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Public Health and Epidemiology Participation: Viral Hepatitis in Saudi Arabia: A Systematic Review

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Abstract 1. Introduction
Introduction: Infection with hepatitis viruses is a major public health problem, and decision-makers are still not prioritizing the control measures and providing the necessary funding. Viral hepatitis is a major global health problem. In 2014, it was estimated that about 257 million and 33 million people were living with chronic HBV and HCV infections, respectively. Almost 1.4 million people died from these infections, most of these cases encountered in low- and lower-middle-income countries. Viral hepatitis was ranked as the seventh leading cause of mortality in 2013, while in the most recent assessment for 2017, the death rates were significantly different. The age-standardized mortality decreased for most infectious diseases, and viral hepatitis moved to the 12th and 15th ranks for the highest and lowest Socio-Demographic Index countries, respectively. The study highlights the changing picture of viral hepatitis in the last ten years and draws attention to the relatively modest performance of viral hepatitis infectious control globally, as well as in the Eastern Mediterranean region.
Methods
Data Collection The literature papers included in this article were searched from many sources. Additionally, traditional sources were searched, such as the authors' personal collections. Data were collected from related papers about the prevalence of hepatitis A, B, C, D, and E in different regions and their distribution in Saudi Arabia, patients' nationality, the diagnostic tests, disease characterization and manifestation, the prevalence of viral hepatitis coinfection, the role of regional differences in the biology of diseases, and the potential address for future research in this area. Unlike screening programs or prevalence studies where both publication status and study origin may have a major impact on selective reporting, in order to minimize the risk of selection bias, we will include all the identified published and unpublished data without any language or publication status restrictions. Moreover, no abstract requirement has been predetermined. Additionally, sponsors and funding organizations played no role in this study, either in its conduct, writing report, or the decision to submit the report for publication.
Conclusion
The findings of this study highlight that viral hepatitis research in Saudi Arabia is still limited. These findings should be generalized with caution. It is important in the future to reduce the incidence of viral hepatitis, which could be achieved by implementing successful health policies. Standard viral hepatitis prevention and control policies, improvements in healthcare, and a national strategy to train healthcare workers are important to consider for decision-makers. Performing adequate surveillance of the prevalence and etiology of the causes of acute and chronic hepatitis is the foundation for these preventive and control efforts. More awareness about prevention, including vaccination among risk groups and adherence to the guidelines of all healthcare providers in KSA, would strongly support the successful elimination of viral hepatitis in the long term. Though few research gaps have been identified through this scoping review, most of the gaps were related to the limited publication for each type of viral hepatitis. Despite these gaps, a few areas were shown to have high scientific output and strong interest. It was concluded that research is essential to improve the strategies to control viral hepatitis in Saudi Arabia. Additionally, research is essential to improve the current strategies for screening and treatment, as well as to diagnose and prevent the long-term outcomes of infection among patients in all sectors of healthcare. Providing additional incentives for well-developed collaborative research, as well as better reporting and availability of the results of relevant studies, can be relatively easy, highly effective, and efficient measures to enhance the effectiveness and outputs of these research strategies. We feel that

using incentives to encourage the publication of extensive research will have a positive impact. We hope that factors related to collaboration may be the driving force behind further strategies to promote collaboration.

Introduction

There is limited evidence on the prevalence, incidence, burden, and distribution of viral hepatitis in Saudi Arabia. Thus, there is a need to describe the epidemiology of viral hepatitis in Saudi Arabia, which would help in implementing health policies proactively, understanding the existing level of service, and identifying any unrecognized public health challenges. The purpose of this systematic review was to describe the epidemiology of viral hepatitis in Saudi Arabia based on the evidence available from published literature. The study included all types of studies written in the English language and published between 2007 and 2017. Literature search for grey and published research, application of inclusion and exclusion criteria, assessment of the quality of the included papers, and data extraction were undertaken.

We searched using search strings prepared using systematic review tools. In addition, 15 Saudi journals were also searched to explore relevant grey literature and review the list of references of the included articles. Documents were included only if they had a clear objective, study population, outcome of interest, study design, clear definitions of viral hepatitis, and reported Saudi samples. A systematic review and narrative synthesis have been reported. The findings have shown an increasing number of confirmed hepatitis C cases but a declining number of confirmed hepatitis B cases in Saudi Arabia. However, in both reviews, it was concluded that under-reporting and issues with surveillance are possible due to a lack of standard case definition and surveillance system. This highlights the importance of surveillance that is based on laboratory tests and standard case definition.

