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Trends in the Reported Cases of Hepatitis C Virus Infection, Ministry of Health, Kingdom of Saudi Arabia, 2008 – 2012

by

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Master of Public Health

Global Health

Scott JN McNabb, PhD, MS

Committee Chair

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M.B.B.S

King Khalid University

2009

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An abstract of

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

In partial fulfillment of the requirements for the degree of

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ABSTRACT

OBJECTIVE: Infection with hepatitis C virus (HCV) is a risk factor for liver disease and responsible for significant morbidity and mortality. Considered one of the most challenging infectious diseases, the prevalence and risk factors are not well known. Therefore, we determined the trends in the distribution of case reports and incidence rates (IRs) of HCV infection in the Kingdom of Saudi Arabia (KSA) from 2008 – 2012.

METHODS: Using a retrospective design, we analyzed all cases of HCV infection reported to the KSA Ministry of Health (MoH) from 2008 – 2012 to determine trends in cumulative numbers and incidence rates (IRs) by gender, nationality, and region.

RESULTS: A total of 12,336 cases of HCV infection were reported to the KSA MoH from 2008 – 2012. A statistically significant reduction in the IRs of reported cases of HCV infection was observed; in 2008, the IR was 10.6 (95% CI = 10.2 – 11) per 100,000 populations, and by 2012, it had fallen to 8 (95% CI = 7.7 – 8.3) per 100,000 population. Males had a consistently higher IR than females. We observed a statistically significant reduction in the IR of HCV infection from 2008 to 2012 for males and females separately. Saudi citizens had a higher HCV infection IR than non-Saudis, and IRs significantly decreased for both Saudis and non-Saudis. In 2012, Makkah had the highest IR for reported cases of HCV infection (13.5 per 100,000 population 95% CI =12.65 – 14.31). The IR in Asir region increased significantly from 8.2 per 100,000 (95% CI = 6.87 – 9.49) in 2008 to 11 per 100,000 (95% CI = 9.61 – 12.49) in 2012. Those >45 years old had the highest number of HCV cases.

CONCLUSION: The reported IRs of HCV infections significantly decreased over the 5-year study period in each of the thirteen administrative regions from 2008 – 2012. Despite some inconsistencies with the population data, the reduction in HCV infection is encouraging, and the KSA MoH should review the policies and procedures of the HCV infection prevention and control program.

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CHAPTER 1: INTRODUCTION

The hepatitis C virus (HCV) infection, discovered in 1988, targets the liver (1). HCV is a single-stranded RNA virus classified into different genotypes and subtypes for clinical and epidemiologic purposes (2). Physicians need clinical genotyping information to follow up on treatment progress, while epidemiologic classification aids in the determination of geographical distribution and modes of transmission (2). WHO estimates that HCV infection is a primary global risk factor for 27% of cirrhosis cases and 25% of hepatocellular carcinoma (HCC) cases (3, 4).

1.1 Mode of Transmission

HCV is a blood-borne infection that can be transmitted in several ways, including the sharing of needles (between intravenous drug users or by way of needle stick injuries to healthcare providers who have contact with HCV patients). In addition, it can be transmitted during hemodialysis treatment sessions for end-stage renal disease (5) or through organ transplantation. It can also be transmitted via sexual contact or childbirth if the mother is infected (5). Fortunately, hepatitis C virus can't be transmitted through kissing, water, food, or breast milk (5).

1.2 Nature of Infection

The disease can range from a mild illness persisting for a short time (< 6 months) to a severe, chronic condition. Approximately 80% of those exposed to HCV end up with serious outcomes (liver cirrhosis or liver cancer), which can lead to liver failure, require liver transplantation, or may result in death (5-7).

Patients with acute HCV infection usually have no symptoms, but 80% progress to a chronic phase (3). Most chronic HCV patients do not know about their infection unless they give blood to be tested for some reason. However, these patients may have symptoms such as decreased appetite, jaundice (yellowish discoloration of the eyes and skin), abdominal pain, and increased chance of bleeding with mild trauma.

1.3 Diagnosis of HCV Infection

HCV infection is diagnosed using confirmation tests such as the enzyme-linked immunosorbant assay (ELISA), recombinant immunoblot assay (RIBA), and polymerase chain reaction (PCR) (3, 5, 8). However, the most common diagnostic tools are the second- and third-generation enzyme immunoassays (EIA-2 and EIA-3) for detecting antibodies against HCV (9). Although PCR has been used for detection of HCV-RNA in serum, it is not yet the international standard due to its inconsistency (9).

When assessing severity of liver disease, the liver biopsy is the gold standard (9). In general, the confirmatory test should be administered to blood donors and people with normal levels of liver enzymes who test positive for HCV antibodies (anti-HCV) (9). Once a diagnosis is confirmed, patients face the harsh realities of HCV treatment: the powerful and unpleasant side effects of interferon or ribavirin, and the fact that there is no vaccine available for their contacts (5, 10). In many cases, HCV can produce resistance to interferon, making treatment even more challenging (11).

1.4 Global Epidemiology of HCV Infection

HCV infection is a main risk factor for liver disease and one key cause of projected increases in morbidity and mortality. It is considered a challenging infection due to the uncertainty of its prevalence and difficulties of detecting risk factors (12).

It is estimated that 3% of people worldwide (150 million) are infected with HCV, and 3 - 4 million become infected every year. Annually, 350,000 die due to liver diseases (3, 5). In the United States in 2006, 3.9 million people were infected with HCV, 2.7 million of whom were chronically infected; most of these chronic cases were from 30 - 49 years old and reported intravenous injection use, which is the most common mode of transmission in the United States (13). The United Kingdom and Scandinavia report the lowest prevalence of HCV (0.01% -- 0.1%) (4). Even in countries where the prevalence is higher, such as Japan, Italy and China, the distribution can vary significantly among regions. Within each of these three countries, HCV is 20-fold higher in some areas compared to 2-fold in others (4).

