UNIVERSITI PUTRA MALAYSIA

RISK FACTORS FOR HEPATITIS C VIRUS INFECTION AMONG ADULT PATIENTS AT A PUBLIC HOSPITAL IN KEDAH, MALAYSIA

MOHD AZRI MOHD SUAN

FPSK(m) 2020 24

RISK FACTORS FOR HEPATITIS C VIRUS INFECTION AMONG ADULT PATIENTS AT A PUBLIC HOSPITAL IN KEDAH, MALAYSIA

By

MOHD AZRI MOHD SUAN

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirement for the Degree of Master of Science

November 2019

Abstract of thesis presented to the Senate of Universiti Putra Malaysia
in fulfilment of the requirement for the degree of Master of Science

RISK FACTORS FOR HEPATITIS C VIRUS INFECTION AMONG ADULT PATIENTS AT A PUBLIC HOSPITAL IN KEDAH, MALAYSIA

By

MOHD AZRI MOHD SUAN

November 2019

Chair : Salmiah Md Said, M. Community Medicine
Faculty : Medicine and Health Sciences

Hepatitis C virus infection has increasingly become a public health concern in both developed and developing countries. The World Health Organization reported that 71 million persons were living with this chronic hepatitis C virus infection worldwide with global incidence rate accounted for 23.7 per 100,000 population. Malaysia is also reported to have nearly 330 000 adults being infected with this virus. In addition to providing treatment, identifying the potential risk factors to prevent the transmission of HCV are essential to control the hepatitis C infection. However, many known risk factors have not been widely explored in Malaysia. Hence, the aim of the study was to identify the risk factors associated with hepatitis C among adult patients in Kedah state, Malaysia.

The conduct of this study has been approved by the Medical Research and Ethics Committee of the Ministry of Health of Malaysia. This matched, hospital-based, case-control study was conducted at Hospital Sultanah Bahiyah, Alor Setar, in Kedah state. Cases were adults (aged ≥18 years) diagnosed with hepatitis C from January 2015 until December 2018, while controls were age-, gender-, and ethnic-matched and tested negative for hepatitis C virus. The purpose and method of the study were explained to all participants before obtaining their informed consent. A questionnaire on demographic characteristics and previous exposure to listed risk factors were filled up by all study participants. Association of hepatitis C infection with demographic characteristics, occupational profile, medical history, high-risk activities, and traditional practices were assessed using univariable and multiple logistic regression analysis. All data analyses were performed using R statistical software, Version 3.5.2

A total of 255 case-control patient pairs were enrolled in this study. In both groups, majority of the patients were male, aged 50-59 years, and of Malay/Bumiputra ethnicity. Multiple logistic regression analysis indicate that having a history of blood or blood product transfusion before 1992 (adjusted odds ratio [AOR] 6.99, 95% confidence interval [CI]: 3.73, 13.81), injection drug use (AOR 6.60, 95% CI 3.66, 12.43),

imprisonment (AOR 4.58, 95% CI 1.62, 16.40), tattooing (AOR 3.73, 95% CI 1.37, 12.00), having more than one sexual partner (AOR 2.06, 95% CI 1.16-3.69), body piercing (AOR 1.71, 95% CI 1.04, 2.80), and having only secondary education (AOR 1.92, 95% CI 1.06, 3.57) were independently associated with hepatitis C.

In conclusion, these findings demonstrate that the risk factor for hepatitis C is multifactorial. Screening activities should give greater attention to these high-risk groups to identify undiagnosed HCV-infected individuals. Better access to HCV screening and treatment at prison and drug rehabilitation facilities, improved public awareness on unsafe use of illicit drugs and formulating safety guidelines for tattooing and piercing, were among recommended strategies to control this chronic viral infection in Malaysia.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
sebagai memenuhi keperluan untuk ijazah Master Sains

FAKTOR RISIKO BAGI JANGKITAN VIRUS HEPATITIS C DALAM KALANGAN PESAKIT DEWASA DI HOSPITAL AWAM DI KEDAH, MALAYSIA

Oleh

MOHD AZRI MOHD SUAN

November 2019

Pengerusi : Salmiah Md Said, M. Perubatan Komuniti
Fakulti : Perubatan dan Sains Kesihatan

Jangkitan virus hepatitis C semakin menjadi kebimbangan bagi kesihatan awam di negara-negara maju mahupun membangun. Pertubuhan Kesihatan Sedunia (WHO) melaporkan bahawa 71 juta orang menghidap jangkitan virus hepatitis C ini di serata dunia dengan kadar insidens global mencecah 23.7 bagi setiap 100,000 populasi. Malaysia juga turut dilaporkan mempunyai hampir 330,000 orang dewasa yang dijangkiti virus ini. Selain pemberian rawatan, pengenalpastian faktor risiko untuk mencegah penularan hepatitis C adalah penting untuk mengawal jangkitan tersebut. Namun begitu, banyak faktor risiko yang diketahui masih belum diterokai secara meluas di Malaysia. Oleh sebab itu, kajian ini bertujuan untuk mengenal pasti faktor-faktor risiko yang berkaitan dengan hepatitis C dalam kalangan pesakit dewasa di Kedah, Malaysia.

Kebenaran untuk menjalankan kajian ini telah diluluskan oleh Jawatankuasa Etika dan Penyelidikan Perubatan, Kementerian Kesihatan Malaysia. Kajian kes-kawalan sepadan ini telah dijalankan di Hospital Sultanah Bahiyah, Alor Setar, di negeri Kedah. Kes ialah orang dewasa (berumur ≥ 18 tahun) yang didiagnosis dengan jangkitan hepatitis C dari Januari 2015 hingga Disember 2018, manakala kawalan dipadankan mengikut umur, jantina dan etnik serta diuji negatif untuk virus hepatitis C. Tujuan dan kaedah kajian diterangkan kepada semua peserta kajian sebelum kebenaran diperoleh daripada mereka. Borang soal selidik tentang demografi dan pendedahan sebelumnya kepada faktor risiko yang disenaraikan telah diisi oleh semua peserta kajian. Perkaitan antara jangkitan hepatitis C dengan ciri-ciri demografi, profil pekerjaan, sejarah perubatan, aktiviti berisiko tinggi, dan amalan tradisional telah dinilai menggunakan analisis regresi logistik univariat dan multivariat. Semua analisis data dilakukan menggunakan perisian statistik R versi 3.5.2.

Sejumlah 255 pasangan kes-kawalan telah terbabit dalam kajian ini. Dalam kedua-dua kumpulan, majoriti pesakitnya ialah lelaki, berumur 50–59 tahun, dan daripada etnik

Melayu/Bumiputera. Analisis regresi logistik berganda menunjukkan bahawa peserta yang mempunyai sejarah transfusi darah atau produk darah sebelum tahun 1992 (nisbah ods terlaras [AOR] 6.99, 95% selang keyakinan [CI]: 3.73, 13.81), penggunaan dadah secara suntikan (AOR 6.60, 95% CI 3.66, 12.43), pemenjaraan (AOR 4.58, 95% CI 1.62, 16.40), bertatu (AOR 3.73, 95% CI 1.37, 12.00), mempunyai lebih daripada seorang pasangan seks (AOR 2.06, 95% CI 1.16, 3.69), bertindik (AOR 1.71, 95% CI 1.04, 2.80), dan hanya mendapat pendidikan menengah (AOR 1.92, 95% CI 1.06, 3.57) berkait secara tidak bersandar dengan hepatitis C.

Kesimpulannya, penemuan ini menunjukkan bahawa faktor risiko bagi hepatitis C adalah multifaktoral. Aktiviti penyaringan hendaklah lebih tertumpu kepada kumpulan berisiko tinggi ini untuk mengenal pasti individu yang dijangkiti HCV yang belum didiagnosis. Capaian yang lebih baik kepada penyaringan dan rawatan HCV di penjara dan pusat pemulihan dadah, kesedaran awam yang lebih tinggi mengenai penggunaan dadah terlarang yang tidak selamat, dan penyediaan garis panduan keselamatan untuk bertatu dan bertindik merupakan antara strategi yang disarankan untuk mengawal jangkitan virus kronik ini di Malaysia.

ACKNOWLEDGEMENTS

I am forever grateful to my thesis advisor and Committee Chair, Assoc. Prof. Dr Salmiah Md Said for her guidance and sharing her expert knowledge and wisdom with me throughout this master program. A huge thank you to my supervisory committee; Dr Ahmad Zaid Fattah Azman and Datuk Dr Muhammad Radzi Abu Hassan, for their guidance in completing this thesis project. Special thanks to Dr Lim Poh Ying for her assistance in R statistical analysis. I also thank the Research Management Center, Universiti Putra Malaysia for providing the financial support to conduct this Master project through Putra Grant. I want to give a special thanks to my wife, Azrina Ayob, family members and friends in Clinical Research Center, Hospital Sultanah Bahiyah, Alor Setar, who also supported me and encouraged me to pursue and complete my Masters program. Without all of these people, this thesis would have never been completed. Thank you all for being there for me and helping me reach my goals.