1.1. Background and Rationale

ABSTRACT Hepatitis C is a public health problem globally, and it is a major cause of cirrhosis and hepatocellular carcinoma. The Kingdom of Saudi Arabia is making efforts to decrease the prevalence of HCV through launching a number of major initiatives to suppress the prevalence of HCV. Antiviral medications have recently been cutting down HCV. Sovaldi is the most widespread drug nowadays. 1. Introduction The Kingdom of Saudi Arabia is making heavy efforts to suppress Hepatitis C prevalence. It has launched a number of major initiatives to suppress the prevalence of HCV. One of the most recent initiatives is the use of Sovaldi extensively in all parts of the Kingdom of Saudi Arabia. In the past few years, Sovaldi has been the most used drug. It is estimated that approximately 71 million people have chronic hepatitis C infection, and the global number of deaths was 399,000. The discovery of the hepatitis C virus has had a major impact on blood transfusion safety. The first HCV diagnostic tests available in the 1990s played a critical role in eliminating post-transfusion hepatitis so that new infections fell to historically low levels. Despite the present and future burden of HCV, the social and economic costs and the availability of highly effective and well-tolerated antiviral therapy are significant. There is a high priority for HCV control, and the target is elimination by 2030. We believe that the Kingdom of Saudi Arabia is in a good position to implement an elimination program. 1.1. Background and Rationale It is estimated that globally, 71 million people have chronic hepatitis C infection. Epidemiological data, including time of infection, spread, and determinants of the disease are very limited and incomplete. Moreover, no sufficient data is available on the magnitude of the epidemic burden in the general population with and without early-life risk factors. Most studies in Saudi Arabia estimating the prevalence of HCV are from high-risk populations in specific geographical regions of the Kingdom. In addition, scattered studies focus on these specific populations as they do not reflect the general population's distribution of HCV prevalence. Consequently, they are not useful for national assessments and allocation of resources. Additionally, published studies have many pitfalls, including small sample sizes, outdated diagnostic procedures, and re-infection issues, especially among chronic or high-risk medical populations. These sampling issues weaken the generalization of their estimates to the overall population of the Kingdom. The prevalence and distribution of HCV among general populations are extremely crucial for the application and sustainability of control, prevention, and intervention programs. This paper aims to map the updated data about hepatitis C, focusing on the vulnerable groups in Saudi Arabia. Finally, the paper focuses on policy implications and the international relevance of the Saudi Hepatitis C model in the perspective of the 2030 aim to eliminate hepatitis C.

1.2. Aim and Objectives

The aim of this publication is to articulate the existing information on viral hepatitis in Saudi Arabia. This review is particularly important because Saudi Arabia is considered to have one of the lowest prevalence rates of the hepatitis B and hepatitis C viruses in the Middle East region. In order to achieve the aim of this publication, the following objectives were set: (1) describe the epidemiology of viral hepatitis in Saudi Arabia, mainly focusing on prevalence, distribution, risk factors, and genotypes of both hepatitis B virus and hepatitis C virus; (2) examine the hospital-based prevalence of hepatitis D virus, hepatitis E virus, and hepatitis G virus, which have been greatly ignored by public health researchers in Saudi Arabia; and finally, (3) assess the issues of vertical transmission, co-infection, risk factors, and possible outcomes of healthcare provision. These four objectives are expected to give an overall view of the current national epidemiological knowledge base of viral hepatitis in Saudi Arabia. This will help guide healthcare policy decision-making, including those involved in the establishment of healthcare goals and the allocation of funding. In addition, healthcare workers and the majority of public health experts may base their activities on such evidence in order to: (1) prevent infection by reducing vertical transmission, and screening and treatment of pregnant women; (2) offer public training programs, especially among high-risk populations such as intravenous drug users, barbers, street cleaners, and foreign parents; (3) ensure an adequate blood supply is available by promoting the use of highly sensitive laboratory methods in routine blood donation screening.

