

Hepatitis B and C virus prevalence in couples attending an in vitro fertilization clinic in a tertiary care hospital in Saudi Arabia: comparison with ten years earlier

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BACKGROUND: Viral hepatitis B (HBV) and C (HCV) are a major public health problem in Saudi Arabia. Recent data has indicated a major reduction in viral hepatitis prevalence in Saudi population. However, there is limited data for infertile Saudi couples.

OBJECTIVES: To determine the prevalence of HCV and HBV attending an in vitro fertilization (IVF) clinic in Saudi Arabia between 2012 and 2015 to compare with the prevalence 10 years earlier in the same center.

DESIGN: Retrospective prevalence study.

SETTING: Tertiary care center in Riyadh.

PATIENTS AND METHODS: Data on the prevalence of HBV and HCV was collected on all couples seen at the IVF unit between 2002 - 2005 and 2012 - 2015.

MAIN OUTCOME MEASURE(S): Prevalence of HBV and HCV.

RESULTS: In 4442 patients during 2002-2005 and 5747 patients during 2012-2015, the prevalence of HBV was significantly less in 2012-2015 compared with 2002-2005 (1.67% [97 patients] vs 4.7% [210 patients], $P < .0001$), respectively, but HCV prevalence was similar for the two periods (0.7% for both periods) ($P = .887$). The hepatitis B seroprevalence rate was higher in males compared to females during 2002-2005 (6.3% vs 3.1%) ($P < .0001$) and 2012-2015 (2.4% vs 1.1%) ($P < .0001$), respectively.

CONCLUSION: The significant drop in HBV prevalence was most likely due to the introduction of the vaccination program in 1989, while reasons for HCV prevalence remaining unchanged are unclear.

LIMITATION: No data on confounding factors that may have affected the prevalence.

Viral hepatitis B (HBV) is a major health problem in Saudi Arabia and worldwide. HBV infection chronically afflicts 240 million people while more than 780000 people die annually due to complications.¹ The picture is similar for hepatitis C (HCV) with 130-150 million people infected and 500000 people dying every year from hepatitis C infection.² In Saudi Arabia, HBV infection was hyperendemic.³ Three decades ago HBV prevalence was 7% in the first epidemiological study of Saudi children.⁴ The country addressed the issue in a serious manner, and hepatitis B vaccination become a part of the mandatory vac-

ination program in the country in 1989.⁵ Screening for HBV and HCV is currently part of the premarital screening program.⁶ HIV, HBV and HCV infections were first tested in premarital screening in January 2008. The aim of testing is not to prevent marriage of discordant couples, but to provide them with information and education to prevent transmission of infection. Since 2008, several studies have shown a major reduction in HBsAg prevalence to negligible values in children, indicating the success of the HBV vaccine program.⁷⁻¹⁰

In assisted reproduction, there is a concern about transmission of the infection to newborns and to medi-

cal or laboratory staff, as well as cross-contamination of other virus-free gametes or embryos in cryocontainers during storage.¹¹⁻¹⁵ In vitro fertilisation (IVF) programs, couples are tested routinely for HCV and HBV to reduce the potential risk for transmission in the same laboratory, especially during cryopreservation of embryos.¹⁶ Studies of HBV and HCV prevalence in the IVF population have mostly focused on pregnancy outcomes.¹⁷⁻¹⁹ Other studies have demonstrated the effect of viral infection on male and female fertility.²⁰⁻²² Only a few studies have addressed prevalence of hepatitis in infertile patients.²³ One study by Mansoor et al conducted in Saudi Arabia between 2006 and 2008 reported an overall prevalence of 1.8% for HBV.²⁴ The overall HCV prevalence in the same group was 0.5%. The aim of our study was to determine the prevalence of HCV and HBV in the IVF population in Saudi Arabia between years 2012-2015 and compare it with the prevalence 10 years earlier in the same population.