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

Salmiah Md Said, M. Community Medicine
Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Ahmad Zaid Fattah Azman, DrPH
Medical Lecturer
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Muhammad Radzi Abu Hassan, MRCP
Consultant Physician and Gastroenterologist
Department of Medicine,
Hospital Sultanah Bahiyah, Kedah
(Member)

_____

ZALILAH MOHD SHARIFF, PhD
Professor and Deputy Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

Declaration by Graduate Student

I hereby confirm that:

- this thesis is my original work;
- quotations, illustrations and citations have been duly referenced;
- this thesis has not been submitted previously or concurrently for any other degree at any other institutions;
- intellectual property from the thesis and copyright of thesis are fully-owned by Universiti Putra Malaysia, as according to the Universiti Putra Malaysia (Research) Rules 2012;
- written permission must be obtained from supervisor and the office of Deputy Vice-Chancellor (Research and Innovation) before thesis is published (in the form of written, printed or in electronic form) including books, journals, modules, proceedings, popular writings, seminar papers, manuscripts, posters, reports, lecture notes, learning modules or any other materials as stated in the Universiti Putra Malaysia (Research) Rules 2012;
- there is no plagiarism or data falsification/fabrication in the thesis, and scholarly integrity is upheld as according to the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) and the Universiti Putra Malaysia (Research) Rules 2012. The thesis has undergone plagiarism detection software.

Signature: _____ Date: _____

Name and Matric No.: Mohd Azri Mohd Suan, GS48384

Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

Signature: _____

Name of Chairman
of Supervisory Committee: Salmiah Md Said

Signature: _____

Name of Member of
Supervisory Committee: Ahmad Zaid Fattah Azman

Signature: _____

Name of Member of
Supervisory Committee: Muhammad Radzi Abu Hassan

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AOR	adjusted odd ratio
CDC	Centre of Disease Control
CI	confidence intervals
EIA	enzyme immunoassay
HBV	hepatitis B Virus
HCC	hepatocellular carcinoma
HCV	hepatitis C Virus
HIV	human immunodeficiency virus
HSB	Hospital Sultanah Bahiyah
MOH	Ministry of Health
MSM	men who had sex with men
NAT	nucleic acid testing
OR	odd ratio
PCR	polymerase chain reaction
ROC	receiver operating characteristics
RR	risk ratio
WHO	World Health Organisation

LIST OF APPENDICES

CHAPTER 1

INTRODUCTION

This chapter provides an overview on the background of hepatitis C infection. At the end of this chapter, it states the significance of this study, study objectives and research hypotheses conducted among adult patients in Kedah state.

1.1 Background

Hepatitis C is a blood-borne disease that results from hepatitis C virus (HCV) infection. The virus was first discovered from the serum of patient with non-A, non-B hepatitis patient in 1989 (Choo et al., 1989). The virus is a RNA virus that belongs to the family *Flaviviridae* (Lauer & Walker, 2001). There are six major genotypes (numbered as 1 through 6) and more than 50 subtypes (e.g. 1a, 1b, 2a) of these viruses (Zein, 2000) have been recognized worldwide. Due to its chronic effect on the liver, the global burden of disease attributable to HCV-related liver disease seem to be substantial and expected to increase in the next few years (Razavi et al., 2014).

Globally, about 1.75 million new HCV infections and 400,000 HCV-related deaths were reported annually (World Health Organization [WHO], 2017a). There is a wide variation in the incidence of HCV in the world's general population. According to the Global Hepatitis Report, the global incidence rates is highest in the WHO Eastern Mediterranean (23.7 per 100,000 population) and European regions (61.8 per 100,000 population) (WHO, 2017a). In contrast, the Region of the Americas and Western Pacific Region had shown a single digit incidence rate, 6.4 and 6.0 per 100,000 population, respectively. Nevertheless, several studies reported a decreasing trend of HCV infection rate since the 1960s (Armstrong, Alter, McQuillan, & Margolis, 2000; Williams, Bell, Kuhnert, & Alter, 2011). The global prevalence of HCV infection was 1.0%. Similar to HCV incidence, the highest prevalence was recorded in the Eastern Mediterranean Region (2.3%), with the European Region ranked second (1.5%) (WHO, 2017a). Only a small prevalence of HCV was estimated for the South-East Asia Region (0.5%).

In term of mortality, viral hepatitis (which include hepatitis A, B, C, D, and E infection) had caused more death (1.34 million) than those due to human immunodeficiency virus (HIV) infection (1.06 million deaths) (WHO, 2017a). The global mortality rate from viral hepatitis is 18.3 deaths per 100,000 population. The Western Pacific region has the lowest incidence rate but also showed the highest mortality rate (24.1 deaths per 100,000 population), followed by the Southeast Asian region (21.2 deaths per 100,000 population) (WHO, 2017a). The number of deaths reported from the Western Pacific, South-East Asia and African regions were 446 000, 408 000 and 136 000 deaths, respectively (WHO, 2017a). In another study by Lozano et al. (2012), the number of deaths related to hepatitis C were doubled, from 8100 deaths in year 1990 to 16,000 deaths in year 2010. The above incidence and mortality rate signify the burden of disease

and the importance of early detection and treatment to reduce death from hepatitis infection.

HCV severity can range from a mild illness lasting a few weeks to serious life-long illness with potentially fatal liver-related consequences that include cirrhosis and hepatocellular carcinoma (Modi & Liang, 2008). Cirrhosis accounts for more death (280,000 deaths) compared to liver carcinoma (100,000 deaths) (WHO, 2017a). Furthermore, over 350,000 people die from hepatitis C-related liver diseases annualy (WHO, 2017a). In the United States, HCV-associated liver disease was the major indication for liver transplant (Wong et al., 2015). Besides liver, several other conditions can be linked to hepatitis C. Extrahepatic manifestation means diseases or conditions that affect organs other than liver. More than 70% of HCV patients experience extrahepatic condition in which some of these features are well documented and common, while others are rarely found (Cacoub et al., 1999, 2000).

HCV is a bloodborne virus and commonly spread through contact with contaminated blood or blood products (WHO, 2017a). Thus, the risk was greater among person with injection drug use (Ho et al., 2012) and healthcare workers (Ahmed, Irving, Anwar, Myles & Neal, 2012; Averhoff, Glass, & Holtzman, 2012). Other known risk factors are haemodialysis, tattooing, body piercing, acupuncture and having sex with infected partner (Ahmed et al., 2012; Sohn et al., 2016). In Europe, Australia and the United States of America (USA), it was also found that hepatitis C is common among men who have sex with men (MSM) that are infected with human immunodeficiency virus (HIV) (Chan, Sun, Wong, Lee, & Hung, 2016). Other uncommon risk factors associated with hepatitis C were cupping therapy, circumcision (Abd El-Wahab, Mikheal, Sidkey, & Shatat, 2014), home delivery (Metwally et al., 2014), and contact sport (Karmochkine, Carrat, Dos Santos, Cacoub, & Raguin, 2006). Despite the known risk factors of hepatitis C mentioned above, there was still cases with an unrecognised source of infection, as high as 40% (Raguin et al., 1998).

A vaccine for preventing hepatitis C infection is still unavailable (WHO, 2017b). Thus, the infection is prevented mainly by identifying and controlling any possible risk factor that promotes virus transmission. Prevention can be accomplished through the implementation of safety precaution by healthcare workers, introduction of reuse prevention devices, reduction of unnecessary healthcare injection (WHO, 2016a), implementation of harm reduction interventions for people who inject drugs (Csete et al., 2016), and providing of access to treatment and early screening for high-risk groups (WHO, 2017a).

Malaysia is also confronted with the burden on HCV infection. According to the Ministry of Health (MOH) Malaysia, the incidence rate of hepatitis C was 2.56 per 100,000 population in year 2010 and increased to 7.3 per 100,000 population in year 2014, an increase by 185.2%. The incidence rate was slightly reduced to 6.91 per 100,000 population for year 2015 (MOH Malaysia, 2010a, 2012, 2013, 2014, 2015, 2016). The national mortality rate for hepatitis C was 0.1 per 100,000 population in year 2010. The mortality rate was almost doubled (0.18 per 100,000 population) in year 2011, before came down to 0.11 per 100,000 in year 2012. While the incidence rate reduced in year

2015, the mortality rate recorded the highest figure in 6-year period, at 0.19 per 100,000 population (MOH Malaysia, 2010a, 2012, 2013, 2014, 2015, 2016). The incidence rate of hepatitis C in Malaysia is summarised in Table 1.1.

