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# Should routine serological screening for HCV be mandatory in HIV/AIDS patients enrolling for HAART in South Africa?

**Maemu P Gededzha, M Jeffrey Mphahlele, Azwidowi Lukhwareni, Selokela G Selabe**

**To the Editor:** Globally, an estimated 170 million people (about 3% of the world's population) have been infected with hepatitis C virus (HCV). HCV, a member of the Hepacivirus genus in the *Flaviviridae* family, possesses a single stranded, positive-sense RNA genome of approximately 9.6 kilobase (kb), and is the major cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma.[1] In Africa, HCV prevalence ranges from <3% in South Africa to >20% in Egypt. In South Africa, there is a low prevalence from 0.16% to 1.8%,[2-5] but this is higher in high-risk individuals, e.g. 39.4% in haemophiliacs and 4.8% in chronic dialysis patients.[2]

Some 4 - 5 million people globally are co-infected with HCV and human immunodeficiency virus (HIV).[6] Co-infection with HCV and HIV is common owing to shared routes of transmission – via blood and blood products and sharing of needles for injecting drugs.[7] The introduction of highly active antiretroviral therapy (HAART) dramatically improved the management of HIV patients. However, co-infections with opportunistic infections such as HCV and hepatitis B virus (HBV) remain a major problem. Patients with HIV/HCV co-infection have less immune reconstitution than patients with HIV infection alone,[8] and HAART may worsen the outcome of HCV disease, through enhancement of drug-induced hepatotoxicity.[9]

South Africa has scaled up HAART for treatment of HIV/AIDS in the public health sector since April 2003. However, research programmes to monitor the efficacy of HAART in HIV/AIDS patients co-infected with HBV and HCV do not exist. We have shown that 63% of HIV-positive South African patients initiating HAART have past or present HBV infection.[10] However, few data exist on the burden of HCV prevalence in HIV patients. One study demonstrated a low prevalence of 1.9%,[11] and another a high prevalence of 13.4% in KwaZulu-Natal.[12]

## Methods

We investigated the burden of HCV co-infection in HIV-positive patients enrolling for HAART at a tertiary hospital in Pretoria. The study population comprised 653 serum samples stored at -70ºC from adult HIV/AIDS patients who were candidates for HAART at Tshepang Clinic, Dr George Mukhari Hospital (DGMH), Pretoria, from 2004 to 2006. The Research, Ethics and Publication Committee of the University of Limpopo, Medunsa Campus, approved the study. All sera were screened for anti-HCV marker using the AxSYM assays version 3.0 (Abbott Laboratories, North Chicago) following the manufacturer's instructions.

Owing to limited serum volumes to confirm the initial screening results with a second serological assay, all anti-HCV positives (samples with S/CO, i.e. ratio of the sample rate (S) to the cut-off rate (CO) for each sample and control) above 5.23 and preliminary positives (samples with S/CO between 1.00 and 5.00) were subjected to in-house qualitative reverse transcription-polymerase chain reaction (RT-PCR) assay. Viral RNA was extracted from serum with the QIAmp viral mini RNA kits (Qiagen Gmbh, Germany), followed by PCR targeting of the highly conserved 5'-untranslated region (UTR) as previously described with slight modifications.[13] PCR positive samples were sequenced to confirm the specificity of the PCR products (SpectruMedix SCE 2410 Genetic Analysis System, LLC, PA).

## Results

Only 1.2% (8/653) of samples were positive for anti-HCV, with S/CO values ranging from 5.69 to 37.8. Of these 8 samples, HCV RNA was detected in only one, which had the highest anti-HCV titre of 37.8 (Table I). Sequencing confirmed that the RT-PCR product is HCV-

*HIV and Hepatitis Research Unit, Department of Virology, University of Limpopo and National Health Laboratory Service, Pretoria*
**Maemu P Gededzha,** MSc (Med)
**M Jeffrey Mphahlele,** PhD
**Azwidowi Lukhwareni,** PhD
**Selokela G Selabe,** PhD

***Corresponding author:*** *S Selabe (selokela@yahoo.com)*

**Table I. Summary of patients with reactive anti-HCV**

| Patient | Age | Gender | Anti-HCV (S/CO) | RT-PCR assay |
|---|---|---|---|---|
| 1 | 37 | F | 37.08 | + |
| 2 | 51 | M | 6.29 | - |
| 3 | 30 | M | 7.77 | - |
| 4 | 30 | F | 5.69 | - |
| 5 | 43 | M | 11.62 | - |
| 6 | 36 | F | 6.42 | - |
| 7 | 33 | F | 11.48 | - |
| 8 | 37 | F | 6.05 | - |

specific. In contrast, 20.7% (135/653) of preliminary positive samples had S/CO values ranging from 1.02 to 4.48. None of these samples tested positive for HCV by RT-PCR.

## Discussion

Laboratory diagnosis of HCV has major limitations as most available serological assays do not distinguish between acute, chronic and past infections. HCV RNA positive is regarded to be a marker of replication, whereas HCV RNA negative in anti-HCV positive patients indicates either resolved infection or very low viraemia with HCV RNA levels below the detection limit of the RT-PCR assay.

South Africa has one of the highest number of people living with HIV.[14] This study found a sero-prevalence of only 1.2% in HIV/AIDS patients enrolling for HAART in Pretoria. All but one appeared to have past or resolved HCV infection as indicated by a negative RT-PCR assay. Comparable findings were reported in pregnant women from Gabon.[15] During the natural history of HCV infection, 20 - 30% of infected individuals eliminate the virus spontaneously.[16] The low prevalence of HCV antibodies in our study could be due to missed HCV antibodies, as many HIV/AIDS patients fail to generate antibodies owing to immunosuppression,[17] and RT-PCR assay was used only to confirm anti-HCV positives or preliminary positives. The high number of HCV RNA negative results may also be the result of false anti-HCV positives with AxSYM 3.0 assay as the initial screening results were not confirmed with another serological assay owing to insufficient sera. Other limitations include lack of fresh samples, insufficient volume and that the study was conducted on patients attending a tertiary HIV referral clinic in a hospital setting.

Our study shows that most HIV/AIDS patients initiating HAART at DGMH have low exposure to, or active, HCV infection. In contrast to high rates of HBV and HIV co-infection in similar patients at DGMH, it appears that HIV/AIDS is not a risk factor for increased detection of HCV co-infection. While our findings do not support mandatory HCV screening in HIV/AIDS patients initiating HAART in South Africa, consideration should be given to patients who may be at an increased risk, such as HIV-positive haemophiliacs, injection drug users and diabetics. HCV antiviral therapy that may benefit such high-risk patients is increasingly becoming available in South African tertiary public hospitals through public-private partnerships.

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