Hepatitis B infection in Malta: a retrospective cross sectional study

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Abstract

Chronic Hepatitis B infection can lead to significant morbidity and mortality**.** Case notes of patients who tested positive for HBsAg between 1st Dec 2007 and 29th October 2009 were reviewed (*n*=197) . The results show that 2/3 (65%) of the study population were male and that HBV infection was detected across all age groups. About ¼ (25.4%) of the study group were foreigners. 79% of Maltese patients testing postive did not have any identifiable risk factors documented in their case notes for acquiring HBV. In more than 60% of patients who tested positive further assessment to determine suitability for treatment was not performed and only 6.6 % of the study population received treatment for HBV.

Keywords

Hepatitis B, HBsAg, HBV infection, Malta

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Introduction

Hepatitis B (HBV) is a DNA virus which belongs to the family of hepadnaviruses .After exposure to the virus the patient develops an acute infection which may or may not progress to a chronic hepatitis. Acute Hepatitis B infection is subclinical in 70% of infected patients while the rest develop jaundice. A small minority (0.1-0.5%) of acutely infected patients develop fulminant hepatic failure[1] which is life threatening. Chronic HBV hepatitis (CHB) is often silent for many years, however, it can lead to cirrhosis in 8-20% of patients within 5 years of diagnosis[2]. About one fifth of HBV cirrhotics will go on to develop liver failure in 5 years time and would have a poor prognosis unless transplanted.CHB also predisposes the patient to develop hepatocellular carcinoma (2-5% per annum).[2]

Worldwide, two billion people have serological evidence of past or present infection with HBV, whereas more than 350 million people are chronically infected. Globally HBV cirrhosis and hepatocellular carcinoma cause more than 1 million deaths per year and account for approximately 5-10 % of liver transplants in the developed world.[3,4,5]

In developed countries the prevalence of chronic infection (HBsAg prevalence) is about 2%. In these low prevalence areas the main modes of transmission are through sharing of contaminated needles amongst intravenous drug abusers and unprotected sexual intercourse. Although rare, some individuals acquire the infection iatrogenically when there is non-compliance with infection control practices. Infection in these areas is often acquired in adulthood and only 10% of those infected go on to develop chronic HBV hepatitis.

On the other hand in areas of high prevalence (8%) such as SE Asia , Sub-Saharan Africa and the Amazon basin, the infection is often aquired perinatally or in early childhood either through vertical transmission (mother to child) or through the use of non-disposable medical equipment. The majority (90%) of individuals who are exposed at a young age

develop chronic HBV hepatitis with its associated risks of cirrhosis and hepatocellular carcinoma.[3]

Reduction in HBV transmission is best achieved through vaccination programs prior to infection. The world's first nationwide universal vaccination program for HBV vaccination was launched in 1984 in Asia (Taiwan).[7] The vaccine is 95% effective in preventing the development of chronic infection. In 1991, the World Health Organization (WHO) recommended adding HBV vaccination to all national immunization programs.[3] In Malta universal HBV vaccination is recommended at 15 months of age.[10]

Patients with acute severe hepatitis are candidates for treatment as this can reduce the need for liver transplantation.[11] In patients with chronic hepatitis, avoiding the development of cirrhosis and hepatocellular carcinoma leads to improved survival and this is best achieved through a sustained and profound suppression of HBV replication.[6] Treatment in these patients is recommended if there is evidence of active viral replication as well as ongoing liver injury. Ongoing liver injury is evidenced by raised liver transaminases (ALT/AST) as well as fibrosis and inflammation on liver biopsy.[6,8] Active viral replication is evidenced by detecting HBV DNA in the patient's blood. Chronic HBV infection is an evolving process passing through various phases depending on how the virus and the host immune system interact (Table 1). According to the EASL guidelines the chronically infected patients who require treatment are those in the Immune Reactive Phase as well as the HBeAg negative HBV DNA positive chronic HBV hepatitis (Pre-core mutation) patients.[6] All patients with chronic HBV however, should be followed up by a gastroenterologist or an infectious disease specialist even when there are undetectable HBV DNA levels as these patients can still develop complications later on in life.