Furthermore, the local prevalence of HCV among specific high-risk population varied as reported in several studies. The highest prevalence was recorded among injection drug user (89.9%) (Chawarski, Mazlan, & Schottenfeld, 2006) and the lowest prevalence was seen among local blood donor (0.45%) (Haslina et al., 2012). Since the availability of HCV screening test in Malaysia, injection drug use was identified as the main risk factor for HCV infection. In a study between 1985 and 1991, Sinniah and Ooi (1993) have

Table 1.1: Number of cases and incidence rate of hepatitis C in Malaysia

Year	No of Cases	Incidence Rate*
2003	520	2.08
2004	745	2.91
2005	995	3.81
2006	1163	4.37
2007	1412	5.2
2008	928	3.35
2009	1049	3.71
2010	724	2.56
2011	1047	3.61
2012	1734	5.91
2013	2011	6.77
2014	2196	7.30
2015	2108	6.91
2016	2645	8.35
2017	3089	9.54

* Incidence rate per 100,000 population

(Source: Malaysia Health Indicator Report (MOH Malaysia, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010a, 2012, 2013, 2014, 2015, 2016, 2017b, 2018b).

screened various risk groups for the anti-HCV antibody. They found that the highest percentage of positive anti-HCV antibody was among patient with injection drug use (85%), followed by blood recipients (64%) and dialysis patients (54%). Similar finding was found by Tan et al. (2015) in which 77.8% of patients diagnosed with hepatitis C were injection drug user. Only a small percentage of HCV positive patient reported a history of blood transfusion (4.9%) and having sexual contact with infected partner (3.9%).

1.2 Problem Statements

Despite the disease high burden, hepatitis C is curable if it is diagnosed and treated timely (WHO, 2017c). The introduction of highly effective direct-acting antivirals (DAAs) such as the NS3 protease inhibitors (e.g. Glecaprevir), the NS5B nucleotide inhibitor (e.g. Sofosbuvir), and the NS5A inhibitors (e.g. Daclatasvir and Ledipasvir), are a major advancement in hepatitis C treatment (WHO, 2016b). In Malaysia, Sofosbuvir and Daclatasvir are available in 25 public hospitals throughout the country. However, the high cost of DAAs have imposed a financial burden on the public healthcare system and have limited access for the hepatitis C patient in Malaysia. In 2017, there were more than 12 000 HCV-infected patients awaiting access to DAAs (Hiebert et al., 2019). Thus, in addition to providing treatment, identifying the potential risk factors and preventing the transmission of HCV are still essential to control the hepatitis C infection.

Several studies on risk behaviours associated with HCV acquisition have been conducted in Malaysia. However, most of the studies are only limited to high-risk populations, particularly drug users (Tan, Yihui & Abu Hassan, 2015; Vicknasingam, Narayanan, & Navaratnam, 2009), haemodialysis patients (Jaafar et al., 2011), fishermen (Choo et al., 2015), and blood donors (Ng et al., 1995). In addition, the roles of other known risk factors, such as cupping, acupuncture, occupational exposure and surgical procedures, have not been widely explored. Moreover, a notable concern is the existence of patients with unknown risk factors for hepatitis C that had been reported locally to be as high as 8 to 42% (Siti, Hairul, & Hadzri, 2017; Tan et al., 2011; Tan & Adlin, 2017; Tan, Yihui, & Abu Hassan, 2015).

For the present study, Kedah state was chosen for several reasons. First, the incidence rate of HCV infection in Kedah was high, ranked as second highest among other states in Malaysia where in the year 2013, 260 cases of HCV were registered in Kedah with the incidence rate of 12.91 per 100,000 population (MOH Malaysia, 2014). Furthermore, since year 2013 till 2015, the Kedah state had higher rate of HCV infection than the national rate (MOH Malaysia, 2014, 2015, 2016). Second, there was an increased number of local adult population involved in the high-risk activities. For instance, almost four thousand drug addicts were recorded from Kedah state, representing 12.5% of total drug abusers caught in Malaysia for the year 2016 (Ministry of Home Affairs Malaysia, 2017). Third, as Kedah state is neighbouring with Southern Thailand, a known place for shopping and night entertainment among local population, sexual transmission may also become a major risk factor for HCV infection for this state. It is estimated that 3 million Malaysian crossed the country border via Bukit Kayu Hitam gate to visit Thailand (Mohd-Noor, 2018), and the number of visitors were escalated during weekends. With a high prevalence of HCV among Thailand sex workers (Luksamijarulkul &

Deangbubpha, 1997), the virus may be transmitted through sexual contact with commercial sex workers there. Suggestion to open the border gate round-the-clock at Bukit Kayu Hitam could increase the rate of HCV infection (Abas, 2017).

In a nutshell, all of the figures and findings mentioned earlier are reaffirming that HCV infection is undoubtedly a public health threat in Kedah state and identifying its risk factors is warranted. Using a case-control study design, the present study was conducted to determine any association between occupational profile, medical history, involvement in high-risk activities, and traditional practices with HCV infection among adult patient in Kedah state.

1.3 Significance of the Study

The conduct of this study is a significant endeavour in extending the existing local knowledge on HCV infection and its risk factor. Not like other previous studies, the the present study was conducted among the hospital-based population and incorporated several factors that are potentially associated with HCV infection that have not previously been well studied in the Malaysia population. These factors were working as a health care professional, high-risk behaviours (intranasal drug use, imprisonment and men who have sex with men) and common traditional practices (acupuncture, cupping, home birth and male circumcision). Thus, the present study and its findings are proposed to provide better results to support the existing knowledge of the related issue. Furthermore, the result from the present research will help to identify possible local practices that have an association with the HCV infection. The findings in this study will be the basis for other researchers to conduct future research on the same area. It is also anticipated that the study results will provide information for the local health authorities and policy makers on key areas to formulate effective screening programs to identify undiagnosed individuals with HCV infection in Kedah state and Malaysia.

1.4 Research Questions

What is the risk factors for HCV infection among adult patients at Hospital Sultanah Bahiyah, Kedah?

1.5 Objectives of the Study

1.5.1 General Objective

This study aims to determine the risk factors that are associated with HCV infection among adult patients at Hospital Sultanah Bahiyah, Kedah, Malaysia.

1.5.2 Specific Objectives

The specific objectives of this study are:

i. To describe the sociodemographic characteristics, occupational profile, medical history, high-risk activities, and traditional practices of adult patients at Hospital Sultanah Bahiyah, Kedah.
ii. To determine the association between HCV infection among adult patients at Hospital Sultanah Bahiyah, Kedah with the following risk factors:
    a. Sociodemographic characteristics (e.g. educational level, marital status).
    b. Occupational profile (e.g. healthcare worker, fishery/maritime worker, unemployed).
    c. Medical history (e.g. blood or blood product transfusion recipient, needle stick injury, haemodialysis, previous surgical procedures, HIV status, vertical transmission, had evacuation of retained product of conception).
    d. High-risk activities (e.g. injection drug use, intranasal drug use, tattooing, imprisonment, cosmetic procedures, contact sports, sexual contact with HCV-positive spouse, men having sex with men, having more than one sexual partner).
    e. Traditional practices (e.g. acupuncture, cupping, body piercing, male circumcision by traditional practitioner, home delivery by traditional midwife)
iii. To determine the independent risk factors for HCV infection among adult patients at Hospital Sultanah Bahiyah, Kedah.

1.6 Hypothesis

The research hypotheses are:

i. The odds of acquiring HCV infection is higher among participant with lower education than those with higher education.
ii. The odds of acquiring HCV infection is higher among participant with high risk occupation (healthcare worker, fishery/maritime worker, unemployed) than those who did not worked in this group of occupation.
iii. The odds of acquiring HCV infection is higher among participant with risky medical history (history of blood or blood product transfusion, needle stick injury, haemodialysis, surgical procedures, HIV-coinfection, born to HCV-infected mother and had evacuation of retained product of conception) than those without such history.
iv. The odds of acquiring HCV infection is higher among participant involved in high risk activities (injection drug use, intranasal drug use, tattooing, imprisonment, cosmetic procedures, contact sports, sexual contact with HCV-positive spouse, men having sex with men, having more than one sexual partner) than those who not involved in these activities.
v. The odds of acquiring HCV infection is higher among participant carry out risky traditional practices (acupuncture, cupping, body piercing, male circumcision by traditional practitioner, home delivery by traditional midwife) than those who not practising it.

REFERENCES

Abas, A. (2017, June 17). Malaysia-Thailand run 24 hour ICQS operations midnight. *New Straits Times*. Retrieved from https://www.nst. com.my/news/nation/ 2019/06/496899/malaysia-thailand-run-24-hour-icqs-operations-midnight

Abd El-Wahab, E., Mikheal, A., Sidkey, F., & Shatat, H. Z. (2014). Factors associated with hepatitis C infection among chronic HCV Egyptian patients. *Iranian Journal of Public Health*, *43*(11), 1510–1518.

