



CHRONIC HEPATITIS C; FREQUENCY OF OCCULT HEPATITIS B VIRUS (DNA) IN CASES IN A TERTIARY CARE HOSPITAL OF KARACHI

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INTRODUCTION

In the background of recent studies EASL (European Association for study of Liver) has stated that about one third of population has biochemical proof of recent or remote HBV infection and approximately 350 billion people are suffering from chronic HBV infection. The clinical picture of HBV associated diseases is diverse varying from chronic liver disease to hepatic failure and hepatocellular carcinoma. Over the recent decade it has stood out as one of the top ten cause of mortality in world.¹ In our country the incidence of Hepatitis B sweeps from 4% in common masses to 28 % in cases with cirrhotic liver disease.²

Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infections share the major proportion of liver disease throughout the world. Morphologically HCV is an RNA virus belonging to Flaviviridae

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ABSTRACT... Objectives: The objective of this study is to determine the frequency of Occult hepatitis B virus (DNA) in cases of chronic hepatitis C in a tertiary care hospital of Karachi. **Study Design:** Cross sectional study. **Setting:** Medical Department of Abbasi Shaheed Hospital and Karachi Medical and Dental College after permission of ethical committee. **Period:** 15 December 2015 to 15 December 2016. **Methods:** Patients greater than 18 years of age of either sex were included while those with positive HBsAg, history of alcoholism, blood transfusion, intravenous drug abuse and hemodialysis were excluded. After informed consent blood samples were collected and evaluated for HBV DNA by performing qualitative PCR. Data was analyzed on SPSS version 16.0.p value of <0.05 was taken as significant. **Result:** Out of 377 patients with chronic Hepatitis C Occult hepatitis B virus (DNA) was found in 211 (55.9%) patients. 238(63.1%) were male and 139 (36.9%) were female. Mean age of patient with occult HBV DNA was 56.07 \pm 9.19 years. Highest prevalence 99(46.7%) was found in patients with history of Hepatitis C for more than three year (p value 0.02). **Conclusion:** Occult hepatitis B virus is found significantly among HCV infected patients. A masked HBV infection may interfere with the clinical outcome of chronic hepatitis C and accelerate the evolution to cirrhosis.

Key words: Occult Hepatitis B Virus, Chronic Hepatitis C, Cirrhosis, Hepatocellular Carcinoma.

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family while HBV is a member of Hepadnaviridae family. Blood and sexual contact remains the most allegedly responsible factors of spread of HBV and HCV. Frequency of infection is higher in regions with substantial prevalence of virus and immense likelihood of parenteral contingencies. Specific diagnosis of HCV is made by detection of antibodies and viral RNA in the serum. The presence of HBsAg is required for diagnosis of HBV infection.³ Approximately 80% of cases of acute viral hepatitis caused by HBV clears spontaneously within six months. On the contrary only 20% of cases of HCV are able to clear the virus serologically within six months while remaining 80% transform into chronic liver disease.⁴

Occult Hepatitis B virus (HBV infection) is defined by the presence of HBV DNA in the serum or liver of individuals in the absence of HbsAg.⁵ Over a period of time a number of hypothesis have

emerged for the understanding of this unique entity. Among them the presence of wild type HBV DNA is most commonly accounted for its existence.⁶ However, it is also believed that the widespread use of less sensitive kits for detection of HBsAg which are unable to detect virus when present in low levels has contributed towards the paradigm of Occult HBV.⁷⁻¹¹

The complications caused by Occult HBV infection are still underestimated due to its under recognition. Firstly undiagnosed occult HBV infection can result in HBV transmission through blood transfusion, hemodialysis and organ transplant. Moreover it can contribute to the development of cryptogenic liver disease and progression towards chronic hepatitis B as well as Fulminant Hepatic failure. Further more Hepatocellular carcinoma can develop due to chronic persistence of Occult HBV. It has also been observed that occult HBV infection interferes with treatment response of co-existing chronic hepatitis C.¹²

A wide range of prevalence of occult hepatitis B has been observed throughout the world. International data has reported the prevalence of occult hepatitis B as high as 52.3%.¹³ Therefore this study aims to determine the frequency of occult hepatitis B in patients with chronic hepatitis C to establish the local perspective. By virtue of this data, strategies will be developed for early screening of occult HBV DNA in patients with chronic hepatitis C so that adverse outcomes can be prevented as it can have serious implications in treatment response to antiviral therapy and progression to hepatocellular carcinoma.

METHODOLOGY

This cross sectional study was conducted at Medical unit 1 of Abbasi Shaheed Hospital Karachi during the period of 15 December 2015 to 15th December 2016. Approval from the Hospital Ethics Committees was taken prior to conduct the study. Patients were recruited through simple random sampling fulfilling the inclusion criteria which included adult subjects of both genders having chronic Hepatitis C and negative HBsAg (determined by ELISA). HCV infection was

defined by the presence of anti-HCV antibodies and HCV RNA in serum. Occult Hepatitis B was defined by the presence of HBV DNA by PCR, but negative for Hepatitis B surface antigen. The exclusion criteria included patients with positive HBsAg, patients on hemodialysis, intravenous drug abusers, history of blood transfusion and alcoholism. An informed consent was taken from all patients. Diagnosed patients of Hepatitis C were labeled as having chronic Hepatitis C by following the past medical records for HCV RNA presence over a period of six months. After all aseptic measures 5 ml of sterile blood was drawn by means of a disposable syringe at an ISO certified lab. The blood samples of patients were analyzed for HBV DNA by performing qualitative PCR and HBsAg by Elisa. Patients were labeled as having Occult Hepatitis B when results showed presence of HBV DNA in the absence of HBsAg. A predesigned Performa was used to collect the bio data, history and record the final outcome. Data was analyzed on SPSS version 16.0. Qualitative data was analyzed by Chi square test and p value of <0.05 was taken as significant.