PATIENTS AND METHODS

In this retrospective study, data was collected on HBV and HCV prevalence for all couples seen at the IVF unit, King Faisal Hospital and Research Centre in Riyadh, between 2002-2005 and 2012-2015. The study was approved by KFSHRC Institutional Review Board. If the hepatitis B surface antigen (HBsAg) or hepatitis B core antibody (HBcAb) were positive, the patient was considered hepatitis B seropositive. For HCV, couples were tested for HCV antibodies or by recombinant immunoblot assay (RIBA). The chi-square test was used to test for statistically significant differences and for trends. A *P* value <.05 was considered statistically significant.

RESULT

For 4442 patients during 2002-2005 and 5747 patients during 2012-2015, there were significantly more HBV positive patients in the period from 2002-2005 (210 positive, 4.7%) compared to 2012-2015 (97 positive, 1.6 %) *P*<.0001 (**Table 1**). However, the seropositivity rate for HCV was not different between the two study periods (*P*=.887). HBV seropositivity was significantly higher in males compared to females in for both periods (6.3% vs 3.1% and 2.4% vs 1.1%, respectively, *P*<.0001) (**Table 2**). Seropositivity for HCV between the two genders was not significantly different (**Table 2**).

DISCUSSION

The present study shows that the prevalence of HBV during 2012-2015 (1.67%) was low as defined by the WHO. This seroprevalence was similar to other studies conducted about the same period in Saudi Arabia,

Table 1. Prevalence of hepatitis B and C virus in the study population.

	2002-2005 n (%)	2012-2015 n (%)	P value
HBV	210 (4.7)	97 (1.68)	.0001
HCV	32 (0.7)	40 (0.7)	.887

HBV-hepatitis B virus, HCV-hepatitis C virus.

Table 2. Prevalence of hepatitis B and C virus in study population by sex.

	Male n (%)	Female n (%)	P value
2002-2005			
HBV	141 (6.3)	69(3.1)	<.0001
HCV	19 (0.8)	13(0.59)	.287
2012-2015			
HBV	61 (2.5)	36 (1.1)	<.0001
HCV	17 (0.68)	23 (0.7)	.92

HBV-hepatitis B virus, HCV-hepatitis C virus.

as in Mansoor et al in infertile Saudi couples between 2006 and 2008, which reported an overall prevalence of 1.8% for HBV in the study population.²⁴ In addition, HBV prevalence was 1.3% in premarital screening data for 2008.⁶ We noticed a major decline in HBV prevalence compared to results 10 years earlier when the seroprevalence was 4.7%. This dramatic change in HBV prevalence in Saudi Arabia is attributed to several factors such as improvement in health care facilities, better socioeconomic status, and the successful vaccination program against HBV. However, this decline in the prevalence of HBV reached a steady state between 2008 and 2015. More studies are needed to assess whether there is a further decline in HBV prevalence.

HCV prevalence in our study remained about the same during the last 10 years, with a seroprevalence rate of 0.7% ifor both periods. Why the change in HCV prevalence is different than HBV is unclear. The difference is most likely due to lack of a large community-based study to estimate the true prevalence of HCV in the country. The prevalence in Saudi blood donors was estimated to be 0.4-1.1%.²⁵⁻²⁷ The premarital screening program showed an HCV prevalence of 0.33%.⁶ These different seroprevalence results are due to different populations in each study. Better socioeconomic status, and improvement in

health care facilities, especially after introduction of blood screening program in Saudi Arabia in the early 1990s, helped reduce the prevalence of HCV at that period. That period was not included in our study. Afterwards, HCV prevalence remained constant in Saudi Arabia.²⁷ Unlike HBV prevalence, which declined mainly due to the availability of HBV vaccine, implementation of HCV vaccination is under development. A national screening program, increased public awareness of HCV transmission, and a new generation drugs to treat HCV infection, may help to reduce the prevalence in future.

There was an obvious difference in HBV prevalence between males and females in Saudi Arabia.²⁸ In our study, the incidence of HBV seropositivity showed a higher prevalence of HBV infection in males vs. females during both time periods. This difference has been observed in several studies.^{28,29} There is no clear explanation for the gender variation. The difference is probably related to the conservative society with less female exposure outside the family, but may also be due to opposite effects of sex hormones. In several experimental animal models, viral transcription is stimulated by androgen, while estrogen suppresses HBV transcription.³⁰ In HCV seroprevalence there were no male vs female differences (0.8% vs 0.5%,

and 0.7% vs 0.6%) between 2002-2005 and 2012-2015.