Abdelwahab, S., Rewisha, E., Hashem, M., Sobhy, M., Galal, I., Allam, W. R., … Strickland, G. T. (2012). Risk factors for hepatitis C virus infection among Egyptian healthcare workers in a national liver diseases referral centre. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *106*(2), 98–103. doi:10.1016/j.trstmh.2011.10.003

Ahmed, F., Irving, W. L., Anwar, M., Myles, P., & Neal, K. R. (2012). Prevalence and risk factors for hepatitis C virus infection in Kech District, Balochistan, Pakistan: Most infections remain unexplained. A cross-sectional study. *Epidemiology and Infection*, *140*(4), 716–723.doi:10.1017/ S0950268811001087

Ampuero, J., Romero-Gómez, M., & Reddy, K. R. (2014). Review article: HCV genotype 3 – the new treatment challenge. *Alimentary Pharmacology & Therapeutics*, *39*(7), 686–698. doi:10.1111/apt.12646

Antonelli, A., Ferrari, S. M., Giuggioli, D., Di Domenicantonio, A., Ruffilli, I., Corrado, A., … Fallahi, P. (2014). Hepatitis C virus infection and type 1 and type 2 diabetes mellitus. *World Journal of Diabetes*, *5*(5), 586–600. doi:10.4239/wjd.v5.i5.586

Armstrong, G. L., Alter, M. J., McQuillan, G. M., & Margolis, H. S. (2000). The past incidence of hepatitis C virus infection: Implications for the future burden of chronic liver disease in the United States. *Hepatology*, *31*(3), 777–782. doi:10.1002/hep.510310332

Arshad, M., El-Kamary, S. S., & Jhaveri, R. (2011). Hepatitis C virus infection during pregnancy and the newborn period-are they opportunities for treatment? *Journal of Viral Hepatitis*, *18*(4), 229–236. doi:10.1111/j.1365-2893.2010.01413.x

Ashkani-Esfahani, S., Alavian, S. M., & Salehi-Marzijarani, M. (2017). Prevalence of hepatitis C virus infection among hemodialysis patients in the Middle-East: A systematic review and meta-analysis. *World Journal of Gastroenterology*, *23*(1), 151–166. doi:10.3748/wjg.v23.i1.151

Assari, S., Yarmohamadivasel, M., Moghani. L. M., Sehat, M., Narenjiha, H., Rafiey, H., … Ahmadi, K. (2014). Having multiple sexual partners among Iranian intravenous drug users. *Front Psychiatry*. 2014;5:125.

Averhoff, F. M., Glass, N., & Holtzman, D. (2012). Global burden of hepatitis C: Considerations for healthcare providers in the United States. *Clinical Infectious Diseases*, *55*(Suppl 1), S10-15. doi:10.1093/cid/cis361

Benova, L., Mohamoud, Y. A., Calvert, C., & Abu-Raddad, L. J. (2014). Vertical transmission of hepatitis C virus: Systematic review and meta-analysis. *Clinical Infectious Diseases*, *59*(6), 765–773. doi:10.1093/cid/ciu447

Bhopal, R. S. (2016). *Concept of Epidemiology* (3rd ed.). United Kingdom: Oxford University Press. p.278.

Bollepalli, S., Mathieson, K., Bay, C., Hillier, A., Post, J., Van Thiel, D. H., & Nadir, A. (2007). Prevalence of risk factors for hepatitis C virus in HIV-infected and HIV/hepatitis C virus-coinfected patients. *Sexually Transmitted Diseases*, *34*(6), 367–370. doi:10.1097/01.olq.0000240295.35457.b1

Brandão, A. B. M., & Fuchs, S. C. (2002). Risk factors for hepatitis C virus infection among blood donors in southern Brazil: A case-control study. *BMC Gastroenterology*, *2*, 1-8.

Bruggmann, P., Berg, T., Øvrehus, A. L. H., Moreno, C., Brandão Mello, C. E., Roudot-Thoraval, F., … Hindman, S. J. (2014). Historical epidemiology of hepatitis C virus (HCV) in selected countries. *Journal of Viral Hepatitis*, *21*(Suppl 1), 5–33. doi:10.1111/jvh.12247

Bujang, M., & Baharum, N. (2017). Guidelines of the minimum sample size requirements for Cohen's Kappa. *Epidemiology Biostatistics and Public Health*, *14*(2), e126671-e126679. doi:10.2427/12267

Cacoub, P., Dabis, F., Costagliola, D., Almeida, K., Lert, F., Piroth, L., & Semaille, C. (2015). Burden of HIV and hepatitis C co-infection: The changing epidemiology of hepatitis C in HIV-infected patients in France. *Liver International*, *35*(1), 65–70. doi:10.1111/liv.12639

Cacoub, P., Poynard, T., Ghillani, P., Charlotte, F., Olivi, M., Piette, J. C., & Opolon, P. (1999). Extrahepatic manifestations of chronic hepatitis C. *Arthritis and Rheumatism*, *42*(10), 2204–2212. doi:10.1002/1529-0131(199910)42:10<2204::AID-ANR24>3.0.CO;2-D

Cacoub, P., Renou, C., Rosenthal, E., Cohen, P., Loury, I., Loustaud-Ratti, V., … Piette, J. C. (2000). Extrahepatic manifestations associated with hepatitis C virus infection. A prospective multicenter study of 321 patients. *Medicine*, *79*(1), 47–56.

Center of Disease Control. (2013). Testing for HCV infection: An update of guidance for clinicians and laboratorians. *Morbidity and Mortality Weekly Report*, *62*(18), 362–365.

Chan, D. P. C., Sun, H.-Y., Wong, H. T. H., Lee, S.-S., & Hung, C.-C. (2016). Sexually acquired hepatitis C virus infection: A review. *International Journal of Infectious Diseases*, *49*, 47–58. doi:10.1016/j.ijid.2016.05.030

Chawarski, M. C., Mazlan, M., & Schottenfeld, R. S. (2006). Heroin dependence and HIV infection in Malaysia. *Drug and Alcohol Dependence*, *82*(Suppl 1), S39-42.

Chen, D. S., Hamoudi, W., Mustapha, B., Layden, J., Nersesov, A., Reic, T., … Schmelzer, J. D. (2017). Strategies to manage hepatitis C virus infection disease burden-Volume 4. *Journal of Viral Hepatitis*, *24*(Suppl 2), 44–63. doi:10.1111/jvh.12759

Chen, S. L., & Morgan, T. R. (2006). The natural history of hepatitis C virus (HCV) infection. *International Journal of Medical Sciences*, *3*(2), 47–52.

Choo, M. K. K., El-Bassel, N., Adam, P. C. G., Gilbert, L., Wu, E., West, B. S., … Kamarulzaman, A. (2015). Prevalence and correlates of HIV and hepatitis C virus infections and risk behaviors among Malaysian fishermen. *PloS One*, *10*(8), e0118422. doi:10.1371/journal.pone.0118422

Choo, Q. L., Kuo, G., Weiner, A. J., Overby, L. R., Bradley, D. W., & Houghton, M. (1989). Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science*, *244*(4902), 359–362.

Cook, R. .D., & Weisberg, S. (1982). *Residuals and Influence in Regression*. London: Chapman and Hall. p.145.

Csete, J., Kamarulzaman, A., Kazatchkine, M., Altice, F., Balicki, M., Buxton, J., … Beyrer, C. (2016). Public health and international drug policy. *Lancet*, *387*(10026), 1427–1480. doi:10.1016/S0140-6736(16)00619-X

Dumont, D. M., Brockmann, B., Dickman, S., Alexander, N., & Rich, J. D. (2012). Public health and the epidemic of incarceration. *Annual Review of Public Health*, *33*, 325–339. doi:10.1146/annurev-publhealth-031811-124614

Duraisamy, G. (1994). Blood transfusion service in Malaysia. *Japanese Journal of Transfusion Medicine*, *40*(5), 776–778. doi:10.3925/jjtc1958.40.776

Duraisamy, G., Zuridah, H., & Ariffin, M. Y. (1993). Prevalence of hepatitis C virus antibodies in blood donors in Malaysia. *The Medical Journal of Malaysia*, *48*(3), 313–316.

El-Ghitany, E. M., Abdel Wahab, M. M., Abd El-Wahab, E. W., Hassouna, S., & Farghaly, A. G. (2015). A comprehensive hepatitis C virus risk factors meta-analysis (1989-2013): Do they differ in Egypt? *Liver International*, *35*(2), 489–501. doi:10.1111/liv.12617

Feinstone, S. M., Kapikian, A. Z., Purcell, R. H., Alter, H. J., & Holland, P. V. (1975). Transfusion-associated hepatitis not due to viral hepatitis type A or B. *The New England Journal of Medicine*, *292*(15), 767–770. doi:10.1056/NEJM 197504102921502

Fissell, R. B., Bragg-Gresham, J. L., Woods, J. D., Jadoul, M., Gillespie, B., Hedderwick, S. A., … Young, E. W. (2004). Patterns of hepatitis C prevalence and seroconversion in hemodialysis units from three continents: The DOPPS. *Kidney International*, *65*(6), 2335–2342. doi:10.1111/j.1523-1755.2004. 00649.x

Fleiss, J., Levin, B., & Paik, M. C. (2003). *Statistical methods for rates and proportions* (3rd ed.). New York, NJ: John Wiley. p.604.

