

Screening of hepatitis B and C and human immunodeficiency virus in infertile couples in Saudi Arabia

Aisha A. Mansoor, MD, MBBS, Abdalla I. Salih, MD, FRCOG, Dania H. Al-Jaroudi, SSCOG, ABOG.

ABSTRACT

الأهداف: التحقق من مدى انتشار التهاب الكبد ب، وج، وفيرس نقص المناعة البشري في مجموعة من الأزواج السعوديين المصابين بالعقم.

الطريقة: أُجريت هذه الدراسة المقطعية الاسترجاعية في قسم الغدد الصماء والعقم بمستشفى النساء التخصصي، مدينة الملك فهد الطبية، الرياض، المملكة العربية السعودية وذلك خلال الفترة من يناير 2006م إلى ديسمبر 2008م، وقد تم الرجوع إلى السجلات الطبية لحوالي 500 زوجاً مصاباً بالعقم. لقد تم الكشف عن المؤشرات المصلية بواسطة التحاليل المناعية المرتبطة بالإنزيمات (ELISA)، وهذه المؤشرات كانت: المستضد السطحي لفيروس التهاب الكبد ب، والجسم المضاد لهذا المستضد، والجسم المضاد اللبي لالتهاب الكبد ب، والجسم المضاد لالتهاب الكبد ب البائي، والجسم المضاد لالتهاب الكبد ج، والجسم المضاد لفيروس نقص المناعة البشري من النوع الأول والثاني.

النتائج: أشارت النتائج إلى أن النسبة الكلية لانتشار التهاب الكبد ب وصلت إلى 1.8% (العدد=17)، حيث كانت نسبة انتشار المرض بين الإناث 1.5% (العدد=7)، وبين الذكور 2.1% (العدد=10). وكانت نسبة انتشار التهاب الكبد ج 0.5%، حيث بلغت نسبة الإصابة بين الذكور 1.1% (العدد=5)، فيما كانت نتائج الإناث سلبية. ولقد كانت نتائج الكشف عن فيروس نقص المناعة البشري سلبية في كلي الجنسين.

خاتمة: أثبتت الدراسة مدى انتشار التهاب الكبد ب، وج بين الأزواج السعوديين المصابين بالعقم، فيما لم يكن هناك ظهوراً لفيروس نقص المناعة البشري. ويجب الكشف عن مؤشرات التهاب الكبد وفيروس نقص المناعة البشري قبل الشروع بعلاج العقم من أجل تفادي خطر انتقال الإصابة بالمرض، وذلك بصرف النظر عن تدني الإصابة بفيروس نقص المناعة البشري، وتكلفة اختبارات الكشف.

Objectives: To determine the prevalence of hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in a group of infertile couples attending a tertiary care facility in Saudi Arabia.

Methods: A retrospective cross-sectional observational study was performed by reviewing medical records of 500 couples referred to the Reproductive Endocrine and Infertility Medicine Department of the Women's Specialized Hospital at King Fahad Medical City, Riyadh, Kingdom of Saudi Arabia between January 2006 and December 2008. All patients were screened for HBV markers (hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antibody, hepatitis Be antigen), anti-HCV, anti-HIV types I and II using enzyme linked immunoassay technique.

Results: The overall prevalence of HBV in the population studied was 1.8% (n=17). For females HBV prevalence was 1.5% (n=7), and for males it was 2.1% (n=10). Overall HCV prevalence in this group was 0.5%. All females were negative for HCV, while males had a prevalence of 1.1% (n=5). All males and females were negative for HIV.

Conclusion: We found a high prevalence for HBV and HCV in a group of Saudi infertile population. The HIV prevalence was found to be 0%. Due to the risks of cross sectional and vertical transmission of these infections, and despite the low incidence of HIV infection and the cost implications, it is important to screen all Saudi infertile couples for these infections prior to embarking on fertility treatments.

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From the Obstetrics and Gynecology Department (Mansoor), and the Reproductive Endocrine and Infertility Medicine Department (Salih, Al-Jaroudi), Women's Specialized Hospital, King Fahad Medical City, Riyadh, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr. Dania H. Al-Jaroudi, Reproductive Endocrine and Infertility Medicine Department, Women's Specialized Hospital, King Fahad Medical City, Riyadh, Kingdom of Saudi Arabia. Tel. +966 (1) 2889999 Ext. 8503. Fax. +966 (91) 2935613. E-mail: daljaroudi@kfmc.med.sa

