Prevalence of hepatitis B and hepatitis C viral infections and impact of control program among blood donors in Al-Baha region, Saudi Arabia

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Background: A low prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections has been previously reported in Al-Baha. The present study reexamines the prevalence of HBV and HCV infection among blood donors 3 years following a previous study in an attempt to detect an impact of control measures. Materials and Methods: This 29-month retrospective study was conducted from October 2014 to May 2017. A total of 3,461 blood donors were screened for serological and molecular markers for HBV and HCV.

Results: The mean age of the donors was 32.4 ± 10.1 (range: 17–67). Of all donors, 10 (0.3%) had HBsAg while 253 (7.3%) had anti-HBc in absence of HBsAg. Anti-HCV was detected in 8 (0.2%) donors, of whom 6 (75.0%) were also HCV-RNA positive. HBV-DNA was detected in 12 (0.4%) donors, of whom 10 (83.3%) had concurrent HBsAg, whereas 2 (16.7%) had HBV-DNA with anti-HBc as the only HBV marker. The donors born after inclusion of HBV vaccine in expanded program of immunization (EPI) had a significantly (P < 0.05) lower prevalence of HBsAg, anti-HBc, and HBV-DNA. Although insignificant (P = 0.197), a lower prevalence of HCV infection was detected among the donors who were born after implementing the screening policy for HCV infection.

Conclusion: Compared to a previous report, this study detected a further reduction in the prevalence of HBV, whereas the decline in the prevalence of HCV infection merits further investigation.

Key words: Al-Baha, blood donors, hepatitis B virus, hepatitis C virus, Kingdom of Saudi Arabia

INTRODUCTION

Viral hepatitis caused a total of 1.34 million deaths in 2015 around the world. Most of these were due to chronic liver disease that led to 720,000 cirrhoses and 470,000 hepatocellular carcinoma (HCC). Viral hepatitis ranks the seventh major cause of death worldwide. Globally around 2 billion individuals have serological markers of past or current hepatitis B virus (HBV) infection, with 248 million being HBV carriers. The current estimate is that 170 million people around the world are infected with hepatitis C virus (HCV). About 30% of those infected with HCV spontaneously recover, whereas the majority develops chronic hepatitis which slowly progresses in the first two decades of life or can be hastened as a consequence of advancement of age and cofactors such as heavy alcohol intake and HIV coinfecion leading ultimately to liver fibrosis, cirrhosis, and HCC. Infection with HCV is a principal cause of cirrhosis and HCC around the world and is a cause of death of 350,000 annually.

In the Eastern Mediterranean Region of the WHO, an estimated 4.3 million are infected with HBV and 800,000 are infected with HCV annually and over 75% of HCCs are ascribed to HBV and HCV. Worldwide, the control programs

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launched against HBV and HCV included screening of blood donors and various risk groups, health education in addition to vaccination-based control of HBV infections. The Kingdom of Saudi Arabia (KSA), in the late 1980s had an overall HBsAg prevalence of 8.3%. This placed the country within the high HBV endemic region. However, immunization against HBV which has been included in the EPI in 1989 in addition to the program of screening of blood donors, haemodialysis patients, soon to be married individuals and visa seekers wishing to work in KSA have played a major role in HBV and HCV control. Highly sensitive and specific diagnostic assays have been employed for screening for multiple viral serological markers as well as viral nucleic acid for both HBV and HCV infections. These together have significantly impacted the prevalence of HBV and HCV infections as low prevalence of HBV (0.7 to 3.0%) and HCV (0.04 to 0.6%) have been repeatedly reported in various regions of the kingdom. Testing of blood donors for HBV and HCV infections has an impact on the safety of blood recipients, reduces disease burden, and also offers an indirect approach for monitoring of the prevalence of these viruses in the community. A previous study of blood-borne viruses in blood donors in Al-Baha, KSA, has reported a low prevalence of both HBV and HCV. The reported findings have demonstrated an impact of the control measures that are based mainly on screening of blood donors and other groups at risk in the case of HCV in addition to EPI in the case of HBV. This study reexamines the prevalence of HBV and HCV infection among blood donors 3 years after a previous study in an attempt to detect an impact of control measures.