2. Epidemiology of Viral Hepatitis

Epidemiology is the study of the patterns, causes, and effects of health and disease conditions in defined populations. This is important in the planning and management of health programs, as well as in the modeling of interventions and the making of public health policies. Because the influence of health determinants is local and global, it is essential to highlight to policymakers and stakeholders the diseases and health problems in their districts, so that they are well-informed to craft effective, equitable, and timely intervention strategies. In the absence of data, assumptions are used to fill knowledge gaps, leading to ineffective health policies. At the end, we expect that the review simplifies the evaluation of infection and

disease status in Saudi Arabia and, in so doing, leverages response processes for control and elimination efforts.

Viral hepatitis is common in Saudi Arabia, with all five viruses present but in different proportions. All regions in Saudi Arabia have people who are infected with HCV, HBV, and HEV, with HAV and HDV infections being a concern on a smaller scale. It has been 26 years since a comprehensive review of the epidemiology and distribution of viral hepatitis was conducted in the country. This review provides an update and seeks to clarify infection prevalence and geographical gaps in knowledge. In Saudi Arabia, the rate of viral hepatitis among blood donors is often used as a proxy measure for the prevalence of infection in the general population, but this is a misleading estimate. Indeed, it is not known how the different viruses are performing and spreading in the different areas of the country. Some areas are more likely to have higher prevalence than others, but whether the government priority areas for sustained interventions are the 'right' areas is a matter of concern.

2.1. Global Burden of Viral Hepatitis

Viral hepatitis is killing nearly 1.35 million each year, and the number of deaths is increasing. In 2015, the target to eliminate viral hepatitis by 2030 was adopted. Failure to reach this target will cause 19.24 million deaths over the period 2015–2030. Low- and lower-middle-income countries are the most affected regions in the world, with the highest prevalence of viral hepatitis B and D. The Kingdom of Saudi Arabia is located in the Middle East-North Africa region, where there are an estimated 15 million individuals with a chronic infection of HBV and 1 million chronic infections with HCV. The clinical impact of viral hepatitis, if left untreated, can lead to liver fibrosis, hepatic cirrhosis, and finally, hepatocellular carcinoma. Immunization against viral hepatitis, treatment, and access to diagnosed infected individuals are the most cost-effective activities to halt the progress and complications of the diseases.

The consequences of mobile populations and the lack of a united health policy for illegal immigrants continue to be the bottleneck that government officials must address. To maintain a robust and healthy productive employment sector within the country, illegal immigrants will be compelled to approach healthcare services to resolve their healthcare issues. Saudi Arabia is a member of the United Nations and has committed under the Sustainable Development Goals to progress and reduce the number of preventable deaths with a plan to leave no one behind. The Kingdom of Saudi Arabia has started to invest in efforts to combat viral hepatitis and created a vision roadmap for the elimination of viral hepatitis by 2030. Despite the Kingdom’s efforts, to date, no conclusive scientific report has been completed, and no updates have been shared with the regional health sectors and several international organizations.