Counseling couples that present to infertility clinics remains an important duty of the health care provider. When a couple presents, it is important to ensure that the women are Rubella immune, has a normal Pap smear, and has been taking folic acid pre-conceptionally. It is important that assisted reproduction centers have in place, effective means of identifying patients with blood borne viruses. Screening for hepatitis B and C, and human immunodeficiency virus (HIV) prior to embarking on fertility treatments has become widely accepted.¹ There are approximately 350×10^6 chronic hepatitis B infections worldwide.^{2,3} Despite the presence of active immunization, there remains 2500 new infections per year, and men are affected more than women.⁴ Persistence of hepatitis B virus (HBV) infection occurs in 5% in adults, among which 25-40% develop liver cirrhosis, and 2-5% of those develop liver cell carcinoma.² Hepatitis B is one of the common infectious diseases in the Kingdom of Saudi Arabia (KSA).⁵ In a recent study carried out in KSA,⁵ the reported average annual rate of HBV was 46 per 100,000 populations, and hepatitis B accounted for 49% of the hepatitis cases. Another major health problem is hepatitis C virus (HCV).⁶ In 1989, transfusion-associated non-A, non-B hepatitis was identified, and named HCV.⁶ The World Health Organization (WHO) estimates that approximately 3% of the world's population has been infected with HCV, and that some 170 million are chronic carriers, at risk of developing liver cirrhosis, and/or liver cancer. These chronic carriers represent a reservoir sufficiently large for HCV to persist.⁶ The introduction of anti-HCV screening has reduced the transmission by up to almost 100%. Chronic hepatitis C results in 10,000 deaths annually.⁷ Chronic liver disease is a consequence of HCV infection, and this also true in KSA. The highest prevalence of HCV in KSA is in the Western and Southern provinces.⁸ Due to the increased knowledge regarding the disease and improved socioeconomic status, a good number of studies among blood donors documented a decrease in HCV prevalence.⁸ The prevalence of HIV in the Middle East is low.⁹ The risk of HIV infection through sexual contact is between 0.1 and 0.5%.⁹ However, in 2003 there was a descriptive analytic study from KSA that showed there were 1,743 Saudi nationals with HIV infection, among which 872 were AIDS cases, and 6064 non-Saudi HIV cases.¹⁰ There was a predominance in the male group (77%). There has been evidence that the health care providers through handling infected samples, and patients who are undergoing assisted reproduction can be infected with HBV, HCV, and HIV.¹¹ In addition to patients who are undergoing assisted reproduction, cross contamination can occur in tanks when storing biological materials, as

well as, during oocyte retrieval and embryo transfer.¹¹ Screening enables patients presenting a risk to their sibling, partner, health care staff, and patients to be identified, and the risks of transmission to be reduced by proper counseling, and resorting to appropriate precautions when handling infected patients and specimens. The aim of this study is to describe the prevalence of HBV, HCV, and HIV virus infections among a population of infertile couples attending a tertiary care facility between 2006 and 2008.

Methods. This is a retrospective review of 500 charts of infertile couples referred to the Reproductive Endocrine and Infertility Medicine Department (REIMD) of the Women's Specialized Hospital at King Fahad Medical City (KFMC) between January 2006 and December 2008. The couples included in the review were Saudi nationals, infertility of more than 2 years irrespective of cause, female age less than 45 years, and male's age less than 60 years. The study was approved by KFMC Institutional Review Board.

Sample size. Taking a probability of error of 1%, as the infertile population is small compared to the general population, and setting the margin of error at 1%, the calculated sample size was 384. Of the 500 couples enrolled, 38 had incomplete data, and they were excluded from the study, leaving a total of 462 couples (924 individuals). Data was abstracted from history reviews, laboratory reports, and progress notes from the 500 medical records of infertile couples. Demographic data included age, gender, and region. The clinical data included number of previous husbands, parity, type and cause of infertility, number of attempts of IVF, and any relevant medical or surgical history. Laboratory data included serum markers; hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), hepatitis B core antibody (anti-HBc), and hepatitis B e antigen (HBeAg) to confirm hepatitis B status. Anti-HCV and anti-HIV type 1 was checked for hepatitis C, and type 2 antibodies was checked for HIV screening. All serological procedures were performed in the serology laboratory of the Department of Laboratory Medicine of KFMC. Enzyme linked immunoassay (ELISA) technique was used for all serological markers. The ELISA has a sensitivity and specificity of more than 99% for hepatitis B and HIV markers, and a specificity of 94.6% and sensitivity of 100% for anti-hepatitis C. For HBV, patients were labeled positive upon the seropositivity of HBsAg.

