The surveillance systems of infectious diseases are fully employed during the annual Hajj, and they have emerged from paper-based reporting tools to automated electronic systems, recording and storing large datasets, and reporting from mobile units, clinics, primary health facilities, and hospitals that serve pilgrims (Memish *et al.*, 2014c). The strides in real-time surveillance have enhanced public health security for the mass gatherings at the Hajj.

Annual outbreaks are associated with the epidemiology of respiratory infections during the winter and spring seasons with relation to temperature. However, these infections can be prevalent throughout the year, especially to those in tropical countries, where the correlation of respiratory viral activity with climate are not being reported (Khor *et al.*, 2012). Respiratory infections had witnessed the emergence of new viruses which threatened the health security all over the world. The emergence of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003 in China and H1N1 influenza pandemic in 2009 are examples of such emergence. Similarly, in the last decade, there is the emergence of an entirely novel strain of human coronavirus known as the Middle East Respiratory Syndrome coronavirus (MERS-CoV) in the Kingdom of Saudi Arabia (KSA) in 2012 rising fear and immediate attention (Sharif-Yakan and Kanj, 2014). Another study suggests a potential risk of SARS-CoV re-

emergence from viruses currently circulating in bat populations (Menachery *et al.*, 2015).

Respiratory diseases inflict an enormous global health burden. These diseases are among the most regular cause of severe illness and death across the world (Wang *et al.*, 2016b). These diseases and their associated complications are responsible for infection in millions of people with varying degree of severity. Furthermore, respiratory diseases cause more than 10% of all disability-adjusted life-years (DALYs), a measure that calculates the number of active and productive life lost due to a condition (Cassini *et al.*, 2016). Respiratory diseases are next to cardiovascular diseases (including stroke) only as the leading cause of DALYs (Fitzmaurice *et al.*, 2017). RTI is the most frequently occurring disease in many countries than any other acute illness, including diarrhea and other tropical diseases. It is also the third leading cause of mortality globally and the figures are growing (Burney *et al.*, 2015). Although the burden is hard to analyze, it is estimated that lower respiratory tract infection results in approximately 4 million deaths yearly (WHO 2017). The burden of RTI is most eminent in a population of low socioeconomic status and immunocompromised populations (Bhutta *et al.*, 2013). However, there is a rise in the burden in individuals above 70 years of age (Troeger *et al.*, 2018).

A study conducted in 2016 estimated death as a result of LRTIs to be more than 2.8 million worldwide (Naghavi *et al.*, 2017). Global efforts to reduce the burden of LRIs using different preventive and treatment strategies require timely information about the burden of LRIs, their risk factors, and associated pathogens. Furthermore, acute lower respiratory tract infections in children lead to chronic respiratory diseases in future time. In general, RTIs as a result influenza virus kills about 250,000 and 500,000 people and with financial implications between US$71 and 167 billion yearly

(Nguyen *et al.*, 2016). In 2015, 10.4 million people acquired tuberculosis (TB) and with mortality at a figure of 1.4 million (WHO 2018).

2.5 Surveillance of respiratory tract infection

The World Health Organization (WHO), in the last 60 years has carried out global surveillance of influenza over an interface of experiments known as the Global Influenza Surveillance and Response System (GISRS) (World Health Organization, 2017c). Notwithstanding the epidemiological variations in respiratory disease, commonalities such in the population including children under surveillance, sentry places, sample source, laboratory diagnostic infrastructure, and personnel, the long-secured, well-operating GISRS program gives a financially prudent possibility to ease existing potential to test for other respiratory viruses without disrupting continuing influenza surveillance.

The development of novel techniques for early identification or prediction of outbreaks in community settings or the advancement of the methods that are currently employed is of improving systematic and public health importance. This method is fundamentally based on monitoring appropriate data related to surveillance that is a potential aggregate of cases of RTIs that cross beyond a presumed threshold. In terms of surveillance for influenza-like illness, it is conducted primarily through systems of monitoring services provided by various agencies. The RTI cases in the surveillance are defined as individuals who present clinical manifestations matching specifically defined clinical criteria of the syndrome.

Advanced statistical techniques are required for the analysis of surveillance data to check and identify the occurrence of epidemics on RTIs (Spanos *et al.*, 2012). The universal system of this kind of scheme is the utilization of long-term archival

documents for assessing anticipated rates for prospective temporal-dependent topmost thresholds of the appropriate distribution, to which the real measurements performed are subsequently correlated (Costagliola *et al.*, 1991). Under the general principle of the statistical methods, there are several alternatives in the approach that are proposed to these statistical techniques requiring a relatively few recent historical data and resulting in favorable findings (Cowling *et al.*, 2006). These statistical techniques are part of the broader classes of time-series, regression and industrial quality control systems. Other statistics employed are Cumulative sum (CUSUM) statistics that are widely applied in biomedical studies and consists one of the parts of the Early Aberration and Reporting System (EARS) that is utilized for syndromic surveillance by the United States Centers for Disease Control and Prevention (Cowling *et al.*, 2006; Hutwagner *et al.*, 2005).

