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The decline in hepatitis B and C in women: A 5-year retrospective case study in Ha'il, Saudi Arabia

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ABSTRACT

Background: Hepatitis infections, particularly hepatitis B and C, threaten public health to a great extent. They can be directly transferred from pregnant women to their fetuses, either in utero or postpartum. In Saudi Arabia, there is a variation in the prevalence of both infections among women throughout the country's regions. Thus, it is necessary to examine women for probable infections by any of these types of hepatitis to prevent hepatitis transmission.

Objective: To assess the prevalence of hepatitis B and hepatitis C infections among women in Ha'il, Saudi Arabia during 2016-2020.

Methods: A retrospective cohort study was performed on the cumulative sero-prevalence of hepatitis B and C among 23,462 women who attended the maternity hospital in Ha'il, Kingdom Saudi Arabia (KSA), from the period of 2016-2020.

Results: The analysis revealed that the hepatitis B infection (sero-prevalence 0.27%; 64 cases) is more prevalent than hepatitis C infection (sero-prevalence 0.077%, 18 cases) among women. Both infections were higher among Saudi compared to non-Saudi nationals. Moreover, hepatitis B sero-prevalence increases with women's age, while HCVAb was higher in the group 40 – ‹50 years old. The data also showed no trends throughout months, seasons, and years for HCVAb and HBsAg cases.

Conclusion: The results show a dramatic decline in both types of hepatitis (B and C) among the investigated women compared to previous and recent reports from other regions in the country and a further decrease in the prevalence during the study period. These results imply that the hepatitis B vaccination program implemented in Ha'il over the last 30 years has been successful for females. Therefore, surveillance, improved diagnostic facilities, and vaccination efforts should be continued in Ha'il, KSA.

Keywords: hepatitis B, hepatitis C, women, sero-prevalence, epidemiology, Saudi Arabia

1. INTRODUCTION

Infectious diseases are among the leading causes of death globally, being responsible for almost 3.7 million deaths per year [1]. Thus, disease surveillance data is used to determine the need for public health action. Hepatitis B Virus (HBV) and hepatitis C Virus (HCV) infections are among the most significant health issues in the world [1].

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HBV and HCV infections can spread through contact with infected blood and body fluids (e.g., mother-to-child transmission), unsafe healthcare practices, intravenous drug use, and sexual intercourse. They infect the liver and trigger acute and chronic hepatitis, hepatocellular carcinoma, as well as liver cirrhosis, and failure [2,3]. HBV affects more than 350 million people worldwide and killed 1.34 million in 2015 [1]. The prevalence of HBV infection ranges from 1% in North European countries to 9% in Low socioeconomic countries [4,5]. The majority (95%) acquire the infection during the perinatal period and early childhood [6]. Vaccination as a preventive program for HBV was initiated in the 1980s in several countries to eliminate its transmission [7]. HCV primarily attacks the liver. Besides, a wide range of systemic disease processes known as C hepatitis-associated systemic manifestations are found in a significant number of infected people. These include thyroid, cardiovascular, renal, eye, and skin diseases in addition to lymphomas and diabetes [8]. It is a blood-borne virus that spreads through unsafe health-care practices, injecting drugs, unscreened blood as well as blood product transfusion, and sexual practices that lead to exposure to blood. HCV infection is certainly one of the major global causes of mortality and morbidity. Compared to HBV, the prevalence of HCV infection is lower [4]. Overall, in 2017, the World Health Organization (WHO) estimated that 71 million individuals worldwide suffer from chronic HCV infection. Approximately 399 thousand people died in 2016 infected by HCV. To date, an effective vaccine against HCV is unavailable [9].

HBV prevalence and incidence rates vary geographically throughout the Eastern Mediterranean region [10]. HBV infection rates range from 0.6% in Iraq to more than 8% in Sudan [11]. The age-specific prevalence of HBV infection varies, with a perceived decline in prevalence among children [10]. On the other side, the Eastern Mediterranean region shows the highest prevalence of HCV (2.3%) worldwide [12].

The data for the last five years, collected by the Ministry of Health in the Kingdom of Saudi Arabia (KSA), show a notable increase in the HBV and HCV incidence rates (incidence rate/100,000 population: 14.05–22.24 and 5.48–10.27; respectively) [13]. Although several research studies investigating the prevalence of HBV and HCV in the Saudi community were conducted, studies performed among women are still limited and require further attention. This should be of concern as HBV, and to a lesser extent HCV, can be easily vertically transmitted from pregnant women to their fetuses which results in the rise in the infant mortality rate. The Saudi government has adopted a national HBV immunization program for newborns since 1989 [14]. In 2004, HBV sero-prevalence in Saudi women was estimated to be 1.6% [15]. Updated estimation in 2015 revealed that 1.08% of women were sero-positive for HBV [4]. A study representing five different regions of KSA reported no HBV sero-positive among women <18 years old compared to 2.6% in the overall older age groups. However, older age groups in different regions displayed variations. Therefore, studying the prevalence of HBV among a population or a subpopulation (e.g. women) will indirectly evaluate vaccine efficiency.