In the Middle East, HCV infection is considered very critical (14). In Egypt, the prevalence rate was 28% in 2006, the highest worldwide. In Pakistan, it was 1.8% (13). HCV has been categorized into six genotypes based on its geographical distribution, infectivity, pathogenicity and response to medical treatment (14, 15). The most common genotypes through Europe and North America are genotypes 1, 2 and 3. In Africa and the Middle East, the most common genotype is 4 (14, 16).

1.5 Epidemiology of HCV Infection in the Kingdom of Saudi Arabia (KSA)

KSA is the largest Arab country in Asia and second largest Arab country in the world after Algeria, with a total area of approximately 2,150,000 km^2 (830,000 sq. mi) and a total

population of 26,939,583 people (17, 18). Healthcare in KSA is provided to the population through either the national health care system or private providers. The national health system is funded by the government and supervised by the Ministry of Health (MoH), which is the country's main provider of healthcare (preventive, curative, and rehabilitative). The first gateway of this huge health system is the primary health center (PHC); 1,925 PHCs are distributed throughout KSA, with a referral system connecting hundreds of general and specialist hospitals across the whole country (18).

The preventive medicine department under the MoH devotes much attention to infectious diseases as KSA annually receives upwards of 4 million pilgrims who visit the two Holy Mosques. The KSA MoH's concern is evidenced by the extensive distribution of its surveillance centers, located at all airports, seaports, and travel terminals, and its vigilance in screening travelers suspected of having infectious diseases. In addition, the MoH has established departments of public health in all areas under the supervision of Health Affairs, which in turn communicates with the MoH to take appropriate measures and make policy recommendations.

HCV infection gets special attention because of its challenging nature and the difficulty of tracking those who are infected, especially those with chronic HCV infection. The prevalence varies across KSA. In 2007, the MoH classified HCV infection as the second most common viral infection after chickenpox (8, 19). Prevalence of HCV infection among the general population of KSA is estimated to be 1.1 – 1.7% (20). The prevalence of HCV infection among hemodialysis patients is 15 – 80%, with a yearly rate of 7 – 9% (21). Among hemophilic patients, the prevalence is 40% (20). Many HCV genotypes have been identified, and they differ in

distribution by geographical area and the way they are transmitted (22). The most predominant genotypes are genotype 4 (69%) and genotype 1 (12.8%), with rarely reported cases of genotypes 2, 3, 5 and 6 (21, 23-27).

Previously, the main agent of HCV transmission was blood transfusion. The existence of blood donation screening programs and the establishment of an anti-HCV test that screens for the presence of HCV antibodies have had a clear role in decreasing the spread since 1990 (1, 3). In regard to the current role of blood transfusions in the transmission of HCV, a recent study found that 62% of HCV patients in hemodialysis units had never received a blood transfusion; more investigation and research are needed to identify the route of transmission in this group (28).

Currently, the leading cause of infection in KSA is infected needle puncture injuries, which affect hospital staff, and needle sharing, which affects intravenous drug users (IVDU). It has been found that 94% of IVDUs have HCV core Ag. In addition to HCV, HIV and HBV can be transmitted via needle punctures or needle sharing. Another route of blood transmission is hemodialysis; hemodialysis patients had an HCV prevalence rate of 18 – 46%; in a previously mentioned study, the rate was 15 – 80% (20, 21, 29).

Although the number of HCV cases has decreased in KSA since 1990, it still poses a serious health risk. HCV infection is a predisposing risk factor for hepatocellular carcinoma and liver cirrhosis in non-alcoholic patients. Most chronic HCV patients in KSA end up needing liver transplantation (8, 19, 29-34). It has been estimated that 1% - 5% of women and 10% - 20% of men develop hepatocellular carcinoma after developing cirrhosis of the liver (35).

In our thorough review, we found no study focusing particularly on the trend of HCV infection (separate from hepatitis A and B) that relied on data from the MoH. Previous studies concluded that infection with HCV was greater among non-Saudis and older adults, but these studies were done on selected populations, such as blood donors, and not representative of the general population. In addition, these studies focused on either the prevalence or the genotypes of HCV for a specific population without looking at the IR. The distribution of HCV over time is the essential epidemiologic predictor for the burden of disease in the community, but few studies have focused on this analysis. The ones that include incidence have encompassed all types of hepatitis or one specific type like HBV (36) but do not examine HCV infection in depth.

To achieve the goal of limiting spread of HCV in KSA, we should study in-depth the epidemiologic and clinical standpoints so that the research can serve as a reliable reference for public health policymakers. This study aims to determine the changes in distribution of HCV infection throughout the KSA over 5 years from 2008 – 2012.

CHAPTER 2: LITERATURE REVIEW

HCV infection affects a large segment of the world's population. The IR of HCV infection is uncertain in many developing and less developed countries due to the scarcity of resources and lack of well-developed healthcare programs. Because HCV infection affects people worldwide and is a main cause of liver cirrhosis and hepatocellular carcinoma, along with increasing rates of morbidity and mortality, it should be a focus of public health research.

Public health policymakers in affected countries should establish preventive measures at all levels—primary, secondary, and tertiary—to stop the spread of the disease. To do that, public health professionals and researchers should conduct a sufficient number of studies from the epidemiologic and clinical perspectives to determine the burden of disease and define the risk factors and routes of transmission. However, because this infection is asymptomatic in most cases, it is challenging for public health professional to determine the IR even with the existence of a well-developed surveillance systems, as exist in the United States (4, 37). Since there are currently no available HCV vaccines, most HCV studies focused on genotype distribution to inform vaccine research and on primary preventive measures that can be taken to avoid contracting this infection (12).

HCV infection is of great interest to KSA researchers because it is widespread and has a significant role in morbidity and mortality. The prevalence of HCV infection varies by region and age. A community-based study of 4,496 children aged 1-10 years was conducted in 1991 to measure the presence of HCV antibodies in the population. The diversity of the HCV antibody (anti-HCV) rate was significant from one region to another, ranging from 0 – 5.7%. The highest prevalence of anti-HCV was seen in Jizan region (34). In 1997, another study encompassing all

13 regions included 5,350 patients aged 1-12 years; among them, the prevalence of HCV was 0.04% (1). Although the prevalence of HCV had declined, the author called attention to the need for an infection control policy evaluation and continuous monitoring in all hospitals and centers in addition to the implementation of health education programs.