RESULTS

A total of 377 patients of chronic Hepatitis C were included in this study. The frequency of occult hepatitis B virus (DNA) in cases of chronic Hepatitis C was found to be 211(55.9%). Out of 377 patients 238(63.1%) subjects were male and 139(36.9%) were female. Occult HBV DNA was observed in 144(67.9%) males in comparison to 68(32.1%) females. Moreover, out of 377 patients, 325(86.2%) subjects were married and 52(13.7%) were single. Out of 377 patients the age of subjects ranged from 38 to 80 years while the mean age was 56.07 years with a standard deviation of +9.19 years. Patients belonging to the age group of 51 to 60 years have the highest frequency of Occult HBV DNA which is 107(50.5%) while patients aged >60 years occupied the second most commonly observed status of HBV DNA which is 52(24.5%). Moreover occult HBV DNA was less oftenly observed in patients aged <51 years in comparison to older age groups. Among 173 patients the duration of Hepatitis C ranged from 6 months to 5 years while the average duration was found to be 2.6 years with standard

deviation of +1.48 years. Highest proportion of occult HBV DNA was found in 99(46.7%) subjects having chronic hepatitis C for more than 3 years as illustrated in Table-I.

Duration Hepatitis C	N	Occult Hepatitis B	
		Yes	No
≤ 1 Year	83	41(19.3%)	42(25.5%)
1 to 3 Years	141	71(34.0%)	69(41.8%)
>3 Years	153	99(46.7%)	54(32.7%)
p=0.023			

Table-I. Frequency of occult hepatitis b in cases chronic hepatitis c with respect to duration of hepatitis C

DISCUSSION

The phenomena of occult Hepatitis B has opened the door for the advancement of liver disease in a number of ways. Newly acquired Hepatitis B in recipient through transfusion of blood with undiagnosed occult hepatitis B in donor can result in exhilaration of HBV infection, evolvement to chronic liver disease and hepatocarcinogenesis in the long term.^{6,14}

It has been observed that the net prevalence of Occult hepatitis B in a country is directly proportional to its general incidence. Thus occult HBV infection is largely reported in endemic regions where 70 % to 90% of community is exposed to HBV. On the contrary Occult HBV is limitedly reported in low endemic zones where only 5% to 20% of population had HBV.^{6,15,16}

A large numbers of studies have postulated that occult Hepatitis B could be accountable for the escalation of chronic Hepatitis C virus proliferation and interruption with treatment responses. Patients with chronic Hepatitis C has shown the existence of occult HBV DNA in upto 30% of serum samples. Recently conducted met analysis showed enhanced probability of Hepatocellular carcinoma in patients having Occult HBV DNA with an odds ratio of 2.9 (95% CI: 1.6–4.1).^{6,17,18}

Our study demonstrated that occult HBV infection is frequently associated with chronic liver disease secondary to Hepatitis C virus. In our study hepatitis B was observed in 55.9% of patients with

chronic hepatitis C and in the absence of HBsAg.

Unfortunately there is paucity of national and international data on this emerging topic. In 1999, Cacciola et al studied the existence of HBV genome in patients with Hepatitis C virus related chronic Hepatitis and reported a prevalence rate of 33% among these patients.³ Similar study was conducted in 1999 by Fukuda et al and observed a noteworthy percentage of 52.3% of occult HBV DNA infection among patients with diverse liver disease due to Hepatitis C virus which is consistent with our study.¹³ On the other hand comparatively low prevalence rate of 7.5% and 5.5 % were reported in studies from Japan and France respectively.^{2,19,20} However a discrepancy was observed when Alencar et al in 2008 reported the prevalence of Occult HBV DNA in chronic Hepatitis C patients to be just 0.5%.²¹ Therefore it is recommended that multicenter trials should be carried out locally so that more accurate results could be obtained.

In our study, limitations include that it is a single Centre study. Also only qualitative HBV DNA was evaluated for the detection of occult infection due to financial constraints although anti HBc and HBV genome in liver parenchymal cells would have contributed in determining the prevalence more confidently.

By conducting this study, we addressed the topic which is insufficiently studied in Pakistan and needs more research in same and related objectives which should be designed in different settings with plentiful resources.

CONCLUSION

This study reveals the strong prevalence of occult hepatitis B among chronic Hepatitis C patients which could be responsible for adverse clinical outcomes encompassing the whole spectrum of chronic liver disease.

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DISCLAIMER

Manuscript has been read and approved by all authors, has not been published in any other journal, neither under consideration for publication in any other journal and is being exclusively contributed to Journal of Pakistan Medical Association.

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PREVIOUS RELATED STUDY

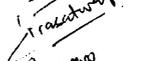
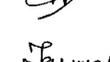
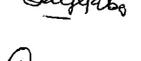
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*Never argue with someone
 who believes their own lies.*
 – Unknown –”

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Sadia Iqbal	Concept and design drafting of article.	
2	Firasat Waqar	Analysis and interpretation of data.	
3	Aisha Javed	Collection, assembly of data, statistical expertise.	
4	Nida Sajid	Critical review for intellectual content.	
5	Tayyaba Iqbal	Analysis, Interpretation of data, Drafting article.	
6	Qamarunnisa	Final approval and guarortor of article.	