Data collection was completed and data analysis was carried out using the Statistical Package for Social Sciences (SPSS Inc, Chicago, IL, USA). Statistical analysis was carried out using arithmetic means.

Results. A total of 500 couples (1000 individuals) were enrolled in this study. The demographic data showed that the overall average age for females was 28 (15-45) years. Patients were predominantly from Riyadh region. Table 1 shows that primary infertility accounted for 62.4%. Infertility was attributed to a male factor etiology in 39.6% of the study population. The overall prevalence of HBV in the group of infertile couples studied was 1.8% (n=17). For female partners, the HBV prevalence was 1.5 % (n=7), and for males it was 2.2% (n=10) (Table 2). The total number of cases who were highly infective due to the presence of HBsAg was 1.2% (11 out of 924 patients). When this was analyzed to females versus males, this was 0.8% (4 females), and 1.5% (7 males). The HCV prevalence was 0.5%. All females screened negative for HCV, while males showed a prevalence of 1.1% (n=5). All subjects, males and females, screened negative for HIV.

Discussion. The overall prevalence of HBV reported in our study is similar to other studies

Table 1 - Summary of clinical data (n=462).

Variables	n	%
Average female age, years (mean)	28 (15-45)	
Infertility duration, years (mean)	3.5 (1.5-23)	
<i>Type of infertility</i>		
Primary	289	(62.5)
Secondary	173	(37.4)
<i>Infertility etiology</i>		
Male factor	183	(39.6)
Anovulation	136	(29.4)
Tubal factor	48	(10.4)
Unexplained	51	(11.0)
Endometriosis	16	(3.5)
<i>Previous marriages</i>		
Male	92	(20.0)
Female	19	(4.1)
More than one current wife	53	(11.5)
Previous ART	118	(25.5)
<i>Previous surgery</i>		
Male	415	(89.8)
Female	414	(89.6)

ART - assisted reproductive technology

conducted in KSA. The HBV prevalence was 1.5% among blood donors at King Khalid University Hospital, Riyadh, over a period of 3 years from January 2000 to December 2002.¹² A cross-sectional survey among 3192 male Saudi blood donors at King Khalid Tertiary Care Hospital in Tabuk from June 2005 to May 2006 showed a prevalence of HBsAg of 3.0%, and anti-HBc was found to be 18.7%.¹³ There are a few studies conducted to describe the prevalence of HBV, HCV, and HIV among infertile couple. Most of the studies published look at the outcome of pregnancies in couples with blood borne viruses,¹⁴ or whether to do or not to do in vitro fertilization (IVF) in carriers of blood borne viruses.¹⁵ Literature regarding outcome of IVF in terms of pregnancy rates and live births are quite conflicting. Pirwany et al¹⁶ found better results in seronegative subjects as compared to sero-positives for HBV and HCV. While other studies showed either no impact or even higher pregnancy and implantation rates for patients with chronic HBV, HCV and HIV.^{14,17} These infections might affect germ cells development. In females, HCV and HIV may be responsible for impaired ovarian response in patients receiving IVF treatment.¹⁸ On the other hand, negative influence has been seen on sperm output in patients with chronic HBV.¹⁹ High rates of chronic infections are also found in the Amazon and the southern parts of eastern and central Europe. In the Middle East and Indian sub-continent, an estimated 2-5% of the general population is chronically infected, whereas in Western Europe and North America, less than 1% of the population were chronically infected.³ Most people in the region become infected with HBV during childhood. In these regions, 8-10% of the adult populations are chronically infected.⁴

The prevalence of HCV in the general Saudi population is 1.6%.²⁰ A 1.2% prevalence in our group of infertile couples is lower than the reported prevalence in the general Saudi population.²⁰ This could be due to the sample size, the fact that the infertile couples studied were generally young, healthy adults who largely come from urban, better educated societies. The present public health schemes have been effective in reducing hepatitis C infection in the general community in KSA.²⁰ A wide

Table 2 - Prevalence of hepatitis B in the study population.