The prevalence of HCV among 24,173 blood donors in King Khalid hospitals in Riyadh region was studied over 3 years (2000 – 2002). The prevalence was 0.4% and was higher among non-Saudis than Saudis. It was also higher among older individuals as compared to younger ones (38).

Another study was conducted at King Khalid National Guard Hospital in Jeddah on 744 male blood donors to detect the prevalence of HCV by using the anti-HCV test and alanine aminotransferase (ALT) test as indicators of HCV. The prevalence of HCV in this study was 3.2% overall and was higher among Egyptian patients (24%) (39).

A study that included 22 hemodialysis centers in KSA was conducted to assess the risk factors and prevalence of HCV infection for 1,147 patients. The study concluded that the prevalence of anti-HCV was 68%, with range of 14 – 94.7% (28). This study showed that a hemodialysis unit is a strong risk factor for HCV transmission and dissemination in the community. This route of transmission requires better quality control and more stringent safety protocols.

Being familiar with the HCV genotypes and knowing their infectivity and pathogenicity aids in facilitating the best treatment options wherever the disease occurs. Due to the role of genotypes in patient management, researchers give them special attention. A study was conducted to determine which HCV genotype had the highest distribution among KSA patients.

The study concluded that genotype 4 was the predominant type among most of the study population; the others were much less common (22). A different study was conducted to determine the genotype and subtype of HCV in KSA for 84 Saudi patients with chronic active hepatitis (CAH), 39 patients undergoing hemodialysis, and 31 intravenous drug users. The study concluded that there was diversity among these groups for HCV genotypes. Genotype 4 was still the most common among the Saudi population; in this study, genotype 4 was predominant in the CAH group (74%) and constituted a large proportion among the hemodialysis group (49%). Among the intravenous drug user group, 39% had subtype 1b (26). Information about the distribution of certain genotypes can be used for planning patient management, but more studies among the general population are necessary in order to more reliably implement clinical and public health interventions.

In terms of the incidence, a 2007 study of 14,224 cases conducted in the National Guard Health Affairs (NGHA) hospitals in three regions in Saudi Arabia showed that HCV incidence was 78.4 per 100,000 and was higher among older patients (having a mean age of 49.9 years and SD of 17.2 years). The incidence of HCV was higher among the non-Saudi population than the Saudi population (8).

A retrospective study was conducted among 1,214 patients with HCV at the Saudi Aramco Medical Services Organization (SAMSO) in the Eastern Region of KSA. This study aimed to evaluate the trend of hepatitis A, B and C between 2000 and 2005. The authors concluded from this analysis that the number of HCV cases was higher than that of HAV, but it was lower than that of HBV: 49% of patients had HBV, 40% had HCV, and 10% had HAV. The study found that HCV mainly affected older adults (40).

CHAPTER 3: MANUSCRIPT

3.1 Introduction

Hepatitis C virus (HCV) infection is a primary risk factor for liver disease and one key cause of projected increases in morbidity and mortality. It is considered a challenging infection due to the uncertainty of its prevalence and difficulties of detecting risk factors (12).

HCV is a blood-borne infection that can be transmitted in several ways, including the sharing of needles (between intravenous drug users or by way of needle stick injuries to healthcare providers who have contact with HCV patients). In addition, it can be transmitted during hemodialysis treatment sessions for end-stage renal disease (5) or through organ transplantation. It can also be transmitted via sexual contact or childbirth if the mother is infected (5). Fortunately, HCV can't be transmitted through kissing, water, food, or breast milk (5).

HCV infection is diagnosed using confirmation tests such as the enzyme-linked immunosorbant assay (ELISA), recombinant immunoblot assay (RIBA), and polymerase chain reaction (PCR) (3, 5, 8). HCV has been categorized into six genotypes based on its geographical distribution, infectivity, pathogenicity and response to medical treatment (14, 15). The most common genotypes through Europe and North America are genotypes 1, 2 and 3. In Africa and the Middle East, the most common genotype is 4 (14, 16).

The disease can range from a mild illness persisting for a short time (< 6 months) to a severe, chronic condition. Approximately 80% of those exposed to HCV end up with serious outcomes (liver cirrhosis or liver cancer) that can lead to liver failure, require liver transplantation, or result in death (5-7). WHO estimates that HCV infection is a primary global

risk factor for 27% of cirrhosis cases and 25% of hepatocellular carcinoma (HCC) cases (3, 4).

It is estimated that 3% of people worldwide (150 million) are infected with HCV, and 3 – 4 million become infected every year. Annually, 350,000 die due to liver diseases (3, 5). In the United States in 2006, 3.9 million people were infected with HCV, 2.7 million of whom were chronically infected; most of these chronic cases were from 30 – 49 years old and reported intravenous drug use, which is the most common mode of transmission in the United States (13). The United Kingdom and Scandinavia report the lowest prevalence of HCV (0.01% - 0.1%) (4). In the Middle East, HCV infection is considered very critical (14). In Egypt, the prevalence rate was 28% in 2006, the highest worldwide.

HCV gets special attention from the Ministry of Health (MoH) in the Kingdom of Saudi Arabia (KSA) because of its challenging nature and the difficulty of tracking those who are infected, especially as the Kingdom receives no fewer than 4 million pilgrims annually who visit the Two Holy Mosques. KSA is the largest Arab country in Asia and second largest Arab country in the world after Algeria, with a total area of approximately 2,150,000 km^2 (830,000 sq mi) and a total population of 26,939,583 people distributed across 13 administrative regions (17, 18).

