PREVALENCE OF ANTIBODIES TO HEPATITIS C VIRUS IN HOSPITALIZED POPULATION SUBSETS

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ABSTRACT

Prevalence of antibodies to hepatitis C virus (anti-HCV antibody) was ascertained in different subsets of hospitalized patients. Anti-HCV antibody testing was done using a third generation test. The anti-HCV positivity in the sera of 308 tuberculosis patients, who had been given streptomycin, was 12.3 per cent. It was 7.1 percent among 84 cardiac patients undergoing invasive cardiac procedures, 15.6 per cent in 77 patients on haemodialysis and 41.2 per cent patients with surgical jaundice. It is surmised that hospitalization, particularly parenteral therapy and invasive procedures during hospitalization, puts patients at higher risk of contracting HCV infection.

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KEYWORDS : Hepatitis C Virus; Hospitalization; Hospital infection; Prevalence.

Introduction

Hepatitis B virus (HBV), human immunodeficiency virus (HIV) and hepatitis C virus (HCV) are blood-borne viruses that can be transmitted in hospitalized subjects through transfusion of blood and blood products. Of these agents, HBV and HIV are usually looked for in blood units in our country whereas HCV screening is not yet in vogue. Several studies have unequivocally established HCV as the major aetiological agent associated with post-transfusion non-A, non-B hepatitis (PTH) [1,2]. The highest incidence of HCV, worldwide, is in haemophiliacs [3]. Other documented sources of HCV infection in hospitals are intravenous immunoglobulins [4], haemodialysis [5], organ transplants [6], needle-stick injuries, surgery without adequate sterilization or without use of disposable equipment, and even hospitalization without transfusion [7]. In many instances the source of infection may remain unidentified [8]. In India, studies on prevalence of HCV are few and mainly focused on blood donors,

hepatitis patients and certain high-risk groups [9-13]. The present study was aimed at determining the prevalence of anti-HCV antibodies in hospitalized patients and exploring the potential of HCV as a candidate transmitted in a hospital setting.

Material and Methods

The study was conducted at the Command Hospital Southern Command, Pune and Military Hospital (Cardiothoracic Centre), Pune from Dec 1993 to Apr 1996. A total of 544 patients and 300 controls were enrolled in the present study. Among the patients 535 were males and among controls 290 were males. Plasma from the cardiac patients and sera from other patients and controls were stored at -20°C until tested.

Subjects

Controls (Group A, n=300) : Controls were healthy adult volunteers of whom 290 were male cadets and soldiers from local units and 10 were female nursing cadets. The mean age of controls was 29.4 years. Control subjects denied any

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history of hospitalization or of receiving or donating blood. History of any high-risk behaviour was elicited by interrogation.

Pulmonary tuberculosis patients (Group B, n=308) : All these patients had been given anti-tubercular regimen consisting of streptomycin and other drugs. Sera were collected 40 days or more after the termination of 60 doses of streptomycin. HIV seropositive tuberculosis patients were not included.

Cardiac patients (Group C, n=84) : These consisted of 17 patients who had undergone open heart surgery for a cardiac disease and had received more than 5 blood transfusions during surgery and 67 who had undergone an invasive cardiac procedure like catheterization. The mean duration between the invasive procedure and collection of sera was 42 days.

Jaundice patients (Group D, n=27) : Patients in this group included 17 subjects with obstructive jaundice who had been subjected to exploratory laparotomy for diagnostic or therapeutic reasons. Blood for HCV testing was collected after a mean period of 41 days after surgery. The remaining 10 patients had not undergone laparotomy. Three of these had obstructive jaundice and 7 had hepatic metastases from other primary cancers. Their blood was collected during periodic review after a mean period of 45 days after discharge from hospital. None of the patients with jaundice had primary hepatocellular carcinoma. All had been subjected to aspiration cytology of the liver at some stage of the disease.

Haemodialysed patients (Group Ei, n=77) : These patients with chronic renal failure (CRF) had undergone 3-19 sittings of haemodialysis with a mean of 11 sittings. Sera of 40 CRF patients (Group Eii) who were yet to be subjected to dialysis were also tested for anti-HCV.

Technique

Anti-HCV testing was carried out on all samples employing the recombinant immunoblot assay test system (RIBA 3.0, Chiron Corporation, USA). This is a strip immunoblot assay that detects antibodies against three recombinant antigens - c33c (produced in *E. coli*), NS-5 and superoxide dismutase (both produced in yeast) and two synthetic

peptides derived from putative nucleocapsid of HCV from c22p and c100p regions of its genome. The results were read either as reactor, non-reactor, or indeterminate based on the criteria given by the manufacturer. The indeterminate results were considered negative since they showed a band against a single antigen only.

Statistical methods : Chi-square test (p value less than 0.05 were considered to indicate significance) and calculation of odds ratio were employed.

Results

The results have been tabulated along with statistical correlation in Table-1.

TABLE 1
Prevalence of anti-HCV antibodies in different patient groups

Group (n)	Percentage positivity	'p' value as compared to parallel control group	'p' value as compared to control group
Controls (300)	2.33	—	—
Pulmonary tuberculosis (308)	12.7	not available	< 0.05
Cardiac patients			
i. Cardiac surgery (17)	17.6	0.05 < p < 0.06	< 0.05
ii. Catheterized pts (67)	4.5		> 0.05
Jaundiced patients			
i. Laparotomy (17)	41.2	p < 0.05	< 0.05
ii. non-laparotomy (10)	0	between i & ii	
CRF			
i. Haemodialysis (77)	15.6	p < 0.05	< 0.05
ii. non-dialysis (40)	2.5	between i & ii	< 0.05

Amongst controls (group A) anti-HCV antibodies were present in 2.3 per cent of cadets and soldiers. None of the 10 female subjects tested positive.