HBV status	Positive serum markers	Female	Male	Total
		462	462	924
		n (%)		N (%)
Chronic HBV infection	HBsAg, anti-HBc positive	7 (1.5)	10 (2.2)	17 (1.8)
Vaccinated	Anti-HBs positive	52 (11.2)	24 (5.2)	76 (8.2)
Immune to natural infection	Anti-HBs, Anti-HBc positive	13 (2.8)	24 (5.2)	28 (3.0)
Highly infective	HBe Ag positive	4 (0.9)	7 (1.5)	11 (1.2)

HBV - hepatitis B virus, HBsAg - hepatitis B surface antigen, anti-HBs - hepatitis B surface antibody, anti-HBc - hepatitis B core antibody, HBeAg - hepatitis B e antigen

variation of HCV prevalence had been reported, and this had ranged between 0.4-40.7%.^{1,12} The WHO estimates that HCV prevalence is between 1-4.6% with 21.3 million people infected in the Eastern Mediterranean.²¹ Vertical transmission of HCV complicates up to 18% of pregnancies in HCV-positive, HIV-negative women, and 6-36% in HCV-positive, HIV-positive women. Higher vertical transmission of HCV provides a great risk to babies born to infertile infected couples. The HCV infection is a significant health problem and has become a major cause of morbidity and mortality as it can lead to chronic active hepatitis, liver cirrhosis, and hepatic carcinoma.⁶ The screening for HCV should, therefore be mandatory for all infertile couples before embarking on fertility treatment.

The prevalence of HIV in our study was 0% among the group of Saudi infertile couples studied. Similarly, the prevalence rate of HIV was 0% among blood donors at King Khalid University Hospital Riyadh, KSA over a period of 3 years from January 2000 to December 2002.¹² Globally, there was an estimated 33 million (30-36 million) people living with HIV in 2007.²² The limited HIV information available for the Middle East and North Africa indicates that approximately 380,000 people were living with HIV in 2007.²² The prevalence among adults aged 15-49 years was 0.2-0.4%.¹⁰ A number of studies carried out in Saudi Arabia¹² reported low prevalence of HIV similar to what has been described in our study. Religious, social, and cultural values are among the reasons for the low incidence of HIV. As there is no vaccine for HIV, early detection through proper screening is a very important measure in the prevention of the spread of HIV infection. Our study demonstrates that the prevalence of HIV is low, and is indeed comparable to that in the general Saudi population.^{10,12} Screening for HIV, hepatitis B and C infection in a population seeking assisted reproduction in an inner London Hospital showed HIV (0.13%), HCV (0.5%), and HBV (1.7%), while in the antenatal population, HBV was 1.4%, and HIV was 0.8%.²³ In another study, Wingfield et al²⁴ conducted a survey between June 2007 and August 2009 among patients undergoing assisted reproductive technology (ART) in 7 Irish clinics. They collected data on viral screening. There was no one positive for HIV among the 13,717 patients. Among these, there were 18 patients positive for HBsAg, and 179 for anti-HBc. Additionally, 16 patients had positive HCV among the 13,716 patients tested.²⁴ In comparison, our study reported a higher prevalence for HBV and HCV in the group of Saudi infertile couples attending a tertiary care facility for ART. Retrieval of information in our study was carried out retrospectively, and this was a limitation. An accurate prevalence of the viruses can be better addressed in a properly conducted study.

The health of expected babies is the responsibility of the health care giver. Therefore, screening of infertile couple for HBV, HCV, and HIV is important, and careful clinical evaluation of both partners is to be carried out before the application of these methods. Risk of the mother's or the developing child health is a relative contraindication for a treatment. This is not only important for the mother and baby, but also for the safety of all the staff involved in the treatment procedures.²⁵ Laboratory transmission risk for HBV, HCV, and HIV is still unknown but not negligible.¹

In conclusion, screening will help to reduce the risk of transmission to partner, fetus, new born baby, or by cross-contamination during embryo cryo-storage. Therefore, despite the low incidence of HIV infection, and the cost implications it is important to screen all Saudi infertile couples for these infections prior to embarking on fertility treatments. Determination of the prevalence of HBV, HCV, and HIV in infertile couples will certainly help in reviewing the screening procedures and making health policy decisions. Further studies must assess the impact of these infections on pregnancy rates and live birth in patients receiving ART.