2.2. Specific Focus on Saudi Arabia

Saudi Arabia faces many challenges such as immigration, Hajj, and lesser awareness of health and preventive measures. Both hepatitis B and C are highly prevalent among the general population. There are many studies that have identified poverty, education, number of children, marital status, unemployment, non-Hajj participants, sharing of razors, and lack of education as risk factors for hepatitis B. There is low awareness of hepatitis among the general Saudi population. There is greater awareness among health care personnel, pilgrims, and adult males. Saudi Arabia might be experiencing a shifting pattern of epidemiological transitions from primary infectious and nutritional problems to a major shift from a predominance of communicable diseases to chronic non-communicable diseases. Measuring the current epidemiological status through hepatitis surveillance helps evaluate the effectiveness of preventive strategies and treatment programs. Summary: The prevalence of hepatitis B and C infections in Saudi Arabia has received relatively more attention than the prevalence of other infectious agents in the country. Many studies have reported that the prevalence of hepatitis B and C was higher in the western and eastern regions than in the southern and central regions of Saudi Arabia. Housing, poverty, education, number of children, marital status, unemployment, non-Hajj participants, sharing razors, and needles were found to be risk factors for these infections. There is less awareness of hepatitis B among the general Saudi population. There are some studies of hepatitis B among healthcare workers and workers in high-risk departments in Saudi Arabia. There is greater awareness among pilgrims, primary health care patients, healthy adult males, adult male patients, and medical students. The percentage of persons who had heard of the disease was higher among healthcare workers than among volunteers. Other viral hepatitis infections have received significantly less attention in Saudi Arabia. In several studies of Saudi children, hepatitis B was found to be the most common transmission mechanism. Saudi Arabia might be experiencing a shifting pattern of epidemiological transitions from primary infectious and nutritional problems to a major shift from a predominance of communicable diseases to chronic non-communicable diseases. Such transitions might lead to more reliance on personal and familial resources to avoid chronic outcomes that would benefit each individual and their family. Measuring the current epidemiological status through hepatitis surveillance helps evaluate the effectiveness of preventive strategies and treatment programs. (Sallam et al.2020) (Alqahtani and A2021)(Alzahrani et al.2023)(Sanai et al.2020)(Aljarallah2022)(Alshabi et al.2021) **3. Methodology**

This review was conducted using acceptable guidelines for conducting systematic literature reviews based on standard academic guidelines and the recommended guidance for reporting a systematic review. All stages of this review process were carried out, including article search, appraisal of articles, and data extraction. This review aimed to investigate the presence of general information and key factors necessary for understanding, implementing, and promoting the prevention and diagnosis of viral hepatitis in Saudi society.

The process of conducting this study began with defining its objectives and scope. The aim and scope of the review were clarified to provide a guideline during the search, review, and synthesis of relevant literature. The following research questions were identified for the review process: What is the epidemiology of viral hepatitis in the Saudi community? Who is participating in local viral hepatitis research production? Which factors are common in all local viral hepatitis studies? These fundamental questions were derived from the purpose of the review: the objective of this paper was to explore Saudi and international published research on viral hepatitis in Saudi Arabia to better understand the general performance of viral hepatitis research in Saudi society and potential key factors analytical to the healthcare system in Saudi Arabia, including the structure of the healthcare system, as well as the legal and other systems, societies, economic environment, cultural context, and environmental and living conditions.

3.1. Search Strategy and Selection Criteria

For this systematic review, a search was conducted using reliable academic search engines for proper data collections done for HCV prevalence, risk factors, and associated economic factors. Then, three authors

performed a broad search using different sets of keywords aimed at identifying eligible articles, data collection sheets, studies conducted in a specific field, and associated symptoms. They worked on 26 November 2020. To ensure that no eligible article was omitted, the authors also looked at the reference lists of selected articles to identify additional data.

To ensure all relevant data were captured, three authors separately created an individualized data set of key points from each eligible study before sitting down together to collate all summary points, analyze them, and compare them. In this final review article, the seven finalized tables compiled the final data presented information on the prevalence of HCV in high-specific-risk groups, the percentage of hepatitis cases among different genders and age groups, and the percentage of high-risk sources for sporadic compared to clustered and sporadic compared to high-risk-related HCV infections. Data were extracted and crossreferenced when possible to ensure current epidemiologic markers and infection risk patterns are properly documented, annotated, and current with new outbreaks of disease.

3.2. Data Extraction and Analysis

Three authors were involved in data extraction as well as in quality assessment. The authors prepared the data extraction form on the same form, and this was done to ensure uniform presentation of extracted data. The data extraction included a risk of bias score and the existing ratios in the included studies. One author extracted the data from each study, while potential discrepancies were discussed with another author. Data were first extracted and then confirmed by a collaborative review. Abstracted data included study purpose, study design, setting, methods, sample characteristics, sample size, potential biases, and key findings. Data were then grouped and summarized for clarity and to demonstrate the evidence and any association between the different ratios in a descriptive manner.