Disease Phase	HBsAg	HBeAg	HBV DNA	Liver Injury	Treatment required
Immune tolerant	+	+	+	No	No
Immune reactive	+	+	+	Yes	Yes
Inactive HBV carrier	+	-	-	No	No
HBeAg Neg CHB (precore mutation)	+	-	+	Yes	Yes
HBsAg Negative	-	-	-	No	No

Table: 1 *The various phases of chronic HBV infection.*

Two classes of drugs are used to treat chronic HBV infection, namely nucleoside/nucleotide analogues (NUCS) and Interferon-alpha. The precise way Interferon-alpha works is not known. It is released by infected cells as well as activated lymphoctes and is able to kill infected cells through protein sythesis inhibition and immune mechanisms. It can also protect uninfected cells from viral takeover.[9] NUCS are incorporated into growing viral DNA strands but act as chain terminators hence inhibiting HBV replication.[12]

Aims of study

1. To characterise Hepatitis B infection in Malta.
2. To audit the clinical evaluation and management of HBsAg positive patients in Malta.

Methods

This study was carried out by reviewing case notes of those patients who tested positive to HbsAg or HBV DNA in Malta between 1st December 2007 and 29th October 2009. This data was derived from the Virology Dept at Mater Dei Hospital. A number (n=29) of HBsAg positive results could not be assessed furthur as their identification was coded. The list of patients studied was further amplified by identifying any patients who also tested positive for Hepatitis B through routine screening of blood donors as well as at the Detox and Genitourinary clinics. Prior to retrieving case files, approval by the Director Data Protection as well as chairpersons of the various clinical departments at Mater Dei was obtained. A total of 197 files were analysed looking at the demographic data, the stage of the disease as well as auditing the investigation and management of these cases. For the purposes of the audit, management was compared with the EASL practice guidelines published in 2009.[6]

Results

Demographic data (Figures 1and 2)

Approximately 2/3 of the infected individuals were males. About ¾ (74.6%) of the study population were Maltese whereas the rest (50 cases) were foreigners. Infection was detected in all age groups including young individuals suggesting that transmission of HBV is still ongoing.