The prevalence varies across KSA. In 2007, the MoH classified HCV infection as the second most common viral infection after chickenpox (8, 19). The prevalence of HCV infection among the general population of KSA is estimated to be 1.1 – 1.7% (20). The prevalence of HCV infection among hemodialysis patients is 15 – 80%, with a yearly rate of 7 – 9% (21). Among hemophilic patients, the prevalence is 40% (20). Many HCV genotypes have been identified, and they differ in distribution by geographical area and the way they are transmitted (22). The

most predominant genotypes are genotype 4 (69%) and genotype 1 (12.8%), with rarely reported cases of genotypes 2, 3, 5 and 6 (21, 23-27).

Previously, the main agent of HCV transmission was blood transfusion. The existence of blood donation screening programs and the establishment of an anti-HCV test that screens for the presence of HCV antibodies have had a clear role in decreasing the spread since 1990 (1, 3). Currently, the leading cause of infection in KSA is infected needle puncture injuries, which affect hospital staff, and needle sharing, which affects intravenous drug users (IVDUs). Another route of blood transmission is hemodialysis; hemodialysis patients had an HCV prevalence rate of 18 – 46%; in a previously mentioned study, the rate was 15 – 80% (20, 21, 29).

Although the number of HCV cases has decreased in KSA since 1990, it still poses a serious health risk. HCV infection is a predisposing risk factor for hepatocellular carcinoma and liver cirrhosis in non-alcoholic patients. Most chronic HCV patients in KSA end up needing liver transplantation (8, 19, 29-34). It has been estimated that 1% - 5% of women and 10% - 20% of men develop hepatocellular carcinoma after developing cirrhosis of the liver (35).

Since there is currently no available HCV vaccination, most HCV studies focus on genotype distribution to inform vaccine research and on the primary preventive measures that can be taken to avoid getting this infection (12).

In terms of the incidence, a 2007 study of 14,224 cases conducted in the National Guard Health Affairs (NGHA) hospitals in three regions in KSA showed that HCV incidence was 78.4 per 100,000 and was higher among older patients (whose mean age was 49.9 years with a SD of

17.2 years, as shown in Table 1 and Figure 1). The incidence of HCV was higher among the non-Saudi population than the Saudi population (8).

In our thorough review, we found no study focusing particularly on the trend of HCV infection separate from hepatitis A and B that relied on data from the MoH. Previous studies concluded that infection with HCV was greater among non-Saudis and older adults, but these studies were done on selected populations, such as blood donors, and not representative of the general population. In addition, these studies focused on either the prevalence or the genotypes of HCV for a specific population without looking at the IR. The distribution of HCV over time is the essential epidemiologic predictor for the burden of disease in the community, but few studies have focused on this analysis. The ones that include incidence have encompassed all types of hepatitis or one specific type like HBV (36) but have not examined HCV infection in depth.

To achieve the goal of limiting spread of HCV in KSA, we should do in-depth studies of the epidemiologic and clinical standpoints so that this research can serve as a reliable reference for public health policymakers. To that end, this study aims to determine the changes in distribution of HCV infection throughout the KSA over 5 years from 2008 – 2012.

3.2 Methods

Data Sources

Through the Department of Public Health, the MoH collects case reports monthly and annually from all administrative regions (Figure 1) of confirmed cases of HCV via a passive surveillance system. All cases are laboratory-confirmed by anti-HCV positive results.

Figure 1.Administrative Regions of Kingdom of Saudi Arabia

Case reports of HCV infection occurring from 2008 – 2012 were obtained from the KSA MoH and organized nationality, gender, region, and age. The total population of each province of the administrative regions was obtained from Ministry of Finance, and the total population by gender and nationality were obtained from the online database of the Central Department of Statistics and Information, which is based on the annual census field survey as well as data collected from the records of administrative regions (41, 42).

Statistical Analyses

A descriptive analysis was conducted for all cases reported to the MoH over the 5-year period from 2008 – 2012 to determine the IR trends of HCV by nationality, gender, and region. The IR of HCV infection was calculated per 100,000 populations with a 95% confidence interval. The IR was calculated by dividing the reported cases of HCV infection for a specific variable and year by the corresponding population of the same variable and year.

Ethics

The Emory University Institutional Review Board (IRB00073771) confirmed an exemption from Human Subjects Research for this study.

3.3 Results

There were 12,336 cases of HCV infection reported to the KSA MoH during the 5-year period 2008 – 2012. There was a significant reduction of the IR over time. The IR was 10.6 (95% CI = 10.2 – 11) per 100,000 populations in 2008, gradually declining to 8 (95% CI = 7.7 – 8.3) per 100,000 in 2012 (Table 1). The number of HCV cases also gradually declined over time (2,733 in 2008 to 2,340 in 2012).

Table 1. Reported cases of hepatitis C virus infection and incidence rates, Kingdom of Saudi Arabia, 2008 – 2012

Year	# Cases (IR°)	95% CI*
2008	2733 (10.6)	10.2 – 11
2009	2487 (9)	9 – 9.7
2010	2448 (8.5)	8.5 – 9.2
2011	2328 (7.9)	7.9 – 8.5
2012	2340 (7.7)	7.7 – 8.3
Total	12336	

°IR = incidence rate per 100,000 population
*CI = confidence interval

Over the study period, KSA citizens had consistently higher IRs than non-Saudis. There was a significant reduction in the IR among both Saudi and non-Saudi populations over time. For Saudi citizens, The IR was 11.5 (95% CI = 11 – 12) per 100,000 population in 2008, gradually declining to 8.5 (95% CI = 8.1 – 8.9) per 100,000 in 2012 (Table 2). A similar trend was observed

for non-Saudis. The IR was 8.5 (95% CI = 7.8 – 9.1) in 2008 and declined to 6.9 (95% CI = 6.4 – 7.4) in 2012. However, there was an increase in this IR in 2010 (Table 2).