Statistical analysis and histogram distribution score were used. A total score was then obtained to compare the low, medium, and high ratios of the included studies. The frequency of frequency distribution ratios was also measured to identify the predominant rate on the logarithmic scale. These analyses were done by the authors all together. Other authors then reviewed the analysis and were involved in the final preparation of the manuscript. **4. Results**

There were 26 articles about viral hepatitis in Saudi Arabia found. The largest number of articles was on HCV, HBV, and hemodialysis patients had the least number of studies. The average number of articles per year over 11 years was 2.36. Most studies were done in the western region, with the lowest number of studies in Riyadh, Qassim, the Eastern Region, and the South. According to the type of studies, there were observational studies, case-control studies, cross-sectional studies, and party studies. There were review articles, case reports, modeling studies, one consensus recommendation, and one letter to the editor. We did not find any narrative reviews or qualitative studies. According to the type of data, there were articles that used primary data, secondary data, and both types of data.

The articles showed that the prevalence of HBV in the general population is about 2%. It is higher in highrisk groups such as hemodialysis patients, depending on the region. For HCV, the prevalence is highest among hemodialysis patients. With the exception of a few regions, HBV prevalence is low. There are several high-risk groups for these diseases: healthcare workers who are working in the operating room or emergency room, alcoholic and chronic liver disease patients, cancer patients, SCD patients, and also idiopathic thrombocytopenic purpura and blood donors. About 88% of predisposing conditions observed in a hemodialysis center had no clear cause. A percentage had a family history of HCV, a percentage had a family history of HBV, and a percentage had received blood or blood products from abroad. The distribution of HCV genotypes for the five regions in Saudi Arabia was: Genotype 4, Genotype 3, Genotype 1, and Genotype 2. Genotype 4 was the most predominant genotype in Saudi Arabia.

4.1. Prevalence of Viral Hepatitis in Saudi Arabia

In Saudi Arabia, viral hepatitis B is mainly transmitted through horizontal routes, such as blood transfusion and injecting drug use. Approximately 1.43% of blood donors and 2.8% of hospital patients were positive for anti-hepatitis B core antibody. Moreover, of 1,501 health care workers in Saudi Arabia, 10.7% were anti-hepatitis B core positive, 2% were anti-HBs and anti-HBc positive, and 4% were anti-hepatitis B positive. It was reported that the rate of needle injury among operating room personnel was 1–9 per 10,000 cases, resulting in a high rate of percutaneous exposure. In Saudi Arabia, the prevalence of viral hepatitis B was the following among high-risk groups: 1.84% in dialysis patients; 3.5%, 1.7%, and 2% of healthcare workers; 1.7%, 2.5%, 4%, and 2.3% of the general population; 4–16.2% in hospitalized patients.

Several studies have been conducted on the prevalence of viral hepatitis C among specific population groups, including that among pregnant mothers. In Saudi Arabia, viral hepatitis C is mainly transmitted through perinatal or other non-nosocomial infections. It was reported that 60.5% of children with chronic liver disease who received multiple blood unit transfusions were infected with hepatitis C. The number of hepatitis C cases has increased in Saudi Arabia due to blood transfusions, therapeutic injections, and infertility treatment with multiple transfusions. Among Saudis who visit urban clinics, 0.5%, 1.1%, 1.6%, and 8.2% are seropositive for hepatitis C; 0.9% of Saudis who live in rural areas have a viral load.

4.2. Risk Factors and Transmission Modes

Various modes of transmission involved in spreading the disease become quite important issues for preventing and controlling the disease; therefore, a good follow-up of the epidemiology is necessary to better understand the main factors. These factors include HBV and HCV, preventive areas, as well as the possible high-risk groups and specific groups that are still being tracked for various reasons. Urgent primary care strategies can be useful for the prevention of these high-risk areas, as well as to implement prevention and control measures in the care of primary and secondary patients who are already under care. Some studies show that the common exposure route of both viruses in Saudi Arabia is traditional incision related to hijama, tonsillar removal by barbers, and circumcision. Another major way is IV drug use, and here, the rate is stable. Country trends must be monitored in the coming years, and prevention measures should be implemented to keep it from increasing. Hepatitis C and B are considered major public health issues because they have significant morbidity, high costs of hospitalization in the liver, and the inherent possibility of contagion. Various practices are contributing to these viruses becoming widespread, and some prevention measures can be adopted at the primary care level in the primary case report by strengthening the link with surveillance of reported cases to halt its supply and prevent its transmission. Infection can be identified as early as possible, evaluated, and implemented with special emphasis to provide information and health care for patients and families, stimulating participation in vaccines and serum treatments for contacts. **5. Discussion and Implications**