This work aims to establish a trend for Hepatitis B and Hepatitis C prevalence among women living in Ha'il Saudi Arabia by using a five years retrospective data from Ha'il maternity hospital patient's registry and laboratory records from 2016 to 2020.

2. SUBJECTS AND METHODS

The present study uses retrospective data retrieved from the registry records of the maternity and children's hospital in Ha'il, KSA. This hospital is the sole governmental hospital specializing in obstetrics and gynecology in Ha'il province with bed capacity of 200. According to the Saudi Ministry of Health rules, all women attend maternity and children's hospitals should be examined for HCVAb and HBsAg. The data of 26902 women tested for HCVAb and HBsAg during five years (January 2016–December 2020) were retrieved from the hospital database. The data collected for all cases included age, date of the test, the results of HCVAb as well as of HBsAg. Duplicated file numbers and failed tests were excluded, ending up with a 23462 women's lab reports files. For those sero-positive cases, the nationality information was then requested from the medical records in the hospital. Age groups were categorized as ≤ 20, 21–30, 31–40, 41–50 and >50 years old. Nationalities were sorted into 2 categories: Saudi and non-Saudi. Positive cases of both tests were also aligned in the context of the date of the case's appearance (month, season, and year) and the point and cumulative prevalence were explored. Chi-square test was used to examine the relationship between variables using the Statistical Package for Social Sciences (SPSS) version 20.

3. RESULTS

3.1 Population Characteristics

During the period of 2016-2020, a total of 23,462 reports for HCVAb and HBsAg tests of women attending the hospital were investigated. The mean age ± standard deviation (SD) of the investigated women was 34.22 ±7 years. Most of the population (n = 12,390) was within the age range of 31-40 years old. To facilitate a direct comparison of the studied group, the cumulative prevalence of HCVAb and HBsAg were standardized based on nationality, age, and date of detection.

3.2 HCVAb and HBsAg were higher among the Saudi compared to non-Saudi nationals

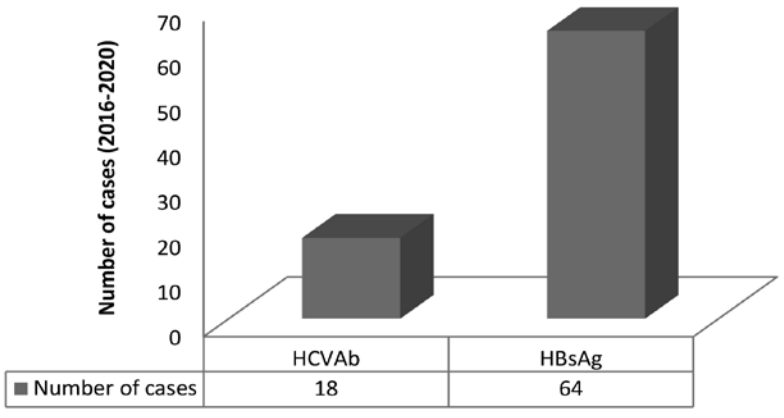
During the time period of the study, the majority of HCVAb (*n* = 15, 83.3%) and HBsAg cases (n = 56, 87.5%) were Saudi compared to 3 (16.7%) and 8 (12.5%) for non-Saudi cases; respectively. Accordingly, the reported cases of HCVAb and HBsAg were 5 and 7-fold higher among Saudi nationals compare to non-Saudi (**Table 1**).

Table 1. Year distribution of reported hepatitis by nationality between 2016 and 2020.

Epidemiological Year	HCVAb			HBsAg		
	Nationality		Total N (%)	Nationality		Total N (%)
	Saudi N (%)	Non Saudi N (%)		Saudi N (%)	Non Saudi N (%)	
2016	1 (100)	0 (0)	1 (100)	14 (100)	0 (0)	14 (100)
2017	10 (83.3)	2 (16.7)	12 (100)	14 (87.5)	2 (12.5)	16 (100)
2018	2 (100)	0 (0)	2 (100)	15 (79)	4 (21)	19 (100)
2019	1 (50)	1 (50)	2 (100)	10 (90.9)	1 (9.1)	11 (100)
2020	1 (100)	0 (0)	1 (100)	3 (75)	1 (25)	4 (100)
Overall	15 (83.3)	3 (17.7)	18 (100)	56 (87.5)	8 (12.5)	64 (100)

3.3 The cumulative prevalence of HBV is higher than HCV infection

The numbers of HBsAg and HCVAb positive cases among the reported 23,462 female patients are shown in **Figure 1a**. Sixty-four cases were reported positive for HBsAg (0.27%), while 18 cases were positive for HCVAb (0.077%), representing 78% and 22% of the cases; respectively. (**Figure . 1b, c**). Thus, the number and the cumulative sero-prevalence of HBsAg positive cases is almost 4-fold higher than HCVAb positive cases among women in Ha'il province during 2016-2020. No co-presence of HBsAg and HCVAb in the studied population was found.