Table 2. Reported cases of hepatitis C virus infection and incidence rates, by year and nationality,Kingdom of Saudi Arabia, 2008 – 2012

Year	Saudi		Non-Saudi	
	# Cases (IR°)	95% CI	# Cases (IR°)	95% CI
2008	2082 (11.5)	11.0 – 12	651 (8.5)	7.8 – 9.1
2009	1882 (10.1)	9.7 – 10.6	605 (7.4)	6.9 – 8
2010	1737 (9.1)	8.7 – 9.6	711 (8.3)	7.7 – 8.9
2011	1677 (8.6)	8.2 – 9	651 (7.3)	6.7 – 7.8
2012	1692 (8.5)	8.1 – 8.9	648 (6.9)	6.4 – 7.4
Total	9070		3266	

°IR = incidence rate per 100,000 population
*CI = confidence interval

Males had a consistently higher IR than females. We observed a statistically significant reduction in the IR of HCV infection from 2008 to 2012 for males and females separately. For male, The IR was 10.8 (95% CI = 10.3 – 11.4) per 100,000 population in 2008, gradually declining to 8.5 (95% CI = 8.1 – 9) per 100,000 in 2012 (Table 3). A similar trend was observed for female. The IR was 10.3 (95% CI = 9.7 – 11) in 2008 and declined to 7.3 (95% CI = 6.9 – 7.8) in 2012 (Table3).

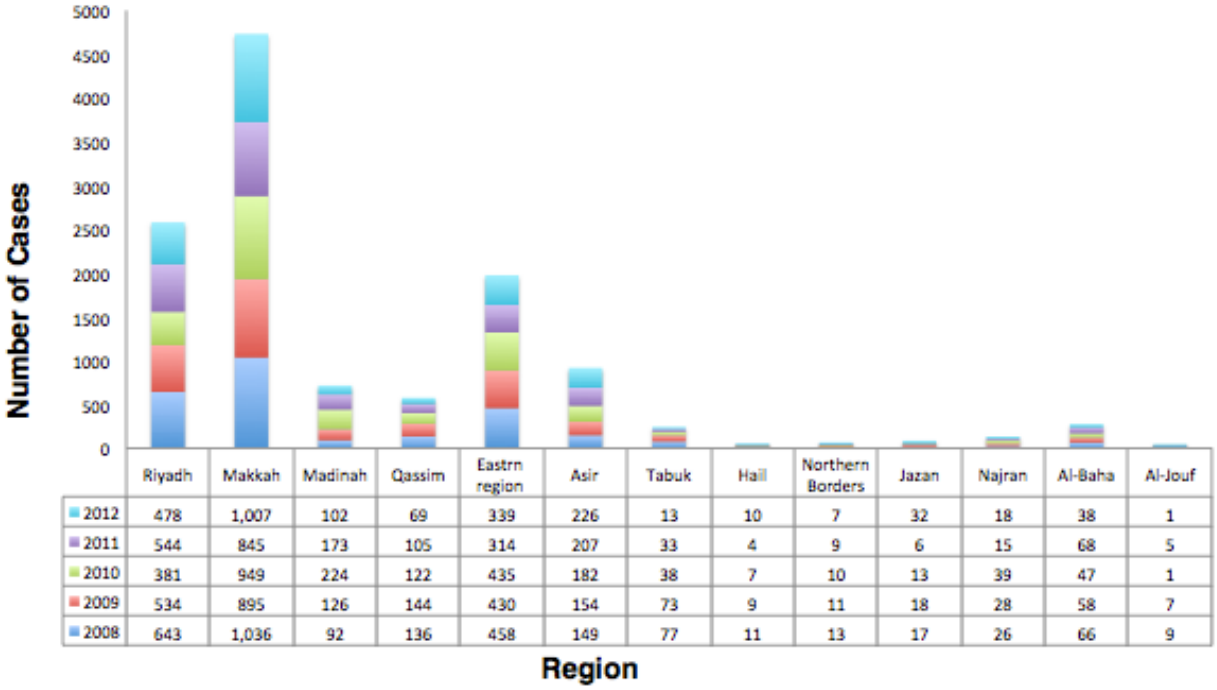
Table 3. Reported cases of hepatitis C virus infection and incidence rates, by year and gender,Kingdom of Saudi Arabia, 2008 – 2012

Year	Male		Female	
	# Cases (IR°)	95% CI	# Cases (IR°)	95% CI
2008	1566 (10.8)	10.3 – 11.4	1167 (10.3)	9.7 – 11
2009	1442 (9.6)	9.1 – 10.1	1045 (9)	8.4 – 9.5
2010	1501 (9.6)	9.1 – 10.1	947 (7.9)	7.4 – 8.4
2011	1439 (8.9)	8.4 – 9.3	889 (7.2)	6.7 – 7.7
2012	1412 (8.5)	8.1 – 9	928 (7.3)	6.9 – 7.8
Total	7360		4976	

°IR = incidence rate per 100,000 population
*CI = confidence interval

In terms of the total number of HCV cases, we noticed a significant difference among all of the provinces (Figure 2). Makkah, Riyadh, and Eastern regions reported the highest numbers of HCV cases. For example, in 2012, Makkah had 1007 cases, followed by Riyadh with 478 cases. At the other end of the scale, many regions had as few as 1 case of HBV, as noted in Aljouf in 2010 and 2012 (Figure 2).

Figure 2. Number of Reported Cases of Hepatitis C Virus Infection, by Year and Region, Kingdom of Saudi Arabia, 2008 - 2012



	Riyadh	Makkah	Madinah	Qassim	Eastrn region	Asir	Tabuk	Hail	Northern Borders	Jazan	Najran	Al-Baha	Al-Jouf
2012	478	1,007	102	69	339	226	13	10	7	32	18	38	1
2011	544	845	173	105	314	207	33	4	9	6	15	68	5
2010	381	949	224	122	435	182	38	7	10	13	39	47	1
2009	534	895	126	144	430	154	73	9	11	18	28	58	7
2008	643	1,036	92	136	458	149	77	11	13	17	26	66	9

HCV was also examined by administrative region. There were numerous variations in the HCV IR within and between the regions. Compared to the HCV trend for the total population, we noticed that many regions had a lower HCV rate, namely Aljouf, Hail, Northern Border, Jazan, Najran, Tabuk, Riyadh, and Madinah (Figure 3). Among these regions, Aljouf had the

lowest incidence rate, which dropped significantly from 2.3 per 100,000 population (95% CI= 0.8 – 3.7) in 2008 to 0.2 per 100,000 population (95% CI = -0.2 – 0.6) in 2012 (Figure 3). The regions that had high HCV IRs were Makkah, Al-Baha, Asir, Eastern region and Qassim (Figure 4). Makkah had the highest IR among these regions, with a rate of 16.6 per 100,000 population (95% CI = 15.6 – 17.6) in 2008, which significantly decreased to 13.5 per 100,000 population (95% CI = 12.6 – 14.3) by 2012 (Figure 4).