Franciscus, A. (2016). *HCSP fact sheet: HCV genotype, quasi-species & subtype*. Retrieved from http://hcvadvocate.org/hepatitis/factsheets_pdf/genotype.pdf. Accessed July 7, 2017.

Goh, B., & Ong, L. (2015). *22nd Report of the Malaysian Dialysis & Transplant Registry 2014*. Retrieved from http://msn.org.my/nrr/mdtr2014.jsp. Accessed July 5, 2017.

Gorar, Z. A., Butt, Z. A., & Aziz, I. (2014). Risk factors for bloodborne viral hepatitis in healthcare workers of Pakistan: A population based case-control study. *BMJ Open*, *4*(7), e004767. doi:10.1136/bmjopen-2013-004767

Gower, E., Estes, C., Blach, S., Razavi-Shearer, K., & Razavi, H. (2014). Global epidemiology and genotype distribution of the hepatitis C virus infection. *Journal of Hepatology*, *61*(Suppl 1), S45-57. doi:10.1016/j.jhep.2014.07.027

Grebely, J., & Dore, G. J. (2011). What is killing people with hepatitis C virus infection? *Seminars in Liver Disease*, *31*(4), 331–339. doi:10.1055/s-0031-1297922

Gupta, E., Bajpai, M., & Choudhary, A. (2014). Hepatitis C virus: Screening, diagnosis, and interpretation of laboratory assays. *Asian Journal of Transfusion Science*, *8*(1), 19–25. doi:10.4103/0973-6247.126683

Hair, J. F., Anderson, R. E., Tatham, R. L. & Black, W. C. (1995). *Multivariate Data Analysis* (3rd ed.). New York: Macmillan Publishing Company.

Hamzah, H., Hasmoni, M., Saad, M., Mustafa, M., Abdullah, N., & Seman, R. (2010). Hepatitis C genotyping in haemodialysis patients and the development of genotyping method based on TaqMan probe real-time PCR. *Hepatology International*, *4*, 179.

Haslina, M. N. N., Khairiah, Y., Zainy, D. Z., Shafini, M. Y., Rosnah, B., & Marini, R. (2012). Seroprevalence of hepatitis C virus infection among blood donors in a teaching hospital in north-eastern Malaysia. *The Southeast Asian Journal of Tropical Medicine and Public Health*, *43*(3), 668–673.

Hiebert, L., Hecht, R., Soe-Lin, S., Mohamed, R., Shabaruddin, F. H., Syed Mansor, S. M., … McDonald, S. A. (2019). A stepwise approach to a national hepatitis C screening strategy in Malaysia to meet the WHO 2030 targets: Proposed strategy, coverage, and costs. *Value in Health Regional Issues*, *18*, 112–120. doi:10.1016/j.vhri.2018.12.005

Ho, E. Y., Ha, N. B., Ahmed, A., Ayoub, W., Daugherty, T., Garcia, G., … Nguyen, M. H. (2012). Prospective study of risk factors for hepatitis C virus acquisition by Caucasian, Hispanic, and Asian American patients. *Journal of Viral Hepatitis*, *19*(2), e105-111. doi:10.1111/j.1365-2893.2011.01513.x

Ho, S. H., Ng, K. P., Kaur, H., & Goh, K. L. (2015). Genotype 3 is the predominant hepatitis C genotype in a multi-ethnic Asian population in Malaysia. *Hepatobiliary & Pancreatic Diseases International*, *14*(3), 281–286.

Hosmer, D. W., & Lemeshow, S. (2002). *Applied logistic regression* (2nd ed.). New York: Wiley & Sons, Inc. p.35-233.

Huang, Y., Guo, N., Yu, Q., Lv, Y., Ma, H., Yun, Z., … Shan, H. (2015). Risk factors for hepatitis B and C infection among blood donors in five Chinese blood centers. *Transfusion*, *55*(2), 388–394. doi:10.1111/trf.12850

Jaafar, R., Isahak, I., Wong, K., Rashid, Z. Z., Sulong, A., Jaafar, M., & Gafor, A. A. (2011). Prevalence and predisposing factors for hepatitis C virus in haemodialysis unit Universiti Kebangsaan Malaysia Medical Centre. *BMC Proceedings*, *5*(6), P210. doi:10.1186/1753-6561-5-S6-P210

Jafari, S., Copes, R., Baharlou, S., Etminan, M., & Buxton, J. (2010). Tattooing and the risk of transmission of hepatitis C: A systematic review and meta-analysis. *International Journal of Infectious Diseases*, *14*(11), e928-940. doi:10.1016/ j.ijid.2010.03.019

Johnston, L. G., & Corceal, S. (2013). Unexpectedly high injection drug use, HIV and hepatitis C prevalence among female sex workers in the Republic of Mauritius. *AIDS and Behavior*, *17*(2), 574–584. doi:10.1007/s10461-012-0278-y

Kamarulzaman, A., Reid, S. E., Schwitters, A., Wiessing, L., El-Bassel, N., Dolan, K., … Altice, F. L. (2016). Prevention of transmission of HIV, hepatitis B virus, hepatitis C virus, and tuberculosis in prisoners. *Lancet*, *388*(10049), 1115–1126. doi:10.1016/S0140-6736(16)30769-3

Kandeel, A. M., Talaat, M., Afifi, S. A., El-Sayed, N. M., Abdel Fadeel, M. A., Hajjeh, R. A., & Mahoney, F. J. (2012). Case control study to identify risk factors for acute hepatitis C virus infection in Egypt. *BMC Infectious Diseases*, *12*, 294. doi:10.1186/1471-2334-12-294

Karmochkine, M., Carrat, F., Dos Santos, O., Cacoub, P., & Raguin, G. (2006). A case-control study of risk factors for hepatitis C infection in patients with unexplained routes of infection. *Journal of Viral Hepatitis*, *13*(11), 775–782. doi:10.1111/j.1365-2893.2006.00742.x

Kin, K. C., Lin, B., Chaung, K. T., Ha, N. B., Trinh, H. N., Garcia, R. T., … Nguyen, M. H. (2013). Less-established risk factors are common in Asian Americans with hepatitis C virus: A case-controlled study. *Digestive Diseases and Sciences*, *58*(11), 3342–3347. doi:10.1007/s10620-013-2884-6

Kuo, C.-L., Duan, Y., & Grady, J. (2018). Unconditional or conditional logistic regression model for age-matched case-control data? *Frontiers in Public Health*, *6*, 1-11. doi:10.3389/fpubh.2018.00057

Lauer, G. M., & Walker, B. D. (2001). Hepatitis C virus infection. *The New England Journal of Medicine*, *345*(1), 41–52. doi:10.1056/NEJM200107053450107

Laumann, A. E., & Derick, A. J. (2006). Tattoos and body piercings in the United States: A national data set. *Journal of the American Academy of Dermatology*, *55*(3), 413–421. doi:10.1016/j.jaad.2006.03.026

Laurent, C., Henzel, D., Mulanga-Kabeya, C., Maertens, G., Larouzé, B., & Delaporte, E. (2001). Seroepidemiological survey of hepatitis C virus among commercial sex workers and pregnant women in Kinshasa, Democratic Republic of Congo. *International Journal of Epidemiology*, *30*(4), 872–877.

Lavanchy, D. (2011). Evolving epidemiology of hepatitis C virus. *Clinical Microbiology and Infection*, *17*(2), 107–115. doi:10.1111/j.1469-0691.2010.03432.x

Lee, S., Lee, S. H., Lee, S. J., Kim, K.-H., Lee, J. E., Cho, H., … Kwak, I. S. (2016). Incidence and risk factors of hepatitis C virus infection among human immunodeficiency virus (HIV) patients in a large HIV clinic in South Korea. *The Korean Journal of Internal Medicine*, *31*(4), 772–778. doi:10.3904/kjim.2015.353

Lemos, M. A., Silva, J. B. G., Braga, A. C. S., Carneiro, B. M., Rahal, P., & Silva, R. C. M. A. (2014). Acupuncture needles can carry hepatitis C virus. *Infection Control and Hospital Epidemiology*, *35*(10), 1319–1321. doi:10.1086/678079

Lim, S. G., Aghemo, A., Chen, P.-J., Dan, Y. Y., Gane, E., Gani, R., … Yurdaydin, C. (2017). Management of hepatitis C virus infection in the Asia-Pacific region: An update. *The Lancet Gastroenterology & Hepatology*, *2*(1), 52–62. doi:10.1016/S2468-1253(16)30080-2

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., … Murray, C. J. (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*, *380*(9859), 2095–2128. doi:10.1016/S0140-6736(12)61728-0

Luksamijarulkul, P., & Deangbubpha, A. (1997). Hepatitis C antibody prevalence and risk factors of some female sex workers in Thailand. *The Southeast Asian Journal of Tropical Medicine and Public Health*, *28*(3), 507–512.

