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# Analysis of hepatitis C virus core antigenemia in Saudi drug users

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Hepatitis C virus (HCV) occurs worldwide with an estimated 170 millions people infected.[1] The majority of infected individuals progress to chronic infection, which can lead to cirrhosis or hepatocellular carcinoma. Enzyme-linked immunosorbent assay (ELISA) is the principal diagnostic test to detect anti-HCV antibodies in blood, recombinant immunoblot assay (RIBA) is used as supplemental assay. Only direct detection of viral RNA or antigens can differentiate ongoing from resolved infection and can help in the follow up after therapy. Therefore, a number of qualitative and quantitative assays for detection of HCV RNA have been developed. Recently, a new assay capable of detecting and quantifying HCV core antigen has been developed. This new assay incorporates at least 2 modifications leading to a theoretically improved sensitivity: 1. an immune complex dissociation step that allows detection of both free and antibody-bound core antigen, and 2. an improved conjugate reagent that provides superior signal amplification.[2]

Screening of blood and blood products for anti-HCV antibodies and HCV RNA has reduced the incidence of post-transfusion HCV infection to negligible levels. However, drug users remain at high risk of acquiring HCV infection. Intravenous drug use (IVDU) was found to be responsible for approximately 60% of the new cases of HCV infection.[1] The prevalence of antibodies to hepatitis C virus (anti-HCV) in a population of IVDU in Jeddah, Kingdom of Saudi Arabia (KSA) was reported as 74.6%, whereas the prevalence of anti-HCV in drug dependent patients who did not use the intravenous route was 10.5%.[3] On the other hand, Shawky et al[4] reported that high prevalence of hepatitis C virus infection that amounted to 63.9% in drug addicts from the same area of the country. Similarly Fathalla et al[5] found that the prevalence of HCV antibodies among drug users in the Eastern Province of KSA reached only 6.5%. The objective of the present study was to assess HCV core antigen in sera from Saudi drug users and to compare this with anti-HCV antibodies and HCV RNA data from the same patients.

All patients (n=201) who are enrolled in drug rehabilitation program in a drug rehabilitation hospital over a period of one year (October 2003 to September 2004) were included in this study upon their written informed consent. Anti-HCV antibodies were detected by a third-generation ELISA (Axsym HCV version 3 [Abbott Diagnostics, Chicago, Illinois]) and HCV 3 ELISA test system [Ortho-Clinical Diagnostics, Raritan, New Jersey]) and by a third-generation RIBA (RIBA HCV 3; Ortho-Clinical Diagnostics).[2] A simple enzyme immunoassay for detection and quantification of total HCV core Ag has been recently developed (Ortho-Clinical Diagnostics), and this test was used according to the manufacturer's recommendations described previously.[2] Results were expressed in picograms per milliliter, with a limit of detection established by the manufacturer at 1.5 pg/ml. To detect HCV RNA, the COBAS AMPLICOR HCV test version 2.0 (Roche Molecular Systems, Branchburg, New Jersey) was used according to the manufacturer's instructions. This assay has a limit of detection of 2.0 log 10 IU of HCV genotype 1 RNA per ml of serum.

The study population was 201 Saudi drug users, males, and of mean age of 33 years. Among this cohort of patients 82 were IVDU and 119 non-IVDU. The mean duration of drug use was 10 years. The seroprevalence of HBsAg in the study population was 5.9%, the seroprevalence of HCV antibodies was 35.6%, and seroprevalence of HIV antibodies was 0.99% as determined earlier in our laboratory. Out of the tested 201 samples 68 (33.8%) yielded positive results for HCV core Ag. Among the 68 samples positive for HCV core Ag, 54 (79%) had detectable anti-HCV antibody, and only 14 (21%) were anti-HCV antibody negative. On the other hand, among those 68 samples positive for HCV core Ag, 60 samples (88%) had detectable HCV-RNA by qualitative reverse transcription-

polymerase chain reaction, whereas only 8 (12%) samples were HCV-RNA negative (**Table 1**). The HCV is hyperendemic among injection drug users (IDUs), who contract the virus through contaminated syringes and drug preparation equipment shared with other IDUs. The prevalence of HCV is also high, but to a lesser degree, among non-injection drug users, many of whom report no identifiable HCV risk exposures. Given the economic and health costs of hepatitis C virus (HCV) infection, and the ongoing transmission within the IDU population, there is a need for improved understanding of HCV epidemiology within this risk group. Several problems still limit the wide use of HCV-Nucleic Acid Testing (NAT). These limitations include requirement for a long incubation period, requirement for considerable skills, low yield versus benefit and the limited reproducibility. In addition, HCV-NAT has high cost-efficiency ratio. The detection of HCV core antigen with ELISA could be an alternative to NAT in the early diagnosis of HCV infection. The ELISA offers operational advantages due to the shorter time to results, ability to screen individual samples (rather than pooled samples) using existing laboratory system, and no capital investment is required in a specialty laboratory. The HCV core Ag positive and simultaneously anti-HCV antibody negative samples may well be in the window period of HCV infection, or they may be low responders for the HCV antigens, thus, are unable to mount detectable antibody level. The high level of HCV core antigenemia detected in the studied population may reflect the high prevalence of HCV infection amongst drug users in KSA. There was good correlation between the HCV core antigenemia and the HCV-RNA data, which confirms previous studies.[2] The fact that 14 samples were positive for HCV core Ag and negative for anti-HCV antibodies, indicates that the patients may well be in the window period of HCV infection. The window period is characterized by absence of detectable antibodies, especially in the first few days following HCV infection. During this period, there will be evident viremia, which was detected by HCV RNA assay in 5 out of the 14 samples. Another possibility for the lack of antibodies in the 14 samples positive for HCV core Ag is that the patients may be low responders for the HCV antigen, thus are unable to mount detectable antibody level. For each antigen in nature, humans are either high responders (produce high level of antibody to the particular antigen) or low responders (produce low level of antibody to the particular antigen). Low and high responder status of an individual in genetically controlled, probably through the HLA gene cluster.

Table 1 - Detection of anti-HCV antibodies and HCV-RNA in HCV-core-Ag-positive samples (N=68).

| Anti-HCV | | | | HCV-RNA | | | |
|---|---|---|---|---|---|---|---|
| Positive | | Negative | | Positive | | Negative | |
| n | (%) | n | (%) | n | (%) | n | (%) |
| 54 | (79) | 14 | (21) | 60 | (88) | 8 | (12) |

HCV - hepatitis C virus, RNA - rebonucleic acid

In conclusion, the high prevalence of HCV infection in drug users necessitates rigorous testing of this population. Since drug users were found to be responsible for approximately 60% of the new cases of HCV infection, identifying HCV positive drug users may help in controlling HCV infection in this group of individuals as well as in the general population. The HCV core Ag assay could be a potentially useful assay for screening blood donors, as such an assay will minimize the risk of using HCV positive blood from a patient in the window period of HCV infection

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