Our data suggest that viral hepatitis remains a major health problem in Saudi Arabia and that continued observation and monitoring are important to evaluate disease prevalence and the impact of new health program interventions. In assisted reproductive centres offering care for patients who are carriers of HBV and HCV, there is a need for more comprehensive preventive strategies and prevention of cross contamination. The issue of being a carrier is important for embryo freezing. Once infection is confirmed some centres do not freeze while others use separate cryocontainers to avoid cross contamination. Our data is the first in the country in the reproductive population showing the patterns of HBV and HCV and comparing the prevalence between two periods of time. The data show a significant decline in HBV prevalence among reproductive age patients, which was most likely due to vaccination, while HCV prevalence was unchanged from 10 years earlier. A limitation of the study was that no data was collected on confounding factors that may have affected the prevalence.

Conflict of interest

The authors declare no conflicts of interest.

REFERENCES

1. Hepatitis B. Fact sheet N1204. WHO Media centre. [Updated July 2015]. Available from URL: <http://www.who.int/mediacentre/factsheets/fs204/en/>
2. Hepatitis C. Fact sheet N1164. WHO Media centre. [Updated July 2015]. Available from URL: <http://www.who.int/mediacentre/factsheets/fs164/en/>
3. Abdo AA, Sanai FM, Al Faleh FZ. Epidemiology of viral hepatitis in Saudi Arabia; Are we off the hook? Saudi J Gastroenterol. 2012; 18: 349-357.
4. Al-Faleh F. Hepatitis B infection in Saudi Arabia. Ann Saudi Med. 1988;8:474-80.
5. Al-Faleh FZ, Ayoola EA, Al-Jeffry M, Arif M, Al-Rashed RS, Ramia S. Integration of hepatitis B vaccine into the expanded program on immunization: The Saudi Arabian experience. Ann Saudi Med. 1993;13:231-6.
6. Alswaidi F, O'Brien S. Is there a need to include HIV, HBV and HCV viruses in the Saudi premarital screening program on the basis of their prevalence and transmission risk factors? J Epidemiol Community Health. 2010;64:989-997.
7. Alswaidi FM and O'Brien SJ. Premarital screening programmes for haemoglobinopathies, HIV and hepatitis viruses: review and factors affecting their success. J Med Screen. 2009;16:22-28.
8. Al-Faleh F, Ayoola EA, Arif M, Ramia S, Al-Rashed R, Al-Jeffry M, et al. Seroepidemiology of hepatitis B virus infection in Saudi Arabian children: A baseline survey for mass vaccination against hepatitis B. J Infect. 1992;24:197-206.
9. Al-Faleh F, Al-Jeffry M, Ramia S, Al-Rashed R, Arif M, Rezeig M, et al. Seroepidemiology of hepatitis B virus infection in Saudi children 8 years after a mass hepatitis B vaccination programme. J Infect. 1999;38:167-70.
10. Al-Faleh F, Alshehri S, Alansari S, Aljeffri M, Almazrou Y, Shaffi A, et al. Long-term protection of hepatitis B vaccine 18 years after vaccination. J Infect. 2008;57:404-9.
11. Tedder RS, Zuckerman MA, Goldstone AH, Hawkins AE, Fielding A, Briggs EM, et al. Hepatitis B transmission from contaminated cryopreservation tank. Lancet. 1995; 346:137-40.
12. Hawkins AE, Zuckerman MA, Briggs M, Gilson RJ, Goldstone AH, Brink NS, et al. Hepatitis B nucleotide sequence analysis: linking an outbreak of acute hepatitis B to contamination of a cryopreservation tank. J Virol Methods. 1996; 60:81-8.