Ly, K. N., Hughes, E. M., Jiles, R. B., & Holmberg, S. D. (2016). Rising mortality associated with hepatitis C virus in the United States, 2003–2013. *Clinical Infectious Diseases*, *62*(10), 1287–1288. doi:10.1093/cid/ciw111

Maaroufi, A., Vince, A., Himatt, S. M., Mohamed, R., Fung, J., Opare-Sem, O., … Razavi-Shearer, K. (2017). Historical epidemiology of hepatitis C virus in select countries-volume 4. *Journal of Viral Hepatitis*, *24*(Suppl 2), 8–24. doi:10.1111/jvh.12762

McDonald, S. A., Mohamed, R., Dahlui, M., Naning, H., & Kamarulzaman, A. (2014). Bridging the data gaps in the epidemiology of hepatitis C virus infection in Malaysia using multi-parameter evidence synthesis. *BMC Infectious Diseases*, *14*, 564. doi:10.1186/s12879-014-0564-6

Meffre, C., Le Strat, Y., Delarocque-Astagneau, E., Dubois, F., Antona, D., Lemasson, J. M., … Desenclos, J. C. (2010). Prevalence of hepatitis B and hepatitis C virus infections in France in 2004: Social factors are important predictors after adjusting for known risk factors. *Journal of Medical Virology*, *82*(4), 546–555. doi: 10.1002/jmv.21734

Mehta, P., & Dhapte, V. (2015). Cupping therapy: A prudent remedy for a plethora of medical ailments. *Journal of Traditional and Complementary Medicine*, *5*(3), 127–134. doi:10.1016/j.jtcme.2014.11.036

Merican, I. (2014). Chronic hepatitis C: The hope for a cure. *The Medical Journal of Malaysia*, *69*(3), 115–118.

Metwally, A., Mohsen, A., Saleh, R., Foaud, W., Ibrahim, N., Rabaah, T., & El-Sayed, M. (2014). Prioritizing high-risk practices and exploring new emerging ones associated with hepatitis C virus infection in Egypt. *Iranian Journal of Public Health*, *43*(10), 1385–1394.

Ministry of Home Affairs Malaysia. (2017). *Statistik Penyalahgunaan Dadah 2010-2016*. Retrieved from http://www.data.gov.my/data/ms_MY/dataset/statistik-penyalahgunaan-dadah. Accessed May 10, 2017.

Ministry of Health Malaysia. (2003). *Health Indicators 2003*. Retrieved from http://www.moh.gov.my/moh/images/gallery/publications/md/hi/hi_2003.pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2004). *Health Indicators 2004*. Retrieved from http://www.moh.gov.my/moh/images/gallery/publications/md/hi/hi_2004.pdf. Accessed December 22, 2017

Ministry of Health Malaysia. (2005). *Health Indicators 2005*. Retrieved from http://www.moh.gov.my/moh/images/gallery/publications/md/hi/hi_2005.pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2006). *Health Indicators 2006*. Retrieved from http://www.moh.gov.my/moh/images/gallery/publications/md/hi/hi_2006.pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2007). *Health Indicators 2007*. Retrieved from http://www.moh.gov.my/moh/images/gallery/publications/md/hi/hi_2007.pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2008). *Health Indicators 2008*. Retrieved from http://www.moh.gov.my/moh/images/gallery/publications/md/hi/hi_2008.pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2009). *Health Indicators 2009*. Retrieved from http://www.moh.gov.my/images/gallery/publications/md/hi/hi_2009.pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2010a). *Health Indicators 2010*. Retrieved from http://www.moh.gov.my/images/gallery/publications/md/hi/hi_2010.pdf Accessed December 22, 2017.

Ministry of Health Malaysia. (2010b). *Policies and Procedures on Infection Control*. Retrieved from http://www.moh.gov.my/moh/images/gallery/Polisi/infection_control.pdf. Accessed on 23 November 2019.

Ministry of Health Malaysia. (2012). *Health Indicators 2012*. Retrieved from http://www.moh.gov.my/images/gallery/publications/md/hi/hi_2012.pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2013). *Health Indicators 2013*. Retrieved from http://www.moh.gov.my/images/gallery/publications/final%20buku%20petunjuk%202013.pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2014). *Health Indicators 2014*. Retrieved from http://vlib.moh.gov.my/cms/content.jsp?id=com.tms.cms.document.Document_32cf369e-a0188549-72493700-55380dee. Accessed December 22, 2017.

Ministry of Health Malaysia. (2015). *Health Indicators 2015*. Retrieved from http://www.moh.gov.my/images/gallery/publications/Buku%20Petunjuk%20Kesihatan%202015[1].pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2016). *Health Indicators 2016*. Retrieved from http://www.moh.gov.my/moh/images/gallery/publications/Petunjuk%20Kesihatan%202016.pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2017a). *Case definitions for infectious diseases in Malaysia. 3rd Edition*. Retrieved from http://www.moh.gov.my/moh/resources/Penerbitan/Garis%20Panduan/Pengurusan%20KEsihatan%20&%20kawalan%20pykit/Case_Definition_Of_Infectious_Disease_3rd_Edition_2017.pdf. Accessed July 23, 2017.

Ministry of Health Malaysia. (2017b). *Health Indicators 2017*. Retrieved from http://www.moh.gov.my/images/gallery/publications/Petunjuk%20Kesihatan%202017.pdf. Accessed December 22, 2017.

Ministry of Health Malaysia. (2018a). *Direktori Perkhidmatan Farmasi Methadone Kementerian Kesihatan Malaysia.* Retrieved from https://www.pharmacy.gov.my/v2/sites/default/files/document-upload/direktori-methadone-updated-januari-2018_0.pdf. Accessed January 10, 2018.

Ministry of Health Malaysia. (2018b). *Health Indicators 2018*. Retrieved from http://www.moh.gov.my/moh/resources/Penerbitan/Penerbitan%20Utama/Petunjuk_Kesihatan_2018new.pdf. Accessed November 17, 2018.

Modi, A. A., & Liang, T. J. (2008). Hepatitis C: A clinical review. *Oral Diseases*, *14*(1), 10–14. doi:10.1111/j.1601-0825.2007.01419.x

Mohamed, N. A., Zainol Rashid, Z., Wong, K. K., Abdullah, S. A., & Rahman, M. M. (2013). Hepatitis C genotype and associated risks factors of patients at University Kebangsaan Malaysia Medical Centre. *Pakistan Journal of Medical Sciences*, *29*(5), 1142–1146.

Mohd Hanafiah, K., Groeger, J., Flaxman, A. D., & Wiersma, S. T. (2013). Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology*, *57*(4), 1333–1342. doi:10.1002/hep.26141

Mohd-Noor, Z. (2018, Feb 9). 24 hour operation at Bukit Kayu Hitam will facilitate more tourists from Thailand. *The Sun Daily*. Retrieved from https://www.thesundaily.my/archive/24-hr-operation-bukit-kayu-hitam-will-facilitate-more-tourists-thailand-EUARCH525076

Mok, J., Pembrey, L., Tovo, P.-A., & Newell, M.-L. (2005). When does mother to child transmission of hepatitis C virus occur? *Archives of Disease in Childhood*, *90*(2), F156-160. doi:10.1136/adc.2004.059436

National Anti-Drugs Agency Malaysia. (2018). *Drugs Statistics*. Retrieved from https://www.adk.gov.my/en/public/drugs-statistics. Accessed February 25, 2019.

Ng, K. P., Saw, T. L., Wong, N. W., Goh, K. L., Chuah, S. Y., & Nagaratnam, M. (1995). The prevalence of anti-HCV antibody in risk groups and blood donors. *The Medical Journal of Malaysia*, *50*(4), 302–305.

Norliza, C., Norni, A., Anandjit, S., & Mohd Fazli, M. I. (2014). A review of substance abuse research in Malaysia. *The Medical Journal of Malaysia*, *69*(Suppl A), 55–58.