MATERIALS AND METHODS

Ethical considerations and subjects
Ethical approval for this study was obtained from the Ethical Research Committee of the Faculty of Medicine, Al-Baha University. In this retrospective cross-sectional study, 3461 blood donors were screened for HBV and HCV, during the period of 29 months, from October 2014 to May 2017. The selection of the donors was based on a personal questionnaire, physical examination in addition to predonation investigations which include hemoglobin (Hb) level, blood pressure, body weight, and temperature.

Study area
Al-Baha region is located in the southwestern part of the Hijaz region. The region comprises four mountainous and three coastal governorates. Al-Baha city is the capital of the region. The area of the region is 11,000 km², and has a population of 533,001.

Serological and nucleic acid testing
Blood samples for testing were collected in a plain tube for serum testing for serological markers and in EDTA anticoagulant when plasma was required for nucleic acid testing. Chemiluminescent microparticle immunoassay using Architect system (Abbott, Ireland) was used for the detection of HBsAg, total anti-HBc, anti-HBs, HBeAg, anti-HBe, and anti-HCV according to the manufacturer’s instructions. The HBsAg-positive results were confirmed by Monolisa HBsAg neutralization confirmatory assay (Bio-Rad, Marnes-la-Coquette, France). Anti-HCV-positive results were confirmed using the third-generation line immunoassay INNO-LIA HCV score (Fujirebio, Europe). The detection of HBV-DNA and HCV-RNA was achieved by the Cobas® TaqScreen MPX Test, version 2.0 (v2.0) (Roche, Basel, Switzerland) intended for use with the Cobas s 201 system. It is a qualitative in vitro test for the direct detection of HCV- RNA, HBV- DNA, RNA of HIV-1 and 2 in plasma of blood donors.

The testing policy for infections with HBV and HCV in blood bank included a primary screening of all donors for HBsAg and retesting the positive donors in duplicate, followed by confirmatory testing by neutralization of the repeatedly positive and the weakly positive donors. All HBsAg-negative/ anti-HBc-positive donors on primary screening were retested in duplicate. The repeatedly anti-HBc-positive donors were tested further induplicate for anti-HBs titer. Those with anti-HBs titer below 100 mIU/ml were considered unsafe for donation and thus were excluded. All confirmed HBsAg donors were further tested for HBeAg and anti-HBe. Donors who were positive for anti-HCV on primary testing were retested in duplicate, and those who were repeatedly positive were further confirmed by third-generation line immunocassay INNO-LIA HCV score. All donors were tested for HBV-DNA and HCV-RNA irrespective of their serological testing results, and those who were positive were excluded from donation.

Data analysis
Data were imported from the computer database of statistic department in blood bank to SPSS version 21.0 (IBM, IBM Corp., Armonk, NY, USA). The data were revised for completeness, and subjects with incomplete data were excluded. The Chi-square tests were used to measure the difference in proportions. P ≤ 0.05 was considered statistically significant.

RESULTS
The mean age of the 3,461 donors included in this study was 32.4 ± 10.1 (range 17-67). Of all donors 10 (0.3%) had HBsAg while 253 (7.3%) had anti-HBc in absence of HBsAg. Of the 253 donors with anti-HBc, 212 (80.6%) had concomitant anti-HBs. Donors with HBsAg and/or anti-HBc were 263/3,461(7.6%). Of donors with HBsAg, only 1 (10.0%) had HBeAg, whereas 9 (90.0%) had anti-HBe. Eight (0.2%) of all donors had HCV antibodies, of whom 6 (75.0%) were also HCV-RNA positive. Of all donors, 12 (0.4%) had HBV-DNA, of whom 10 (83.3%) had concurrent HBsAg, whereas 2 (16.7%) had HBV-DNA with anti-HBc as the only HBV marker [Table 1]. With the progress of age, the prevalence of HBsAg and HBV-DNA increased,
DISCUSSION