Figure 3. Incidence Rates° of Reported Cases of Hepatitis C Virus Infection, by Year and Region, Kingdom of Saudi Arabia, 2008 – 2012

(Regions with a lower IR than the total population each year for at least 3 out of 5 years)

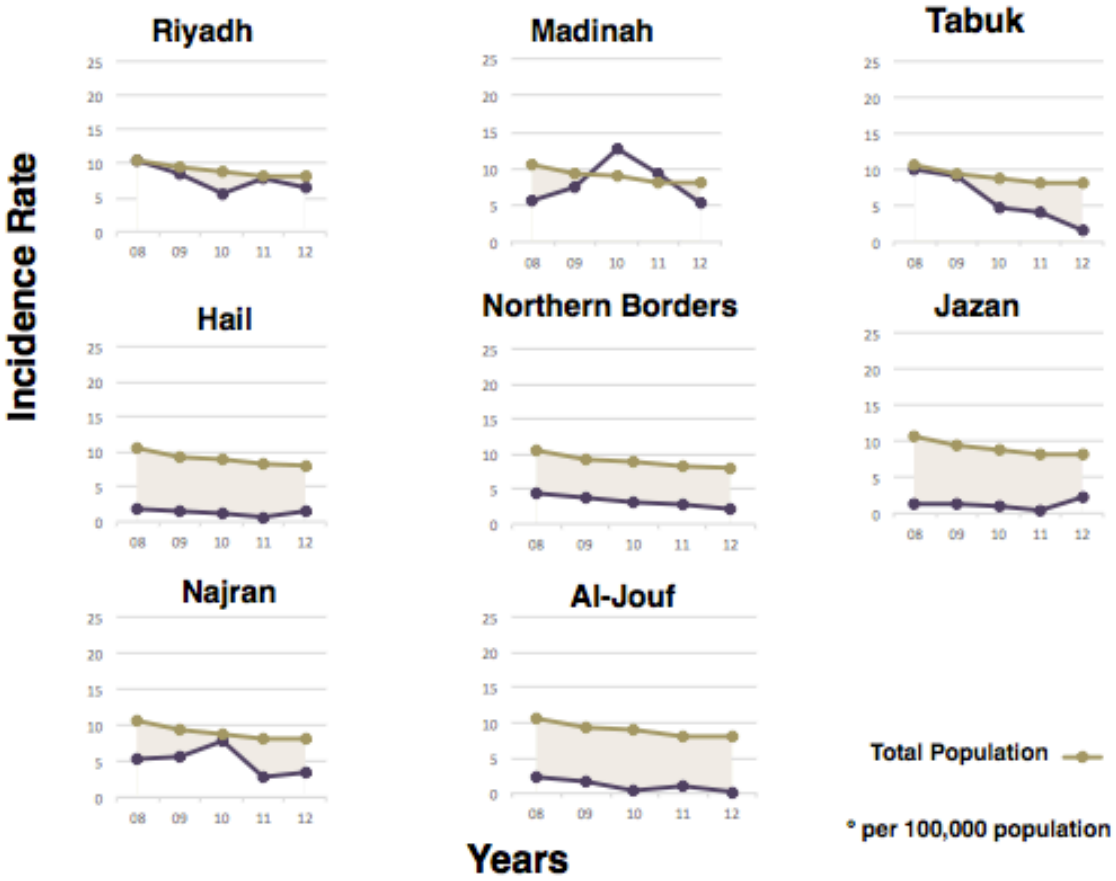
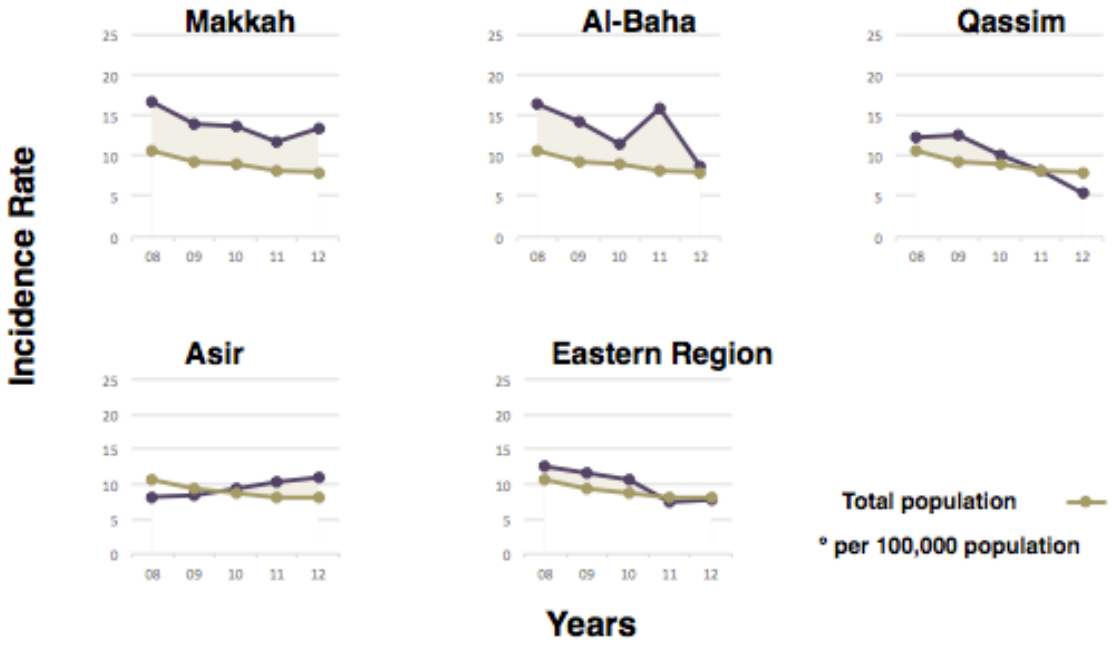