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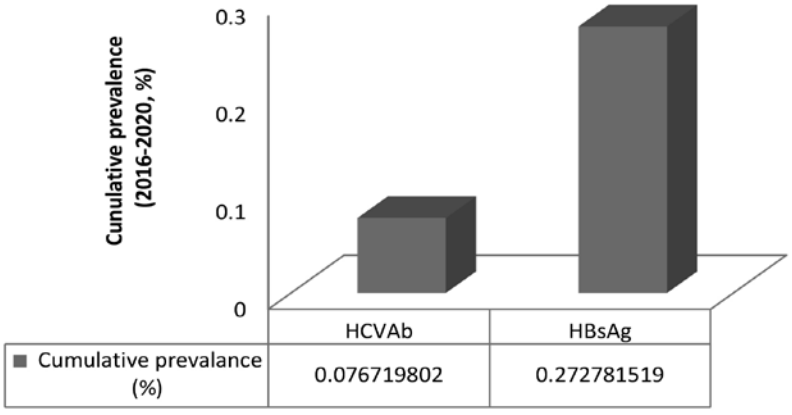
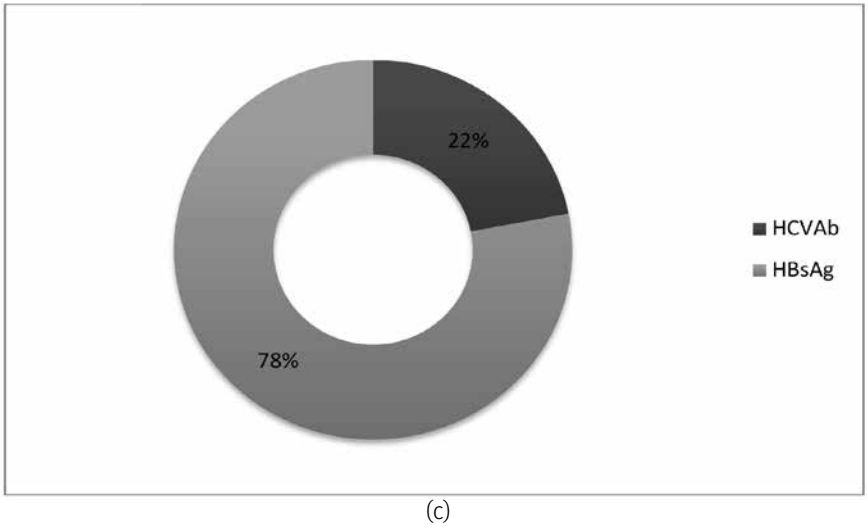




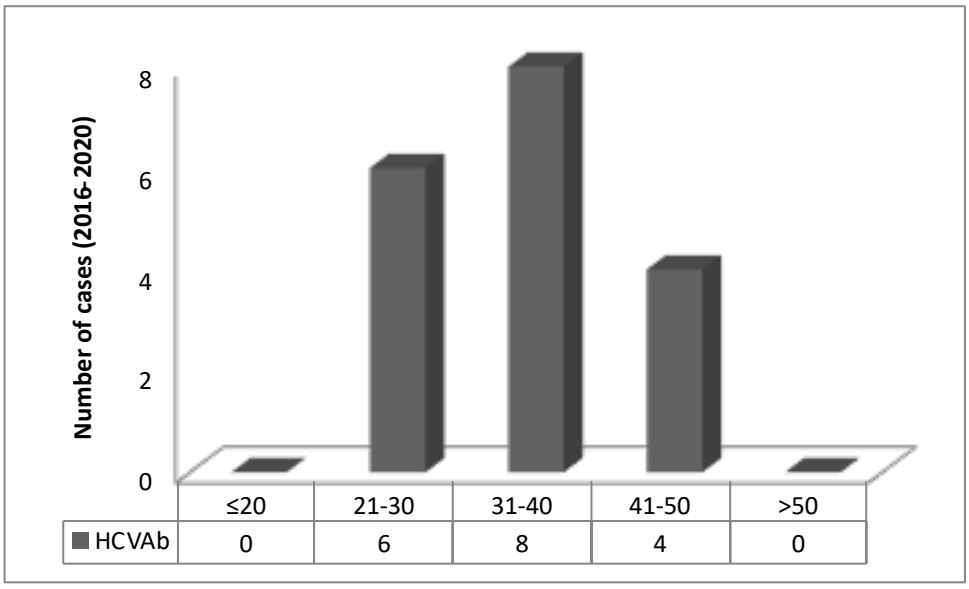
(c)

Figure 1. Reported cases and cumulative prevalence of HCVAb and HBsAg in women in Ha'il. (a) Number of HCVAb (n = 18) and HBsAg (n = 64) cases. (b) Cumulative prevalence of HCVAb (0.077%) and HBsAg (0.273) through 2016-2020. (c) Proportions of HCVAb (22%) and HBsAg (78%) among positive cases.

3.4 The number of HCV cases varies among the different age groups

Figure 2 shows the distribution of positive cases of HCVAb across different age groups. Remarkably, no HCVAb positive cases were found among women ≤20 or >50 years old. In contrast, the number of positive HCVAb positive cases was dominant (8 cases) in women aged 31–40 years old (**Figure 2a**). Overall, the number of positive HCVAb cases showed a varied distribution across age groups. the results revealed no significant association between HCVAb positivity and age, x2 (4, n = 23,462) = 0.97, p-value = 0.91. Moreover, the cumulative sero-prevalence in each age group relative to the total number of investigated women in that age group was analyzed. The highest cumulative prevalence of HCVAb (0.065%) was in the group 41–50 years old (**Figure 2b**). Similarly, the cumulative prevalence of HCVAb showed a varied distribution among the different age groups. Thus, HCV infection is likely age-independent among women in Ha'il.