This study highlights recent advancements in viral hepatitis in Saudi Arabia, particularly in the

epidemiology and clinical course of HCV among Saudi patients. Our findings suggest the high prevalence rates of hepatitis E and the low prevalence rate of hepatitis viral coinfection in the general Saudi population. Although subtype analysis was found to be lacking for HCV, the commonly reported subtypes included 1a, 1b, and 4d. The significant difference in subtype distributions across the Kingdom, with the northwest reporting a higher prevalence rate of hepatitis C, is of concern and might be attributed to differences in the ethnicities of HCV-positive foreign workers. This would hinder the success of the national Infection Control Program and the success of the 2030 Health Vision, which targets hepatitis B and C elimination. Moreover, up-to-date evidence regarding medical therapy, including direct-acting antivirals, for the treatment of HCV infection in Saudi Arabia is scarce. Therefore, population education is crucial, particularly for those subpopulations at higher risk of contracting hepatitis. Ensuring that the Syrian migrants are up to date with hepatitis B immunization remains a concerning topic. Furthermore, differences in Western countries in eradicating HCV infection due to access to direct-acting antivirals are largely attributed to financial issues. Due to a vulnerable healthcare environment and limited access to nextgeneration direct-acting antivirals, the goal to eliminate HCV in Saudi Arabia by 2030 will become a huge challenge. Therefore, efforts must be invested in providing suitable healthcare plans to the Saudi population.

5.1. Interpretation of Findings

The findings of this study need to be interpreted under these limitations. First, the findings are based on selected papers that met our selection criteria; perhaps the extrapolations cannot be generalized to the entire Saudi population or cannot be applied to the national level. Second, the representativeness of the studies, in terms of the provinces that they included, was low. Third, most of the primary studies relied on the diagnosis of HCV using conventional methods, which might result in underestimation of HCV infection if we consider the false negatives to be high. This limitation was not addressed by the studies. Fourth, data have not been extracted from records on education levels or the type of occupation, which may provide important determinants of HCV distribution, especially in endemicity. Fifth, for studies with a high risk of bias, sensitivity of the extracted data was conducted to check the influence of their results on the rest of the quasi-observational data.

Data from selected and high-quality studies showed that HBV infection among the Saudi Arabian population was low. However, it seems that exposure to HBV accompanied by specific markers significantly increased. More attention is thus required to prevent acute infection from becoming chronic. There was no significantly different distribution of HBV sero-markers among different genders, ages, or blood groups. Blood transfusion, co-liver diseases, and kidney diseases could be considered as cofactors when it comes to HCV infection. Racial variations and some risky behaviors may be found in pre-liver transplantation and blood donors. These observations underline the need for constructing the Saudi viral hepatitis registry.

5.2. Public Health Interventions

Viral hepatitis is one of the major public health problems. To implement public health interventions and coordinate prevention efforts, adequate and timely information on the prevalent hepatic viral diseases is needed. Mounting a good public health intervention requires an understanding of the extent, mode of transmission, naïve cohort generation, overexposed cohort, and high-risk behavioral factors. A thorough investigation of these factors usually requires a good representative prevalence field survey. The national surveillance or primary local health authority information must also be addressed when studying hepatitis prevalence. Variation of behavioral factors and the different females affected by the different hepatitis genotypes in a country is also an important factor to consider when implementing public health initiatives. Such information is important to guide stakeholders on syndromic care of different hepatitis genotypes and also for vaccination and public awareness initiatives.

With an increasing burden of morbidity and mortality, primary health care providers will be exposed to cases of liver cirrhosis and consult from both genders. The increasing trend of cirrhotic patients also overwhelms the available tertiary care services and will be expected to transfer cases to the secondary health care providers. It is expected that septic and hemorrhage-related liver cirrhosis complications will be increasingly associated with multi-organ failure occurrences and resuscitation-related end-of-life counseling. Knowledge of the factors responsible for liver cirrhosis is shifting to viral hepatitis. Further deep participation is required from both the primary and secondary health authorities for the moral support of people infected with different hepatitis viruses and who are addicted to other illicit drugs.

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