The current study shows a far lower overall prevalence (0.3%) of HBsAg than it was reported 3 years ago.[18] In addition, the age-specific prevalence of HBsAg is comparatively lower than the corresponding age groups of the previous study. This further suggests a declining HBsAg prevalence and demonstrates a cumulative impact of HBV vaccine included in EPI in KSA 28 years ago.[15,20] In addition, the significantly lower rate in HBV infection and the prevalence of past and current infections among the cohort of donors who were born during the era of vaccination asserts a sustainable impact of HBV immunization program that has been previously reported in Al-Baha.[18]

Apart from 1 donor who was HBeAg positive, 90.0% of the donors with HBsAg were HBeAg negative and anti-HBe positive indicating HBeAg/anti-HBe seroconversions. The HBeAg/ anti-HBe seroconversion is usually associated with low levels of HBV-DNA and clinical remission of liver disease in the majority of patients.[21] Therefore our donors were likely to be inactive carriers of a virus replicating at low level. This form of HBV infection seems to be common in KSA as it has been previously reported among blood donors in Al-Baha[18] and among various other groups including liver disease patients[22,23] and different apparently healthy subjects from other parts of the KSA.[15,20]

Two donors had anti-HBc and HBV-DNA with no other HBV serological markers. These are likely cases of occult hepatitis which have been newly designated the name HBsAg-negative phase of HBV infection.[26] Occult hepatitis represents a threat to the safety of the blood transfusion. The prevalence of occult hepatitis B infection among blood donors varied between 0.07%–5.4% in various parts of the world.[27–30] Elsewhere in the region, occult hepatitis B was found in 1.6% of donors.[21] The prevalence of occult hepatitis of 0.2% has been previously reported in Al-Baha.[18] The present study showed a major reduction of occult hepatitis B as only 0.01% of all donors have this form of hepatitis. There remains a possibility that these two donors were either “window period” patients or had HBsAg level below the detection limit of the current screening assay. In a few cases, the absence of HBsAg has been linked to the sensitivity of the assay used for detection.[22] Further investigation is required to further verify the status of these two donors. Irrespective of their status, identifying these two donors based on nucleic acid testing further stresses the role of the nucleic acid testing in bridging the gaps missed by the serological testing of blood donors. The prevalence among the various age groups and the pattern of age-dependent increase of prevalence observed in this study is consistent with a previous report in Al-Baha[18] and further supports the previous inference of horizontal transmission of HBV infection acquired during adult life rather than perinatal transmission.

Compared to the finding that has been previously reported in Al-Baha region,[18] the present study has shown an increase, although statistically insignificant, in HCV prevalence (0.2% vs. 0.04). It is even higher than that reported in other regions in Saudi Arabia.[33–35] One obvious reason for this increase is that two (33.3%) of the HCV-infected donors were

| Table 1: HBV and HCV serological markers and viral nucleic acid detected among blood donors |
|---------------------------------------------|
| Markers | Positive/total (%) |
| HBsAg | 10/3461 (0.3) |
| HBsAg and/or anti-HBc* | 263/3,461 (7.6) |
| Anti-HBC* and/or HBV-DNA | 253/3,461 (7.3) |
| Anti-HBs* and/or HBV-DNA | 212/253 (83.8) |
| Anti-HBc only | 43/3,461 (1.2) |
| HBeAg in HBsAg | 1/10 (0.1) |
| Anti-HBe in HBsAg | 9/10 (0.9) |
| HCV antibody confirmatory RIBA | 8/3461 (0.2) |
| HBV-DNA | 12/3461 (0.3) |
| HCV-RNA | 6/3461 (0.2) |
| HBV-DNA/anti-Hbc only | 2/263 (0.8) |