(a)



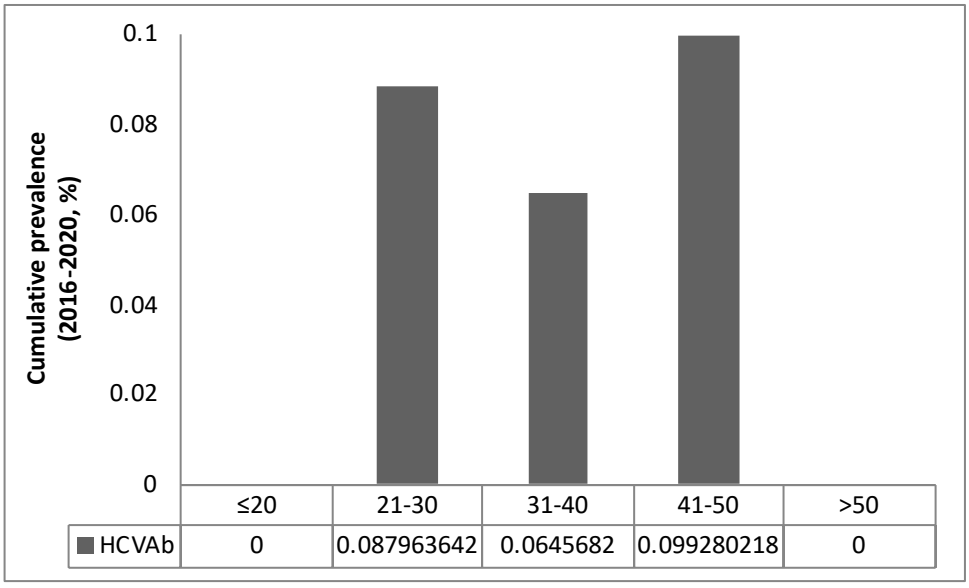
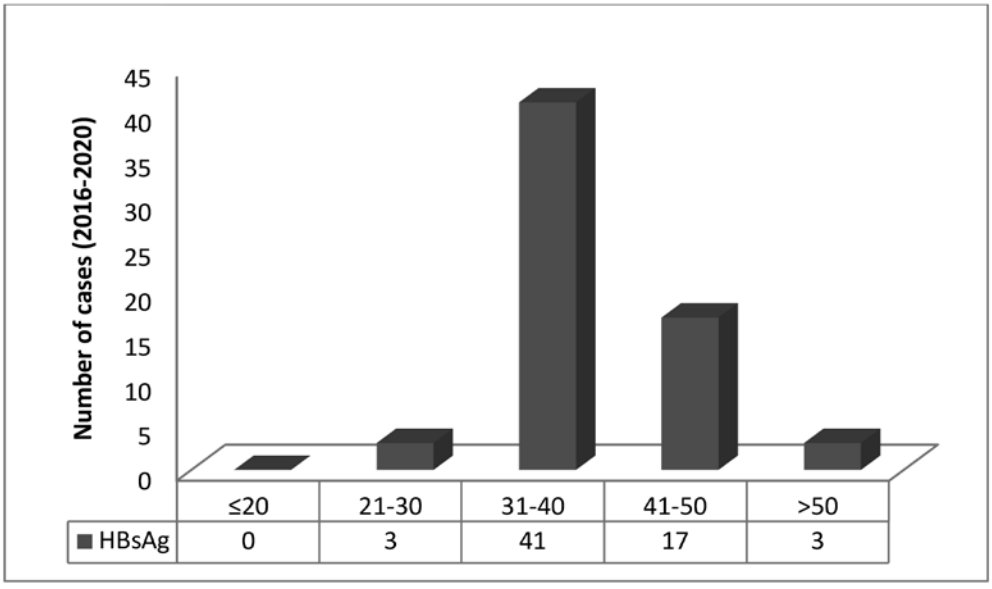


Figure 2. Distribution of cases (a) and cumulative prevalence (b) of HCVAb in women in Ha'il across the age groups. ≤20 (n = 0, 0%), 21-30 (n = 6, 0.088%), 31-40 (n = 8, 0.065%), 41-50 (n = 4, 0.099%) and >50 (n = 0, 0%).

3.5 The number of HBV cases increases directly with age

No HBsAg positive cases were observed among women ≤20 years, while the number of HBsAg positive cases was the highest (41 cases) among the age group 31–40 years old (**Figure 3a**). Interestingly, the cumulative prevalence of HBsAg positive cases increased directly with age periods of the observed women (see the trend line, R^2=0.9592) and reached the highest (0.66%) among the women >50 years old (**Figure 3b**). Thus, our analysis indicates an association between the prevalence of HBsAg sero-positive cases and the age (x2 (4, *n* = 23,462) =20 .77, *p*-value < 0.001).