Omata, M., Kanda, T., Wei, L., Yu, M.-L., Chuang, W.-L., Ibrahim, A., … Sarin, S. K. (2016). APASL consensus statements and recommendations for hepatitis C prevention, epidemiology, and laboratory testing. *Hepatology International*, *10*(5), 681–701. doi:10.1007/s12072-016-9736-3

Omland, L. H., Jepsen, P., Krarup, H., Schønning, K., Lind, B., Kromann-Andersen, H., … DANVIR Cohort Study. (2011). Increased mortality among persons infected with hepatitis C virus. *Clinical Gastroenterology and Hepatology*, *9*(1), 71–78. doi:10.1016/j.cgh.2010.09.014

Omland, L. H., Osler, M., Jepsen, P., Krarup, H., Weis, N., Christensen, P. B., … Obel, N. (2013). Socioeconomic status in HCV infected patients - risk and prognosis. *Clinical Epidemiology*, *5*, 163–172. doi:10.2147/CLEP.S43926

Paez Jimenez, A., Mohamed, M. K., Eldin, N. S., Seif, H. A., El Aidi, S., Sultan, Y., … Fontanet, A. (2009). Injection drug use is a risk factor for HCV infection in urban Egypt. *PloS One*, *4*(9), e7193. doi:10.1371/journal.pone.0007193

Pawlotsky, J. M. (2004). Pathophysiology of hepatitis C virus infection and related liver disease. *Trends in Microbiology*, *12*(2), 96–102. doi:10.1016/j.tim.2003.12.005

Pépin, J., Lavoie, M., Pybus, O. G., Pouillot, R., Foupouapouognigni, Y., Rousset, D., … Njouom, R. (2010). Risk factors for hepatitis C virus transmission in colonial Cameroon. *Clinical Infectious Diseases*, *51*(7), 768–776. doi:10.1086/656233

Petruzziello, A., Marigliano, S., Loquercio, G., Cozzolino, A., & Cacciapuoti, C. (2016). Global epidemiology of hepatitis C virus infection: An up-date of the distribution and circulation of hepatitis C virus genotypes. *World Journal of Gastroenterology*, *22*(34), 7824–7840. doi:10.3748/wjg.v22.i34.7824

Pozzetto, B., Memmi, M., Garraud, O., Roblin, X., & Berthelot, P. (2014). Health care-associated hepatitis C virus infection. *World Journal of Gastroenterology*, *20*(46), 17265–17278. doi:10.3748/wjg.v20.i46.17265

Prüss-Üstün A, Rapiti E, & Hutin Y. (2003). *Sharps injuries: Global burden of disease from sharps injuries to health-care workers*. Retrieved from http://www.who.int/quantifying_ehimpacts/publications/9241562463/en. Accessed May 20, 2017.

Quan, V. M., Go, V. F., Nam, L. V., Bergenstrom, A., Thuoc, N. P., Zenilman, J., … Celentano, D. D. (2009). Risks for HIV, HBV, and HCV infections among male injection drug users in northern Vietnam: a case-control study. *AIDS Care*, *21*(1), 7–16. doi:10.1080/09540120802017610

Rafiq, S. M., Banik, G. R., Khan, S., Rashid, H., & Khandaker, G. (2014). Current burden of hepatitis C virus infection among injecting drug users: A mini systematic review of prevalence studies. *Infectious Disorders Drug Targets*, *14*(2), 93–100.

Raguin, G., Rosenthal, E., Cacoub, P., Veyssier, P., Piette, J. C., & Micoud, M. (1998). Hepatitis C in France: A national survey in the Departments of Internal Medicine and Infectious Diseases. *European Journal of Epidemiology*, *14*(6), 545–548.

Rashid, A., Teh, S., & Narayan, K. (2009). Traditional male circumcision in a rural community in Kedah, Malaysia. *International E-Journal of Science, Medicine & Education*, *3*(2), 19–23.

Razavi, H., Waked, I., Sarrazin, C., Myers, R. P., Idilman, R., Calinas, F., … Estes, C. (2014). The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. *Journal of Viral Hepatitis*, *21*(Suppl 1), 34–59. doi:10.1111/jvh.12248

Rezaei, N., Amini-Kafiabad, S., Maghsudlu, M., & Abolghasemi, H. (2016). Risk factor analysis of hepatitis C virus seropositivity in Iranian blood donors: A case-control study. *Transfusion*, *56*(7), 1891–1898. doi:10.1111/trf.13660

Rosa, R. S., Martinelli, A. de L. C., & Passos, A. D. da C. (2014). Risk factors for hepatitis C virus transmission in the municipality of Catanduva, State of São Paulo: A case-control study. *Revista Da Sociedade Brasileira De Medicina Tropical*, *47*(3), 295–301.

Rotman, Y., & Liang, T. J. (2009). Coinfection with hepatitis C virus and human immunodeficiency virus: Virological, immunological, and clinical outcomes. *Journal of Virology*, *83*(15), 7366–7374. doi:10.1128/JVI.00191-09

Russell, M., Chen, M.-J., Nochajski, T. H., Testa, M., Zimmerman, S. J., & Hughes, P. S. (2009). Risky sexual behavior, bleeding caused by intimate partner violence, and hepatitis C virus infection in patients of a sexually transmitted disease clinic. *American Journal of Public Health*, *99*(Suppl 1), S173-179. doi:10.2105/AJPH.2007.126383

Schlesselman, J. J. (1982). *Case-Control Studies: Design, Conduct, Analysis*. New York: Oxford University Press. p.160-165.

Seong, M. H., Kil, H., Kim, Y. S., Bae, S. H., Lee, Y. J., Lee, H. C., … Jeong, S.-H. (2013). Clinical and epidemiological features of hepatitis C virus infection in South Korea: a prospective, multicenter cohort study. *Journal of Medical Virology*, *85*(10), 1724–1733. doi:10.1002/jmv.23661

Sharma, S. D. (2010). Hepatitis C virus: Molecular biology and current therapeutic options. *The Indian Journal of Medical Research*, *131*, 17–34.

Sinniah, M., & Ooi, B. G. (1993). Hepatitis C-the Malaysian story. *Singapore Medical Journal*, *34*(2), 132–134.

Siti, N., Hairul, A., & Hadzri, H. (2017). Study of hepatitis C virus infection in tertiary hospital: Genotyping, risk factors and comorbidities. *International Medical Journal Malaysia*, *16*, 11–20.

Sohn, H.-S., Kim, J. R., Ryu, S. Y., Lee, Y.-J., Lee, M. J., Min, H. J., … Ki, M. (2016). Risk factors for hepatitis C virus (HCV) infection in areas with a high prevalence of HCV in the Republic of Korea in 2013. *Gut and Liver*, *10*(1), 126–132. doi:10.5009/gnl14403

Sun, J., Yu, R., Zhu, B., Wu, J., Larsen, S., & Zhao, W. (2009). Hepatitis C infection and related factors in hemodialysis patients in China: Systematic review and meta-analysis. *Renal Failure*, *31*(7), 610–620.

Tan, S., Menon, J., Radzi, M., Thein, S., Rosmawati, M., & Annuar, S. (2011). The demography and risk profiles for chronic hepatitis B and C from the Malaysian Liver Registry. *The Medical Journal of Malaysia*, *66*(Suppl. A), 31.

Tan, S. S., & Adlin Nadia, Z. (2017). The clinical features and treatment outcome of chronic hepatitis C with Pegylated Interferon and Ribavirin in routine care. *The Medical Journal of Malaysia*, *72*(3), 165–174.

Tan, W. L., Yihui, G., & Abu Hassan, M. R. (2015). Demographic characteristics and intravenous drug use among hepatitis C patients in the Kota Setar district, Kedah, Malaysia. *Epidemiology and Health*, *37*, e2015032. doi:10.4178/epih/e2015032

Tang, W., Chen, W., Amini, A., Boeras, D., Falconer, J., Kelly, H., … Easterbrook, P. (2017). Diagnostic accuracy of tests to detect Hepatitis C antibody: A meta-analysis and review of the literature. *BMC Infect Dis* 17**,** 695. doi:10.1186/s12879-017-2773-2

Taylor, A., Hutchinson, S. J., Gilchrist, G., Cameron, S., Carr, S., & Goldberg, D. J. (2008). Prevalence and determinants of hepatitis C virus infection among female drug injecting sex workers in Glasgow. *Harm Reduction Journal*, *5*, 1-5. doi:10.1186/1477-7517-5-11

Team, R. C. (2014). *R: A language and environment for statistical computing*. Retrieved from http://www.R-project.org/. Accessed October 31, 2018.

Terrault, N. A., Dodge, J. L., Murphy, E. L., Tavis, J. E., Kiss, A., Levin, T. R., … Alter, M. J. (2013). Sexual transmission of hepatitis C virus among monogamous heterosexual couples: The HCV partners study. *Hepatology*, *57*(3), 881–889. doi:10.1002/hep.26164

Tohme, R. A., & Holmberg, S. D. (2012). Transmission of hepatitis C virus infection through tattooing and piercing: A critical review. *Clinical Infectious Diseases*, *54*(8), 1167–1178. doi:10.1093/cid/cir991

Urbanus, A. T., Van De Laar, T. J. W., Geskus, R., Vanhommerig, J. W., Van Rooijen, M. S., Schinkel, J., … Prins, M. (2014). Trends in hepatitis C virus infections among MSM attending a sexually transmitted infection clinic; 1995-2010. *AIDS*, *28*(5), 781–790. doi:10.1097/QAD.0000000000000126

Vicknasingam, B., Narayanan, S., & Navaratnam, V. (2009). Prevalence rates and risk factors for hepatitis C among drug users not in treatment in Malaysia. *Drug and Alcohol Review*, *28*(4), 447–454. doi:10.1111/j.1465-3362.2009.00087.x

Waheed, Y., Shafi, T., Safi, S. Z., & Qadri, I. (2009). Hepatitis C virus in Pakistan: A systematic review of prevalence, genotypes and risk factors. *World Journal of Gastroenterology*, *15*(45), 5647–5653.