Thirty nine out of 308 (12.7%) pulmonary tuberculosis patients (group B) gave anti-HCV reactivity. All had received streptomycin for 60 days. None gave history of receiving any transfusion of blood, blood products, intravenous fluids, or of having undergone surgery during hospitalization.

Of the cardiac patients (group C), 6 out of 84 (7.1%) gave anti-HCV reactivity. Three of the

reactors were from the group receiving more than 5 transfusions during surgery (17.6%) and 3 reactors were from cardiac catheterized patients (4.5%). Thus a significant difference between transfused operated cardiac patients could be elicited compared to cardiac catheterized patients ($p = 0.058$, odds ratio = 4.57).

Seven patients (41.2%) showed anti-HCV positivity in the laparotomy group (Group D) with surgical jaundice. Jaundiced patients not subjected to surgery did not show anti-HCV positivity. There was thus a statistically significant difference between the group exposed to surgery as compared to those not subjected to laparotomy ($p < 0.05$, odds ratio = undetermined).

Twelve out of 77 (15.6%) CRF patients on haemodialysis and one out of 40 (2.5%) CRF patients not subjected to dialysis tested positive for anti-HCV antibodies. The anti-HCV positivity was significantly higher in the group on dialysis ($p < 0.05$, odds ratio = 7.20, relative risk = 6.23).

Discussion

In the present study, we aimed at detecting the prevalence of anti-HCV antibodies in 4 subsets of a well-defined population who were either hospitalized or exposed to invasive diagnostic or therapeutic procedures.

The control population (group A) gave an anti-HCV prevalence of 2.3 per cent. Such a high background prevalence rate points to several unidentified environmental sources of HCV in any crowded community. The demonstrated or suspected sources include sharing of toilet articles like shaving razors, blades, towels, etc.. It is surmised that conditions akin to intrafamilial transmission, described by Kiyosawa et al [14], must be playing their role in disseminating HCV.

Thirty eight (12.3%) of 300 pulmonary tuberculosis patients (group B) tested positive for anti-HCV at the end of the streptomycin regimen. Pre-hospitalization sera of these patients were not available for comparison. However the elicited seropositivity in this group bears significance when compared to the background seropositivity in the controls ($p < 0.05$). However a study of anti-HCV prevalence in patients with pulmonary tuberculosis on non-streptomycin regimens would have formed

an ideal group for comparison. Studies have speculated the possible role of intramuscular injections in the spread of community acquired hepatitis [15]. A study by Giusti et al [7] showed the occurrence of NANB hepatitis after hospitalization even without transfusion. Another study by Alter et al [9] have shown that in 40 per cent of HCV hepatitis the source may be unknown. It is apparent, therefore, that there is a significant risk of contracting HCV during prolonged hospitalization.

Among cardiac patients (group C) overall anti-HCV positivity was 7 per cent. Mattson et al [16] also studied the incidence of seroconversion to anti-HCV after open heart surgery in transfused and non-transfused patients in Sweden and found PTH developing within 5 months in 17 out of 390 patients (4.4%) and half of these revealed anti-HCV positivity. Plasma from out-patients was collected after a mean period of 42 days post-invasion (expected mean incubation period of HCV is 40 days). Higher anti-HCV positivity among those receiving multiple blood transfusions during cardiac surgery (17.6%) points to association with transfusions and probably surgery. Use of disposable cardiac catheters could have accounted for a lower positivity in those who had undergone cardiac catheterization.

Of the 27 patients with surgical jaundice (group D) anti-HCV positivity of 41.2 per cent was elicited in the obstructive jaundice patients who underwent laparotomy. That surgery has its documented role in HCV transmission [7] is evidenced by this group. Additionally, patients who are operated are exposed to other invasive pre- and post-operative procedures like fine needle aspiration, parenteral drug administration, fluid and blood transfusion, anaesthetic procedures, and repeated blood sampling for investigations. Such invasive procedures are understandably more in operated patients as compared to those managed on conservative lines and may contribute towards acquiring HCV in the former group.

The fact that patients with CRF on haemodialysis (group E-i) showed significantly higher anti-HCV positivity as compared to CRF patients not on haemodialysis, brings out the relationship of dialysis with HCV. The relative risk of contracting HCV infection is more than 6 times ($RR = 6.23$) in

those subjected to haemodialysis. The possible sources of HCV in a dialysis unit needs to be elucidated. They may be due to immune deterioration, renal transplantation, repeated blood transfusions, recurrent percutaneous insults, and improper decontamination of dialysis equipment and other accessories.

Several other studies have shown high degree of anti-HCV positivity in patients in haemodialysis units. Schlikopter et al [5] have shown that 37 per cent of patients in haemodialysis units are anti-HCV positive. Sumathy et al [9] from Madras showed 37.5 per cent anti-HCV positivity in haemodialysis patients. These figures are in agreement with our study.

To conclude, the study has brought out that hospitalized patients subjected to invasive procedures like long-term injectable drug therapy, invasive surgery or blood transfusions, aggressive patient assessment or management in operated subjects with surgical jaundice and cardiac disease, prolonged and recurrent parenteral invasion in the CRF patients on haemodialysis as well as in catheterized cardiac subjects, does expose such patients to blood-borne infective agents like HCV.

That HCV infection is a hospital acquired infection is debatable. This issue can only be resolved by studying pre- and post-hospitalization serum samples. However, in view of the significantly higher ($p < 0.001$, odds ratio = 5.66) cumulative anti-HCV positivity (11.9%) in the patients studied as compared to the control group (2.3%), it can be postulated that HCV transmission is facilitated in a hospital environment.

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