13. Levy R, Tardy JC, Bourlet T, Cordonier H, Mion F, Lornage J, et al. Transmission risk of hepatitis C virus in assisted reproductive techniques. Hum Reprod. 2000; 15:810-6.35.
14. Lesourd F, Izopet J, Mervan C, Payen JL, Sandres K, Monrozies X, et al. Transmissions of hepatitis C virus during the ancillary procedures for assisted conception. Hum Reprod. 2000; 15:1083-5.
15. Rui Nie, Lei Jin, Hanwang Zhang, Bei Xu, Wen Chen, Guijin Zhu. Presence of hepatitis B virus in oocytes and embryos: a risk of hepatitis B virus transmission during in vitro fertilization. 2011; 95(5):1667-71.
16. Hepatitis and reproduction. The practice committee of the American Society for Reproductive Medicine. Fertility and Sterility. 2004;82(6):1754-64.
17. Lee VC, Ng EH, Yeung WS, Ho PC. Impact of positive hepatitis B surface antigen on the outcome of IVF treatment. Reprod Biomed Online. 2010;21(5):712-7.
18. Pirwany IR, Phillips S, Kelly S, Buckett W, Tan SL. Reproductive performance of couples discordant for hepatitis B and C following IVF treatment. J Assist Reprod Genet. 2004 ;21(5):157-61.
19. Lam PM, Suen SH, Lao TT, Cheung LP, Leung TY, Haines C. Hepatitis B infection and outcomes of in vitro fertilization and embryo transfer treatment. Fertil Steril. 2010;93(2):480-5.
20. Su FH, Chang SN, Sung FC, Su CT, Shieh YH, Lin CC, Yeh CC. Hepatitis B virus infection and the risk of male infertility: a population-based analysis. Fertil Steril. 2014;102(6):1677-84.
21. Gimenes F, Souza RP, Bento JC, Teixeira JJ, Maria-Engler SS, Bonini MG, Consolaro ME. Male infertility: a public health issue caused by sexually transmitted pathogens. Nat Rev Urol. 2014;11(12):672-87.
22. Garolla A, Pizzol D, Bertoldo A, Menegazzo M, Barzon L, Foresta C. Sperm viral infection and male infertility: focus on HBV, HCV, HIV, HPV, HSV, HCMV, and AAV. J Reprod Immunol. 2013;100(1):20-9.
23. Pandolfi Passos E, Silveira TR, Salazar CC, Facin AC Souza CAB, Guerin YLS et al. Hepatitis C virus infection and assisted reproduction. Hum Reprod. 2002; 17:2058-2088.
24. Mansoor A, Salih AI, Al-Jaroudi DH. Screening of hepatitis B and C and human immunodeficiency virus in infertile couples in Saudi Arabia. Saudi Med J. 2011;32(3):260-4.
25. El-Hazmi MM. Prevalence of HBV, HCV, HIV-1, 2 and HTLV-I/II infections among blood donors in a teaching hospital in the Central region of Saudi Arabia. Saudi Med J. 2004;25:26-33.
26. Madani TA. Hepatitis C virus infections reported in Saudi Arabia over 11 years of surveillance. Ann Saudi Med. 2007;27:191-4.
27. Aljumah AA, Abaalkhail F, Al-Ashgar H, Assiri A, Babatin M, Al Faleh F, et al. Epidemiology, disease burden, and treatment strategies of chronic hepatitis C virus infections in Saudi Arabia in the new treatment paradigm shift. Saudi J Gastroenterol 2016;22:269-81.
28. Al-Tawfiq JA, Anani A. Profile of viral hepatitis A, B, and C in a Saudi Arabian hospital. Med Sci Monit. 2008;14:CR52-6.
29. Memish ZA, Knawy BA, El-Saed A. Incidence trends of viral hepatitis A, B, and C seropositivity over eight years of surveillance in Saudi Arabia. Int J Infect Dis. 2010;14:115-20.
30. Wang, S.-H., Chen, P.-J. and Yeh, S.-H. (2015), Gender disparity in chronic hepatitis B: Mechanisms of sex hormones. J Gastroenterol Hepatol, 2015; 30: 1237-1245.