Figure 4. Incidence Rates° of Reported Cases of Hepatitis C Virus Infection, by Year and Region, Kingdom of Saudi Arabia, 2008 – 2012

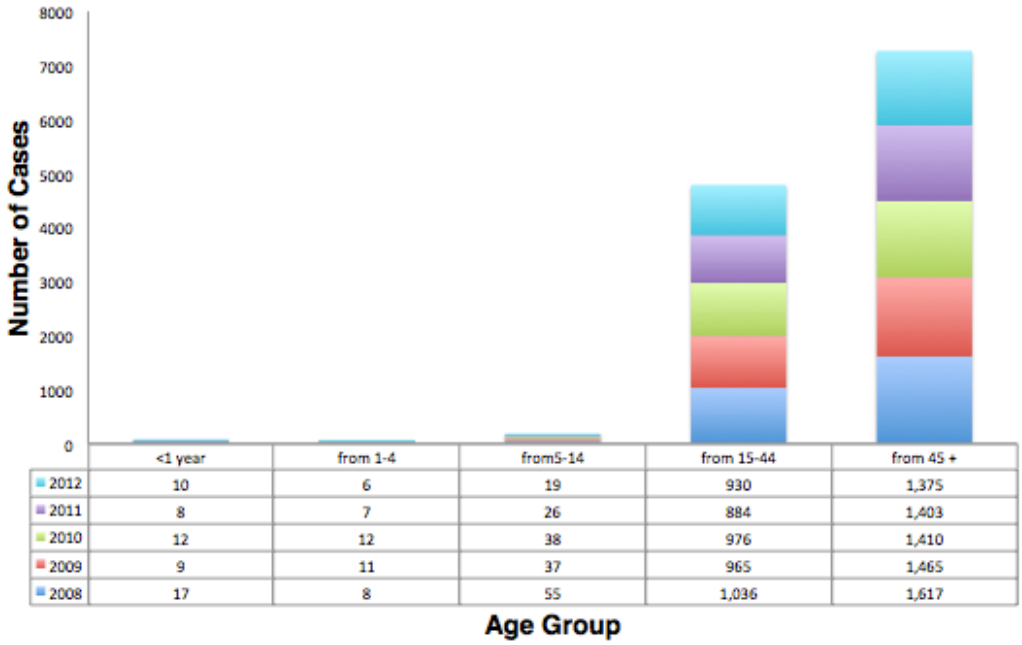
(Regions with a higher IR than the total population each year for at least 3 out of 5 years)



The IRs of HCV demonstrated several trends from 2008 – 2012. We observed significant decreases in the IRs in Riyadh, Makkah, Qassim, Eastern region, Tabuk, Al-Baha and Aljouf in 2012 as compared to 2008, demonstrated by non-overlapping confidence intervals (c.f., appendix). On the other hand, no significant decreases were documented in Madinah, Hail, Northern Borders, Jizan, and Najran in 2012 as compared to 2008, demonstrated by overlapping confidence intervals (c.f., appendix).

Asir was the only region that experienced an upward trend in IR throughout the entire study period; the IR rose significantly from 8.2 per 100,000 population in 2008 to 11.1 per 100,000 population in 2012 (Figure 4). The highest number HCV cases was observed among those > 45 years old (1,671 cases in 2008; 1,375 cases in 2012) followed by those 15 – 44 years old (1,036 cases in 2008; 930 cases in 2012) (Figure 5).

Figure 5. Number of Reported Cases of Hepatitis C Virus Infection, by Year and Age Group, Kingdom of Saudi Arabia, 2008 – 2012



	<1 year	from 1-4	from5-14	from 15-44	from 45 +
2012	10	6	19	930	1,375
2011	8	7	26	884	1,403
2010	12	12	38	976	1,410
2009	9	11	37	965	1,465
2008	17	8	55	1,036	1,617

3.4 Discussion

This study aimed to determine the changes in HCV IRs in KSA over 5 years from 2008 – 2012. Based on our literature review, this is the first study to determine the IR trend of HCV over the entire kingdom. The HCV IR dropped from 11.02 to 8.01 over the 5-year study period. Similarly, previous studies of the IR trends of viral hepatitis A, B, and C, have shown a decline in

the HCV rate by 20 – 30% (8). Many factors have contributed to this remarkable decline, but the most important one is the marked development of the MOH's HCV prevention and control strategies and their adoption by health institutions in all parts of the Kingdom. However, these prevention and control measures might not be being applied fully in many regions, possibly contributing to higher IRs (the high IR in Makkah over the 5 years could be an example), so these strategies do need to be applied consistently.

Makkah is unique among KSA's regions; Makkah city is a holy place where visitors and foreign workers from different KSA regions and other countries visit, work, and live. They have different health backgrounds, and some are from countries with a high HCV prevalence, such as Egypt and Pakistan (13).

Although Al-Baha region experienced a drop in the IR in 2012, its disease burden was high during the previous 4 years. In a previous study examining the IR of HCV between 1995 – 2006, Al-Baha region had the highest HCV prevalence rate (0.32%)(43). This could be due to non-compliance with the measures needed to combat the disease in the region, or it may be due to the aggravating passive surveillance system that can be a generalized Probable Cause for the regions with high IR.

Asir region is the only region that experienced a gradual increase in the IR without any drop over the 5 years. This could be due to report overestimation or a defect in the surveillance or reporting system. Another possible explanation for this ascending rate is that Asir region receives many patients from nearby cities because of the shortage of medical services in those cities. Those regions, which include Jizan and Najran, also have high HCV IRs, and they are

outlets for people from the southern part of KSA and even Yemen, which is known to have a high burden of HCV (44).