Wang, L. S., D'Souza, L. S., & Jacobson, I. M. (2016). Hepatitis C—A clinical review. *Journal of Medical Virology*, *88*(11), 1844–1855. doi:10.1002/jmv.24554

Wang, L., Tang, W., Wang, L., Qian, S., Li, Y.-G., Xing, J., … Wang, N. (2014). The HIV, syphilis, and HCV epidemics among female sex workers in China: Results from a serial cross-sectional study between 2008 and 2012. *Clinical Infectious Diseases*, *59*(1), e1-9. doi:10.1093/cid/ciu245

West, B. S., Choo, M., El-Bassel, N., Gilbert, L., Wu, E., & Kamarulzaman, A. (2014). Safe havens and rough waters: Networks, place, and the navigation of risk among injection drug-using Malaysian fishermen. *The International Journal on Drug Policy*, *25*(3), 575–582. doi:10.1016/j.drugpo.2013.11.007

Westbrook, R. H., & Dusheiko, G. (2014). Natural history of hepatitis C. *Journal of Hepatology*, *61*(1), S58–S68. doi:10.1016/j.jhep.2014.07.012

Westermann, C., Peters, C., Lisiak, B., Lamberti, M., & Nienhaus, A. (2015). The prevalence of hepatitis C among healthcare workers: A systematic review and meta-analysis. *Occupational & Environmental Medicine*, *72*(12), 880–888. doi:10.1136/oemed-2015-102879

Williams, I. T., Bell, B. P., Kuhnert, W., & Alter, M. J. (2011). Incidence and transmission patterns of acute hepatitis C in the United States, 1982-2006. *Archives of Internal Medicine*, *171*(3), 242–248. doi:10.1001/archinternmed. 2010.511

Wong, R. J., Aguilar, M., Cheung, R., Perumpail, R. B., Harrison, S. A., Younossi, Z. M., & Ahmed, A. (2015). Nonalcoholic steatohepatitis is the second leading etiology of liver disease among adults awaiting liver transplantation in the United States. *Gastroenterology*, *148*(3), 547–555. doi:10.1053/j.gastro. 2014.11.039

World Health Organization. (2010). *Neonatal and child male circumcision: A global review*. Retrieved from https://www.who.int/hiv/pub/malecircumcision/ neonatal_child_MC_UNAIDS.pdf. Accessed November 23, 2019.

World Health Organization. (2016a). *WHO guideline on the use of safety-engineered syringes for intramuscular, intradermal and subcutaneous injections in health care settings*. Retrieved from http://apps.who.int/iris/bitstream/10665/ 250144/ 1/9789241549820-eng.pdf. Accessed May 8, 2017.

World Health Organization. (2016b). *Guidelines for the screening, care and treatment of persons with chronic hepatitis C infection. Updated version.* Retrieved from http://apps.who. int/iris/bitstream/10665/205035/1/9789241549615_eng. pdf?ua=1. Accessed July 13, 2017

World Health Organization. (2016c). *Global health sector strategy on viral hepatitis 2016-2021*. Retrieved from http://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en. Accessed June 23, 2017.

World Health Organization. (2017a). *Global Hepatitis Report 2017*. Retrieved from http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en. Accessed May 8, 2017.

World Health Organization. (2017b). *Hepatitis C Fact Sheet*. Retrieved from http://www.who.int/mediacentre/factsheets/fs164/en. Accessed April 29, 2017.

World Health Organization. (2017c). *Guidelines on hepatitis B and C testing*. Retrieved from http://www.who.int/hepatitis/publication/guidelines-hepatitis-c-b-testing/en. Accessed July 13, 2017.

World Health Organization & Joint United Nations Programme on HIV/AIDS. (2007). *Male circumcision: Global trends and determinants of prevalence, safety and acceptability*. Retrieved from http://apps.who.int/iris/ bitstream/10665/43749/1/9789241596169_eng.pdf. Accessed May 20, 2017.

Yang, S., Wang, D., Zhang, Y., Yu, C., Ren, J., Xu, K., … Li, L. (2015). Transmission of hepatitis B and C virus infection through body piercing: A systematic review and meta-analysis. *Medicine*, *94*(47), e1893. doi:10.1097/MD.0000000000001893

Zein, N. N. (2000). Clinical significance of hepatitis C virus genotypes. *Clinical Microbiology Reviews*, *13*(2), 223–235.

BIODATA OF STUDENT

Mohd Azri bin Mohd Suan was graduated from University of Malaya in 2003 with Medical Bachelor and Bachelor in Surgery (MBBS). He started his housemanship training in Hospital Sungai Petani (currently known as Hospital Sultan Abdul Halim) before he joined the Department of Obstetrics and Gynaecology as a medical officer. After served the department for 10 years, he joined Clinical Research Center, Hospital Sultanah Bahiyah, Alor Setar in 2014 as a medical and research officer. His research interest is on communicable and non-communicable diseases, research method, health education and disease prevention.

LIST OF PUBLICATIONS

Mohd Azri Mohd Suan, Salmiah Mohd Said, Ahmad Zaid Fattah Azman, Muhammad Radzi Abu Hassan (2019). A study protocol on risk factors for hepatitis C infection among adult patients at tertiary hospitals in Kedah state. *International Journal of Public Health and Clinical Sciences, 6*(2), 266-281. doi: 10.32827/ijphcs.6.2.266

Mohd Azri Mohd Suan, Salmiah Mohd Said, Ahmad Zaid Fattah Azman, Muhammad Radzi Abu Hassan (2019). A narrative review of natural history, epidemiology and risk factors of hepatitis C virus infection. *Pertanika Journal Science and Technology, 27*(3), 1341-1359.

Mohd Azri Mohd Suan, Salmiah Mohd Said, Lim Poh Ying, Ahmad Zaid Fattah Azman, Muhammad Radzi Abu Hassan (2019). Risk factors for hepatitis C infection among adult patients in Kedah state, Malaysia: A case-control study. *Plos One 14*(10), e0224459. doi: 10.1371/journal. pone.0224459

Mohd Azri Mohd Suan, Salmiah Mohd Said, Lim Poh Ying, Ahmad Zaid Fattah Azman, Muhammad Radzi Abu Hassan (2019). Risk behaviours associated with hepatitis C infection among adult patient in Kedah state, Malaysia. Presented at 6th Asia Pacific Conference on Public Health. Equatorial Hotel, Penang, 22-25 July 2019. Proceeding published in *The Medical Journal of Malaysia, 74*(Suppl 2), 134.

Mohd Azri Mohd Suan, Salmiah Mohd Said, Ahmad Zaid Fattah Azman, Shamsul Azhar Shah, Muhammad Radzi Abu Hassan (2019). Epidemiology and risk behaviours for hepatitis C infection in Malaysia: A narrative review. Submitted to *International Medical Journal of Malaysia*.

UNIVERSITI PUTRA MALAYSIA

STATUS CONFIRMATION FOR THESIS / PROJECT REPORT AND COPYRIGHT

ACADEMIC SESSION : First Semester 2019/2020

TITLE OF THESIS / PROJECT REPORT :

RISK FACTORS FOR HEPATITIS C VIRUS INFECTION AMONG ADULT PATIENTS AT A PUBLIC HOSPITAL IN KEDAH, MALAYSIA

NAME OF STUDENT : MOHD AZRI MOHD SUAN

I acknowledge that the copyright and other intellectual property in the thesis/project report belonged to Universiti Putra Malaysia and I agree to allow this thesis/project report to be placed at the library under the following terms:

1. This thesis/project report is the property of Universiti Putra Malaysia.
2. The library of Universiti Putra Malaysia has the right to make copies for educational purposes only.
3. The library of Universiti Putra Malaysia is allowed to make copies of this thesis for academic exchange.

I declare that this thesis is classified as :

*Please tick (V)

☐	**CONFIDENTIAL**	(Contain confidential information under Official Secret Act 1972).
☐	**RESTRICTED**	(Contains restricted information as specified by the organization/institution where research was done).
☐	**OPEN ACCESS**	I agree that my thesis/project report to be published as hard copy or online open access.

This thesis is submitted for :

☐ **PATENT** Embargo from _____ until _____
(date) (date)

Approved by:

_____ _____
(Signature of Student) (Signature of Chairman of Supervisory Committee)
New IC No/ Passport No.: Name:

Date : Date :

[Note : If the thesis is CONFIDENTIAL or RESTRICTED, please attach with the letter from the organization/institution with period and reasons for confidentially or restricted.]