*Statistical significance. HBV: Hepatitis B virus, HCV: Hepatitis C virus, HBsAg: Hepatitis B surface antigen, RIBA: Recombinant immunoblot assay

| Table 2: HBV and HCV serological and nucleic acid detected among blood donors in various age groups |
|---------------------------------------------|
| Age groups | HBsAg, n (%) | Anti-HBc, n (%) | HBV-DNA, n (%) | HCV-RNA, n (%) |
| 17-26 | 1/1221 (0.08) | 22/1221 (1.8) | 1/1221 (0.08) | 1/1221 (0.08) |
| 27-36 | 3/1100 (0.3) | 55/1100 (5.0) | 4/1100 (0.4) | 0/1100 (0.0) |
| 37-46 | 3/769 (0.4) | 101/769 (13.1) | 3/769 (0.4) | 2/769 (0.3) |
| 47-56 | 3/304 (1.0) | 61/304 (20.1) | 3/304 (1.0) | 3/304 (1.0) |
| >56 | 0/67 (0) | 24/67 (35.8) | 1/67 (1.5) | 0/67 (0) |
| Total | 10/3461 (0.3) | 263/3461 (7.6) | 12/3461 (0.4) | 6/3461 (0.2) |
| P | 0.115 | <0.0001* | 0.07 | 0.006*

*Statistical significance. HBV: Hepatitis B virus, HCV: Hepatitis C virus, HBsAg: Hepatitis B surface antigen

| Table 3: Status of HBV and HCV infections among blood donors before and after inclusion of anti-HBV vaccine to EPI in the Kingdom of Saudi Arabia |
|---------------------------------------------|
| Age groups | HBsAg, n (%) | Anti-HBc, n (%) | HBV-DNA, n (%) | HCV-RNA, n (%) |
| 17-28 | 1/1470 (0.07) | 29/1470 (2.0) | 1/1470 (0.07) | 1/1470 (0.07) |
| >28 | 9/1991 (0.5) | 234/1991 (11.8) | 11/1991 (0.6) | 5/1991 (0.3) |
| Total | 10/3461 (0.3) | 263/3461 (7.6) | 12/3461 (0.4) | 6/3461 (0.2) |
| P | 0.03 | <0.0001* | 0.01* | 0.197

*Statistical significance. HBV: Hepatitis B virus, HCV: Hepatitis C virus, HBsAg: Hepatitis B surface antigen, KSA: Kingdom of Saudi Arabia, EPI: Expanded program of immunization
expatriates. However, the prevalence remains comparatively high (0.15%) even after exclusion of the expatriate donors from the analysis. The reason for this increase is not clear. It is unlikely that the previously reported low prevalence is due to an underreporting that could be ascribed to the testing capacity of blood donors. The testing policy rather involves the use of highly sensitive screening serological assays along with a parallel testing for viral nucleic acid using a 100% sensitivity polymerase chain reaction assay. The other possible reason for the increase in HCV prevalence is the repeated donations by some infected donors. However, the possibility for this to occur is unlikely. This is because the donors identified to be positive for viral infections are prohibited by the law to reattempt donation, and the electronic registration system of donors can identify them. Therefore, the statistically insignificant rise in HCV prevalence in the present study suggests unlikely change in the epidemiology of HCV in Al-Baha region. An increase in global prevalence has been reported and has been attributed to the cross-sectional nature of the prevalence data rather than a change in epidemiology of the disease. Nevertheless, vigilance seems to be essential at this stage to monitor the epidemiology of HCV in Al-Baha region. Based on age groups, HCV is more prevalent among donors aged over 36 years than among the younger ones. Additionally those aged 28 years or younger i.e., born after establishing of the screening of HCV among blood donors 1992 have lower HCV prevalence, albeit statistically insignificant. These together advocate the need for continuing evaluation of the long-implemented HCV control program.

CONCLUSION

Compared with the previous report, the HBV control program based on immunization and screening of blood donors seems to have further reduced the prevalence of HBV infection among blood donors. Although there is an increase in the prevalence of HCV infection among blood donors in general, a lower prevalence of HCV infection among the young donors who were born during the era of screening of blood donors was detected, suggesting an impact of control program. However, a genuine reduction in the prevalence of HCV infection merits further investigation. Continuing monitoring of the prevalence of blood-borne viral infections seems essential to assess the sustainability of the control program and to detect any changes in epidemiology.

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Conflicts of interest

There are no conflicts of interest.

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