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References

- Gilling-Smith C, Emiliani S, Almeida P, Liesnard C, Englert Y. Laboratory safety during assisted reproduction in patients with blood-borne viruses. *Hum Reprod* 2005; 20: 1433-1438.
- Honeck P, Weigel M, Kwon ST, Alken P, Bross S. Assisted procreation in cases of hepatitis B, hepatitis C or human immunodeficiency virus infection of the male partner. *Hum Reprod* 2006; 21: 1117-1121.
- Hepatitis B. Fact sheet N°204. WHO Media centre. [updated 2008 August]. Available from URL: <http://www.who.int/mediacentre/factsheets/fs204/en/>
- Schaefer M, Heinz A, Backmund M. Treatment of chronic hepatitis C in patients with drug dependence: time to change the rules? *Addiction* 2004; 99: 1167-1175.
- Al Tawfiq J, Anani A. Profile of viral hepatitis A, B, and C in a Saudi Arabian hospital. *Med Sci Monit* 2008; 14: 52-56.
- WHO. Hepatitis C. Global Alert and Response (GAR) 2003. Available from URL: <http://www.who.int/csr/disease/hepatitis/whocdscsrlyo2003/en/index.html>
- Koff RS. Hepatitis B and Hepatitis D; Hepatitis C. In: Gorbach SL, Bartlett JG, Blacklow NR, eds. *Infectious Diseases*. 3rd ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2004. p. 765-780.
- Akbar HO. Hepatitis C virus infection in Saudi Arabia. *Saudi J Gastroenterol* 2004; 10: 127-131.
- Obermeyer CM. HIV in the Middle East. *BMJ* 2006; 333: 851-854.
- Yagob Y, Al-Jeffri MH, Fidail A, Al-Huzaim N, El-Gizouli S. HIV/AIDS epidemic features and trends in Saudi Arabia. *Ann Saudi Med* 2005; 25: 100-104.

11. 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: 2085-2088.
12. 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.
13. El Beltagy KE, Al Balawi IA, Almuneef M, Memish ZA. Prevalence of hepatitis B virus markers among blood donors in a tertiary hospital in Tabuk, northwestern Saudi Arabia. *Int J Infect Dis* 2008; 12: 495-499.
14. Prisant N, Tubiana R, Lefebvre G, Lebray P, Marcelin AG, Thibault V, et al. HIV-1 or hepatitis C chronic infection in serodiscordant infertile couples has no impact on infertility treatment outcome. *Fertil Steril* 2010; 93: 1020-1023.
15. Lutgens SP, Nelissen EC, van Loo IH, Koek GH, Derhaag JG, Dunselman GA. To do or not to do: IVF and ICSI in chronic hepatitis B virus carriers. *Hum Reprod* 2009; 24: 2676-2678.
16. 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: 157-161.
17. 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: 480-485.
18. Englert Y, Moens E, Vannin AS, Liesnard C, Emiliani S, Delbaere A, et al. Impaired ovarian stimulation during in vitro fertilization in women who are seropositive for hepatitis C virus and seronegative for human immunodeficiency virus. *Fertil Steril* 2007; 88: 607-611.
19. Vicari E, Arcoria D, Di Mauro C, Noto R, Noto Z, La Vignera S. Sperm output in patients with primary infertility and hepatitis B or C virus; negative influence of HBV infection during concomitant varicocele. *Minerva Med* 2006; 97: 65-77.
20. Shobokshi OA, Serebour FE, Al-Drees AZ, Mitwalli AH, Qahtani A, Skakni LI. Hepatitis C virus seroprevalence rate among Saudis. *Saudi Med J* 2003; 24 (Suppl 2): S81-S86.
21. Shobokshi OA, Serebour FE, Skakni L. Chronic hepatitis C Treatment: A Review. *Ann Saudi Med* 2000; 20: 402-408.
22. UNAIDS 2008 report on the global AIDS epidemic. Available from URL: http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp
23. Hart R, Khalaf Y, Lawson R, Bickerstaff H, Taylor A, Braude P. Screening for HIV, hepatitis B and C infection in a population seeking assisted reproduction in an inner London hospital. *BJOG* 2003; 108: 654-656.
24. Wingfield M, Cottell E. Viral screening of couples undergoing partner donation in assisted reproduction with regard to EU Directives 2004/23/EC, 2006/17/EC and 2006/86/EC: what is the evidence for repeated screening? *Hum Reprod* 2010; 25: 3058-3065.
25. Honeck P, Weigel M, Kwon ST, Alken P, Bross S. Assisted procreation in cases of hepatitis B, hepatitis C or human immunodeficiency virus infection of the male partner. *Hum Reprod* 2006; 21: 1117-1121.

Related topics

Elmetwally IM, Elmahalaway AM, Abuhashem SH, Ahmed AM. Determination of serum fibrosis index in patients with chronic hepatitis and its relationship to histological activity index. *Saudi Med J* 2009; 30: 638-646.

Alim A, Artan MO, Baykan Z, Alim BA. Seroprevalence of hepatitis B and C viruses, HIV, and syphilis infections among engaged couples. *Saudi Med J* 2009; 30: 541-545.

Abdo AA, Azzam NA, Al-Faleh FZ, Al-Jebreen AM, Al-Moffeh IA, Al-Amri SM, et al. Histological and laboratory features of patients undergoing liver biopsy at a university hospital in Central Saudi Arabia. *Saudi Med J* 2006; 27: 1493-1497.