The assessment and monitoring of the 2009 influenza pandemic showed some particular gray areas in the global influenza surveillance capacity which compromise the program. The dearth of authorized surveillance for severe disease in many countries and the relative lack of archival information confined participating countries the capacity to assess the extent of the surveillance in the behavior of the viruses. However, the lack of a defined international means for distributing epidemiological information posed some challenges to explaining global patterns of transmission and disease. Finally, the non-standardized approach to data collection and outbreak investigations early in the event resulted in data that was often incompletely understood outside the local context. Therefore, the collection of historical data for the influenza-associated severe respiratory disease will permit accelerated comparative evaluation of every influenza season and future pandemics, both locally and globally (World Health Organization, 2013).

2.6 Respiratory tract infections during Hajj

Respiratory tract infections are the most reported sickness during Hajj pilgrimage which more often results in hospitalization with pneumonia being the most common cause of severe sepsis and septic shock in patients admitted to intensive care units (ICUs) (Memish *et al.*, 2014b). Additional respiratory conditions such as chronic obstructive pulmonary disease, asthma and sinusitis could further result in complications by exacerbating the respiratory infections in severe cases (Pauwels *et al.*, 2012). Acute upper respiratory tract infections are the most common illnesses during the Hajj period (Al-Tawfiq *et al.*, 2016).

The high prevalence of respiratory tract infections during Hajj is due to some factors such as cigarette smoking, direct contact with infected pilgrims, intermittent use of surgical facemasks and a failure to use alcohol-based hand disinfection. High-density crowds are usually associated with this religious obligation and therefore posed a risk for the possible transmission and outbreaks of infectious agents. With over 90% of pilgrim's suffering from at least one respiratory symptom, the risk of viral respiratory infections can increase in several folds (Barasheed *et al.*, 2016). In Saudi Arabia, the cities hosting Hajj activities have been shown to have a higher prevalence of resistant tuberculosis as well as the annual risk of infection compared to other cities that are not involved with the Hajj ritual. This may be as a result of the number of pilgrims from countries where tuberculosis is endemic (Khan *et al.*, 2001).

Studies from pilgrims during Hajj showed that RTI symptoms are the frequent occurring symptom in the recent years with the prevalence rate of cough at over 90% and ILI ranging from 8 to 72.8% (Alfelali *et al.*, 2015; Benkouiten *et al.*, 2019). However, studies conducted during the 2010 Hajj season to a more recent 2016 Hajj season, there is a continued rise in the prevalence of RTI symptoms among Malaysian

Hajj pilgrims despite the implementation of various preventive practices (Deris *et al.*, 2010b; Hashim *et al.*, 2016; Zuraina *et al.*, 2018). The current approach of the protective measures appears inadequate to reduce it. Many viral respiratory infections have been reported to result in illnesses of which influenza viruses are the most prevalent, followed by respiratory syncytial viruses (RSV) and adenoviruses (Rashid *et al.*, 2008a). However, rhinovirus infection was higher among pilgrims from the United Kingdom when compared to influenza, and the attack rate of ARI was higher when compared with local Saudi pilgrims (25% vs. 13%, respectively).

The incidence of respiratory viruses during Hajj from the various study showed a rising trend. During the 2003 Hajj, a study analyzed throat swabs from 500 participants that reported upper respiratory tract infection and discovered 54 (10.8%) participants with positive cultures. The results further showed the incidence of influenza B at 27 (50%), herpes simplex virus at 13 (24.1%), RSV at 7 (12.9%), parainfluenza at 4 (7.4%) and influenza A at 3 (5.6%) (Balkhy *et al.*, 2004). In another study in 2004 Hajj season, influenza B was isolated in 72.7% of the 46 confirmed influenza cases; with Sichuan as the predominant serotype (70.9%), next is influenza A (not typed, 14.6%; Flu A H1N1, 7.3%; Flu A H3N2, 5.5%) and influenza B Hong Kong (1.8%) (AlSaleh *et al.*, 2005). On the other hand, Rashid *et al.* (2008a) in 2005 Hajj season tested nasal swabs of some symptomatic individuals through the use of real-time polymerase chain reaction (RT-PCR). Influenza A was reported at 56.7% (21/37) among established cases, then RSV at 24% (9/37) and influenza B at 18.9% (7/37). There is a difference in the occurrence of the strains of influenza virus detected over the years, implying a common seasonal influenza epidemic where the viruses in circulation are distinctive in different years (Balkhy *et al.*, 2004). The higher incidence of ARI among the United Kingdom pilgrims was slightly associated with their duration