As for the regions with low IRs, like Al-Jouf, which had the lowest, it could be that they have adopted the preventive measures very effectively and have successfully established a strong HCV control program. Their results could also be due to a defect in the reporting system and lack of communication with the MoH.

We found that males had a higher IRs than females. This might be due to the fact that males are more exposed to risk factors than females. Examples of these factors are almost daily exposure to shaving tools as well as more exposure to intravenous drug use.

The Saudi population had a higher HCV incidence rate than the non-Saudi population, and this might be due to the fact that non-Saudis are screened before entering the KSA. This result could also be due to underestimation; non-Saudis inside the country may not seek screening or treatment even when they know that they are infected for fear of being deported. Another explanation is that Saudi nationals are required to be screened before marriage to make sure they do not have HIV, HBV, HCV, and inherited diseases.

Despite the drop in the HCV IR, this infection is still a major, challenging public health problem, not only in KSA but all over the world. As we noted above, many regions still grapple with this disease, so we need a comprehensive evaluation of the preventive measures and HCV control programs at all levels of healthcare in these regions.

Chapter 4: CONCLUSION

We conclude that the incidence of HCV decreased dramatically over the 5-year study period. Makkah and Al-Baha regions had the highest HCV IRs among all regions. There was an upward trend in the IR in Asir region after 2008. Males had a higher HCV IRs than females and Saudis had double the IR of non-Saudis.

We have noticed two limitations of our study. First, we used population data taken from the official source of the KSA Central Department of Statistics and Information. However there were some inconsistencies in the data. Regional data were not publicly available, so we used that which was found through the KSA Department of Finance. Although yearly population increases were not taken into account by the Ministry of Finance from 2004 to 2012, they were overestimated by the KSA Central Department of Statistics and Information; this had a negligible effect on the yearly IR. The percentage difference in total population by gender across regions, per year, between the Ministry of Finance and Central Department of Statistics and Information ranged from -5% to 0%. The population data of the Central Department of Statistics and Information was overestimated.

Second, we calculated the IR based on the reported cases to the MoH from different administrative regions by nationality and gender, which rely on a passive surveillance system. This reporting system has a high likelihood of many differences in the study variables depending on the thoroughness and extent of participation on the clinical side in the reporting.

Recommendations

Despite the drop in the HCV IR, this infection is still a major, challenging public health problem, not only in KSA but all over the world. As we noted above, many regions still grapple

with this disease, so we need a comprehensive evaluation of the preventive measures and HCV control programs at all levels of health care in these regions. There were huge differences in the numbers of cases reported among the regions, so we recommend that the surveillance system be evaluated in order to ensure that these differences are a reflection of the reality.

Non-Saudi residents need to be motivated to be screened for HCV and to change their behavior toward the disease. New policies for the HCV-positive population should not include deportation from the country. They should be given treatment. Health education programs and campaigns should be established that target high-risk groups and focus on increasing awareness of the transmission routes.

Since Makkah had the highest burden, we recommend that HCV be included as one of the diseases that foreigners must be screened for before entering to the Kingdom. Finally, we suggest a future hypothesis for determining the risk factors for HCV based on different variables (different age groups, gender, and nationality) to detect the real burden of HCV.

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Appendix

Supplementary Table 1. Reported cases of hepatitis C virus infection and incidence rates, by year and administrative region, Kingdom of Saudi Arabia, 2008 – 2012.

	2008			2009			2010			2011			2012		
	Cases	IR*	95%CI	Cases	IR*	95%CI	Cases	IR*	95%CI	Cases	IR*	95%CI	Cases	IR*	95%CI
Riyadh	643	10.57	9.75-11.39	534	8.55	7.82-9.28	381	5.62	5.06-6.18	544	7.67	7.03-8.31	478	6.54	5.95-7.13
Makah	1036	16.63	15.62-17.64	895	14.1	13.18-15.02	949	13.72	12.85-14.59	845	11.66	10.87-12.45	1007	13.48	12.65-14.31
Medina	92	5.49	4.37-6.61	126	7.33	6.05-8.61	224	12.6	10.95-14.25	173	9.31	7.92-10.7	102	5.34	4.3-6.38
Qassim	136	12.24	10.18-14.3	144	12.68	10.61-14.75	122	10.03	8.25-11.81	105	8.28	6.7-9.86	69	5.29	4.04-6.54
Eastern region	458	12.58	11.43-13.73	430	11.58	10.49-12.67	435	10.59	9.59-11.59	314	7.32	6.51-8.13	339	7.68	6.86-8.5
Asir	149	8.18	6.87-9.49	154	8.29	6.98-9.6	182	9.51	8.13-10.89	207	10.38	8.97-11.79	226	11.05	9.61-12.49
Tabuk	77	9.96	7.74-12.18	73	9.19	7.08-11.3	38	4.8	3.27-6.33	33	4	2.63-5.37	13	1.54	0.7-2.38
Hail	11	1.93	0.79-3.07	9	1.55	0.54-2.56	7	1.17	0.3-2.04	4	0.64	0.01-1.27	10	1.57	0.6-2.54
Northern Borders	13	4.32	1.97-6.67	11	3.58	1.46-5.7	10	3.12	1.19-5.05	9	2.7	0.94-4.46	7	2.04	0.53-3.55
Jazan	17	1.28	0.67-1.89	18	1.32	0.71-1.93	13	0.95	0.43-1.47	6	0.42	0.08-0.76	32	2.19	1.43-2.95
Najran	26	5.48	3.37-7.59	28	5.73	3.61-7.85	39	7.71	5.29-10.13	15	2.84	1.4-4.28	18	3.33	1.79-4.87
Al-Baha	66	16.54	12.55-20.53	58	14.33	10.64-18.02	47	11.41	8.15-14.67	68	15.84	12.07-19.61	38	8.64	5.89-11.39
Al-Jouf	9	2.26	0.78-3.74	7	1.71	0.44-2.98	1	0.23	-0.9	5	1.09	0.13-2.05	1	0.21	-0.82