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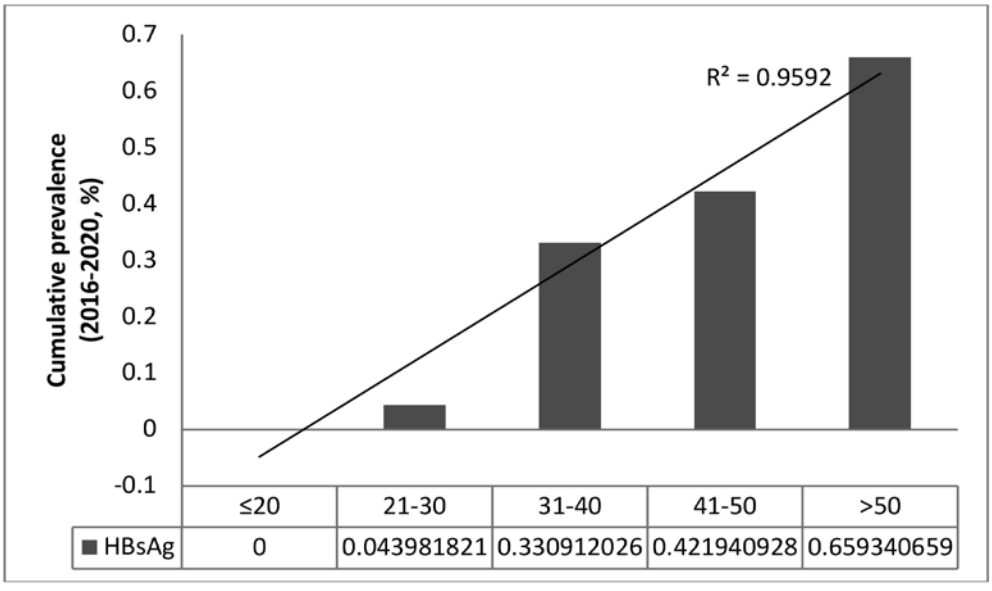
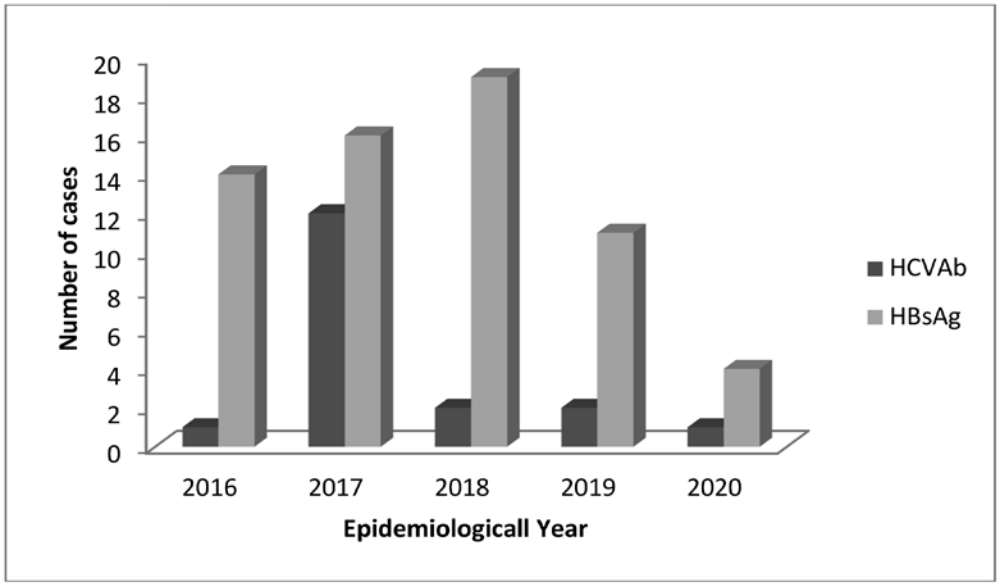


(b)

Figure 3. Distribution of cases (a) and cumulative prevalence (b) of HBsAg in women in Ha'il across the age groups. ≤20 (n = 0, 0%), 21-30 (n = 3, 0.044%), 31-40 (n = 41, 0.331%), 41-50 (n = 17, 0.421%) and ›50 (3 = 0, 659%).

3.6 No trends throughout months, seasons, and years for HCVAb and HBsAg cases

The epidemiological distribution and trends of the reported HCVAb and HBsAg cases over the five years study period (year, season, and month-based) are shown in **Figure 4**. The number of either HCVAb or HBsAg positive cases fluctuates throughout the five studied years. As shown in the graph, 2017 is marked by significant growth in the number of cases (n = 12) as well as the prevalence of HCVAb (0.1%) followed by a marked decrease in the following studied years with no HCVAb cases in 2020 (**Figure 4b**). On the other hand, although the data showed an overall upward trend in HBsAg cases in 2016 (n = 14), 2017 (n = 16) and 2018 (n = 19) followed by a significant decline in 2019 (n = 11) and 2020 (n = 4), the prevalence of HBsAg cases was highest in 2018 (0.28%) followed by 2017 (0.24%), (**Figure 4a, b**). Moreover, the number of cases as well as the prevalence of both HCVAb and HBsAg fluctuated by the season (**Figure 5a, b**) and month (**Figure 6**) and no significant association was established. Collectively, HCV and HBV incidence is month/season independent. However, HCV and HBV were highly prevalent in 2017 and 2018; respectively.