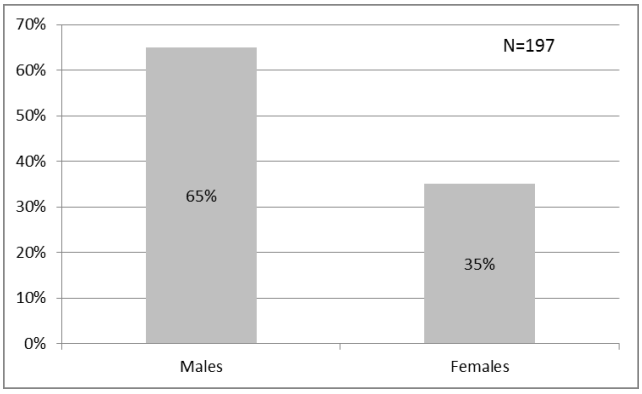

Figure 1: *Gender distribution in study population*

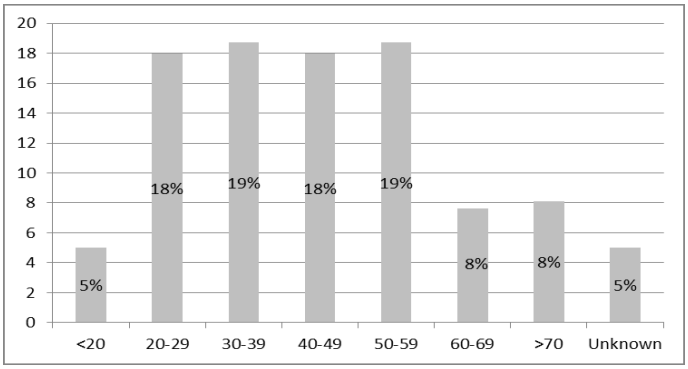

Figure 2: *Age distribution in study population*

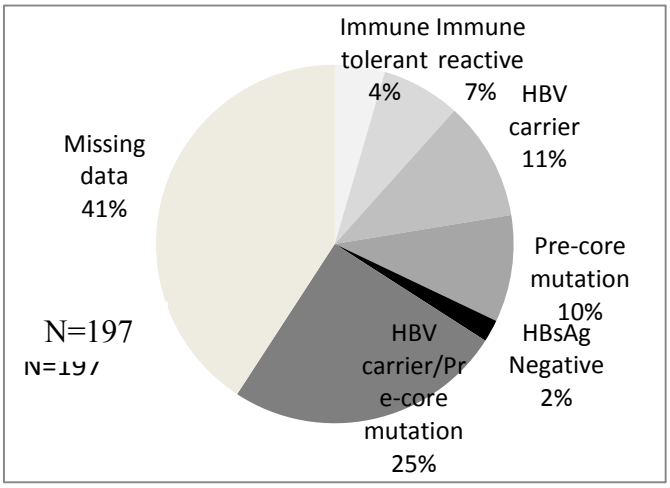

Figure 3: *Distribution of study population according to disease phase.*

Risk factors for transmission

A minority of cases were documented to have tattoos (1%), perinatal transmission (1%), and intravenous drug use (3.5%), history of previous blood transfusion (3.5%) or sexual promiscuity (3.5%). In 2% of the cases, familial clustering was documented. However more importantly in 79% of Maltese cases there was no identifiable risk factor for HBV transmission documented in the case notes. This implies either reluctance of patients to admit to high risk behaviour or less likely the possibility that iatrogenic transmission is commoner than we think.

Further assessment following diagnosis of HBsAg positivity (Figure 3)

Once someone is found to be HbsAg positive it is important that further tests are done (HBV DNA ,HbeAg, Anti HBeAb) so that the phase of the disease is determined. Our results show that in many patients (41%) these tests were not done and therefore it was not possible to classify the phase of the disease. Additionally in another 50 cases (25%) there was no HBV DNA level documented hence the patient could be either an inactive HBV carrier or HBeAg Neg CHB (pre-core mutation).

Treatment (Figure 3)

Given the high proportion of patients who were not assessed further once HBsAg was detected, it was not surprising to find that most HBsAg patients in Malta are untreated. Even on excluding patients with missing data, according to the EASL guidelines, treatment is recommended in patients in the immune reactive phase (7%) as well as patients with the pre-core mutation (10%). This study showed that only 13 patients (6.6%) of the study population received treatment with Interferon-Alpha, NUCS or both.

Prevalence of cirrhosis in HBV (Figure 4)

It is important to determine if the patient is cirrhotic, since cirrhotic patients with active viral replication (HBV DNA positive) will require urgent treatment. The presence of cirrhosis is best diagnosed by liver biopsy but can also be inferred from ultrasound findings (splenomegaly, nodular liver), a low platelet count or oesophageal varices at endoscopy. Only 15 (7.6%) patients were clearly suffering from cirrhosis. Of note in 32% of the study population there was insufficient data documented in their files to determine whether cirrhosis is present or not.

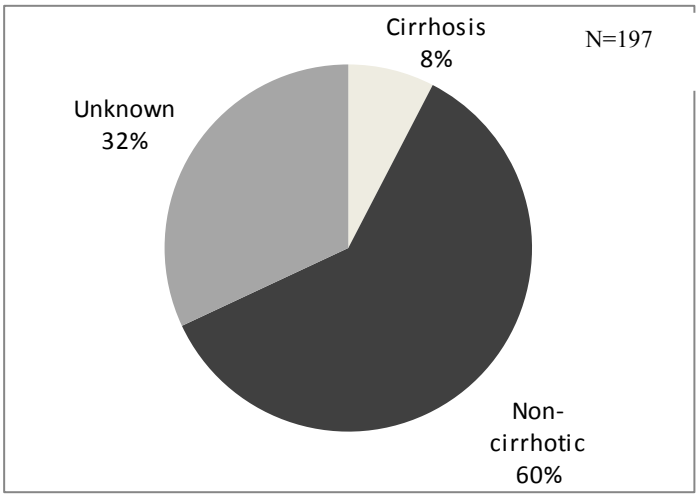

Figure 4. *Prevalence of cirrhosis in HBV*

Discussion

These results clearly show that HBV infection is still ongoing in the Maltese Islands in spite of there being an effective vaccine for the last 20 years. The typical HBsAg positive Maltese patient probably does not admit to high risk behaviour and health care workers should avoid contact with blood at all times. Unfortunately the results also show that HBsAg positive patients are often not referred for further assessment and treatment. This may be secondary to patient reluctance given that considerable stigma is still attached to the disease. Patients may also represent a difficult to treat group with most being noncompliant to follow up visits / actively abusing drugs etc. As most of these patients are entirely asymptomatic in the early phases of chronic infection there is also little motivation for further investigation and treatment. Health care providers may not be aware that major advances in the understanding and treatment of HBV were made in the last few years and that the condition has in fact become very satisfying to treat. All patients found to be HBsAg positive should be referred for specialist care and will require lifelong follow up. The main limitations of this study are that it does not determine prevalence of HBV in Malta since there was no random sampling of the general population and the study has all the limitations of a retrospective study.

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