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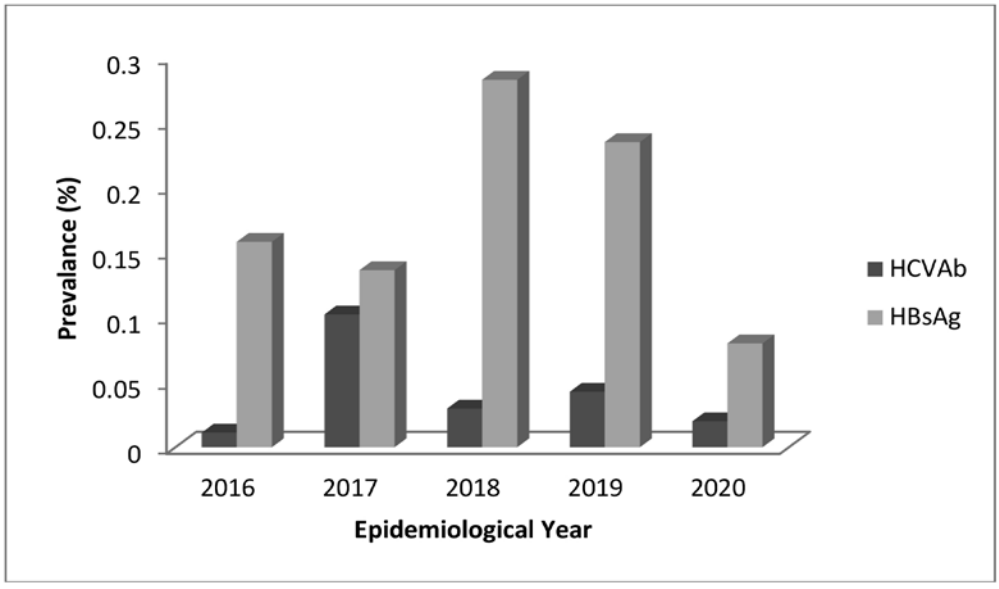
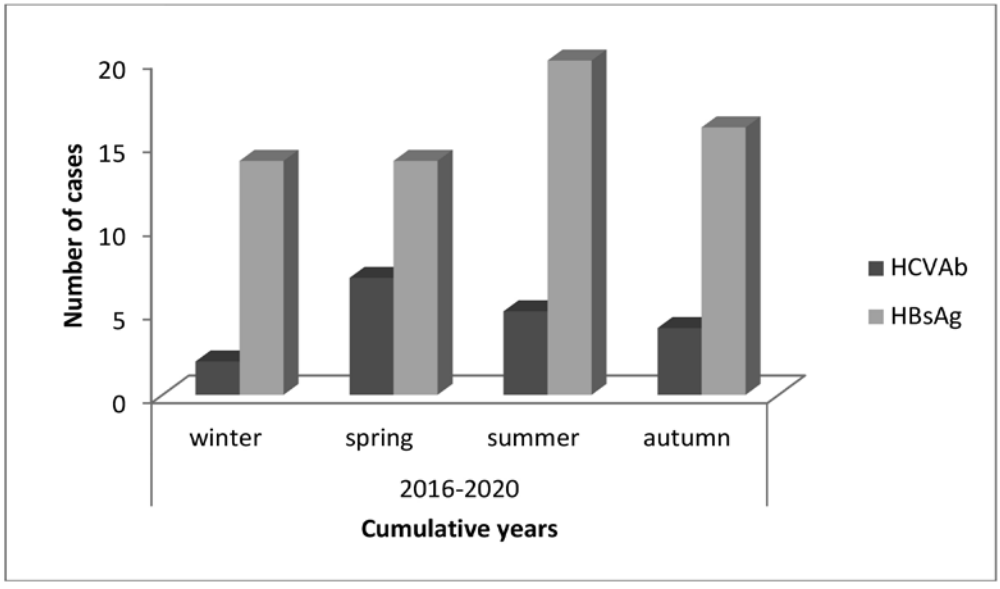


(b)

Figure 4. Annual cases and cumulative prevalence of HCVAb and HBsAg (2016–2020). (A) Annual cases of HCVAb (n= 1, 12, 2, 2 and 1) and HBsAg (n= 14, 16, 19, 11 and 4) through 2016-2020, respectively. (B) Cumulative prevalence of HCVAb (0.011%, 0.102%, 0.03%, 0.043% and 0.02%) and HBsAg (0.0158%, 0.136%, 0.283%, 0.235% and 0.08%) through 2016-2020; respectively.



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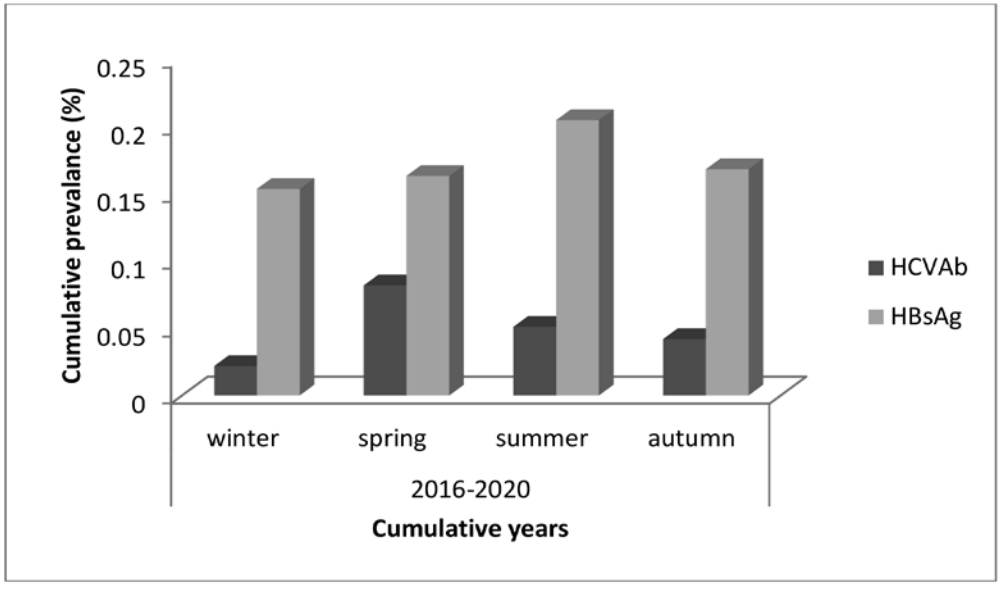

(b)

Figure 5. Reported cases (a) and cumulative prevalence (b) of HCVAb and HBsAg according to seasons (2016–2020). Cases of HCVAb (n= 2, 7, 5 and 4) and HBsAg (n= 14, 14, 20, and 16) in winter, spring, summer and autumn; respectively. (B) Cumulative prevalence of HCVAb (0.022%, 0.082%, 0.051% and 0.042%) and HBsAg (0.153%, 0.163%, 0.205% and 0.168%) in winter, spring, summer and autumn; respectively.

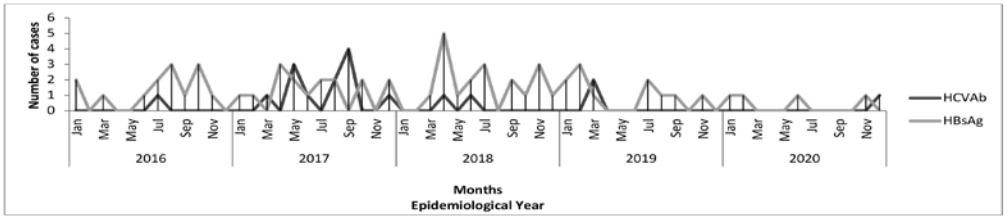

Figure 6. Reported cases (a) and prevalence (b) of HCVAb and HBsAg according to months (2016–2020).

4. DISCUSSION

In 2016, WHO's 2016 resolution sought to eradicate hepatitis as a public health threat by 2030 [7]. The global action on this issue varies among the 194 member states, as 70% responded. Approximately 62% of the responding states had adopted a national plan including vaccination programs and regular testing, particularly for HBV, in risk groups. Screening for HBV, and to a lesser extent for HCV infections, in women is crucial to preventing vertical transmissions. Accordingly, the Saudi Ministry of Health screens women for HBV and HCV when they first visit obstetrics and gynecology clinics. Despite this, the country has been increasingly reporting primary hepatic carcinoma in this decade with marked regional variations. HBV and HCV infections are considered the major etiological factor of liver diseases including hepatic carcinoma [16]. Our study sought to investigate HBV and HCV sero-prevalence and indirectly evaluate the outcome of the national vaccination programs initiated 30 years ago against HBV infection in KSA within a major representative group, the women.

The results in this study revealed a very low sero-prevalence (0.27 %) of HBV among the 23,462 women reports documented. The sero-prevalence among women in Ha'il province is significantly lower than that recently reported worldwide, in Southern Italy (5%), Spain (0.42%), Turkey (1.2%), Egypt (5%), Iran (1.2%), and Sudan (7.5–11%) [17-23]. Nearby, the prevalence of HBsAg among women in the Arab Gulf countries varies from 1% to 7.1% [15, 24-26]. Nationwide, HBV infection is endemic in KSA [27]. Few reports have investigated HBsAg prevalence in women in KSA; and none in the Ha'il province. In 2004, the prevalence of sero-positive HBsAg within Saudi women was estimated at 1.6% [15], decreasing to 1.08% in 2011 [4]. These observations aligned with others' findings that the sero-prevalence of HBV reduced by 65% during 2012–2015 compared to 2002–2005 in KSA [28]. In comparison to other cities/provinces in KSA, a much lower sero-prevalence of HBsAg in Ha'il province was found. This implies that differences in the sero-prevalence of HBsAg within the country vary despite the unified vaccination program and test protocols. These discrepancies are most likely due to socioeconomic and geographical variations between the different cities or non-taking/ incompletion of the three-dose HBV vaccine. Recent studies in the Makkah region revealed that 1.9% of the tested general community had not completed the vaccination course while 20.1% had not received the vaccination at all [29]. The lower prevalence in Ha'il province suggests the adherence of the hospitals in this region to the Saudi Ministry of Health protocols and confirms the effectiveness of the government's steps in 1989 to enforce HBV-preventive vaccination after birth [14]. However, this might require reevaluation of the diagnostic procedures and facilities as this may affect the decreased prevalence value of both diseases in Ha'il.

Although women are commonly deemed representative of HBV prevalence in the general population, our results showed that the sero-prevalence of HBV among women in Ha'il is much lower than that estimated for the general Saudi population, 0.7% in Riyadh, 2.3% in the eastern region, 3.0% in the western region, and 7.9% in the southern region [30-32]. Studies have not yet been conducted to estimate this rate in Ha'il. Additionally, it has been reported that men exhibit a significantly higher HBV infection rate than women in KSA and, therefore, the HBV sero-prevalence in women is unlikely to represent the sero-prevalence in the general population [29].

The sero-prevalence of HCV among women in Ha'il has not yet been sero-estimated. It is found that the seropositive rate for HCVAb among the reported women was 0.077%. The results in this study revealed a low prevalence of HCVAb in women in Ha'il compared to the worldwide prevalence observed among women [33]. For example, it has been reported as 0.2% in Southern Italy, 0.26% in Spain, and 1.2–5% in the United States [21,23,34]. Regionally, HCV prevalence varies greatly among countries, e.g. it is 0.7% in Saudi women while it reaches 8.5% in Yemeni women; respectively [25]. Furthermore, the HCV sero-prevalence among women in Ha'il is much lower than in other Saudi cities; for instance, in Jazan (0.2%), while it is comparable to others, e.g., Riyadh (0.07%) [4]. Collectively, this and other studies revealed a low HCV infection sero-prevalence in women in KSA, particularly in Ha'il. These variations are likely due to differences in socioeconomic and geographical factors, different screening methods as well as less access to hospitals [35]. Additionally, since some of the primary modes of HCV transmission are percutaneous exposure to blood from the injection of illicit drugs and sexual intercourse, the conservative behavior of the Saudi community is likely to have a high contribution to lowering the sero-prevalence of the disease in women.

HBV infection is more prevalent than HCV infection [4,18,25,35-38], which is further confirmed by the results in this work. In the studied population, the distribution ratio of HCVAb and HBsAg positive cases is 22:78. Furthermore, the sero-prevalence of HBV is higher than HCV in all age groups except

for the 21–30-year age group. This is likely because this group had undergone the HBV vaccination. Despite the evidence of the association between HCV and HBV confections (for instance, it was 1.1-1.4% of the population of Western Saudi Arabia), no HCV/HBV confections among women in Ha'il were observed [39].

The results also show that the rate of HBsAg is directly proportional to a women's age. This is likely due to the national immunization program initiated in 1989/1990 for newborns and children at school entry, which led to a higher vaccination rate in younger rather than older women included in this study. Indeed, the introduction of the hepatitis B vaccine worldwide has significantly reduced the rates of HBV infection in women [4].

Despite the higher number of cases and prevalence of HBsAg in 2018, the data revealed a marked decline in these values in 2020 compared to the onset of this study in 2016. These values were also lower for HCVAb in 2020 compared to 2017. These findings suggest a positive progress in the elimination of this infection among women in Ha'il region. Although viral hepatitis infection has been recognized to occur throughout the year, some studies have found that certain months/seasons are associated with higher incidences [41]. However, in this study, no definite and consistent seasonal/monthly pattern for any of these infections was observed, albeit evidence points toward spring and summer peaks for HCV and HBV; respectively. Several researchers attributed the increased incidence of hepatitis infections during summer and spring to increased travel rates to an endemic area in summer, swimming habits in warm months, increase sexual contact…etc., [42]. However, it is challenging to test the correlation between the incidence of hepatitis and seasonality as the incubation period of hepatitis viruses can range from 2 weeks to 6 months. Therefore, theoretically, people who are infected in a certain season can develop active hepatitis shortly after infections in the same season or 2 seasons later. These variables are potential confounders that impede the analysis of hepatitis incidence seasonality.

5. CONCLUSION

This study revealed a marked decline in the prevalence of HCVAb and HBsAg in women in Ha'il. The five-year cumulative sero-prevalence of HBsAg is higher than HCVAb among women and gradually decreases with decreasing age. Neither HBsAg nor HCVAb showed a trend for a specific month or season. Government agencies concerned with community health should continue their efficient immunization programs for HBV which might lead to an HBV-free community in Ha'il, particularly for women, and will subsequently reduce the death rate of fetuses. However, it is recommended to reevaluate the effectiveness of the diagnostic facilities in Ha'il to exclude that the decline in HCV and HBV was due to a deceased quality of diagnosis. The Factors leading to the low prevalence of HBsAg and HCVAb in women in Ha'il should be further identified and considered as a model for lowering HCV and HBV infections worldwide.

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Ethical Considerations
This study was carried out following the ethical guidelines of the Declaration of Helsinki of 1975, revised in 2013. The study was approved by the BioMedical Ethics Committee of the Ministry of Health-Ha'il branch (IRB log number: 2020-22).

Conflict of Interest
The authors declare that they have no conflict of interest.

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