ORIGINAL RESEARCH PAPER

Microbiology

HEPATITIS C VIRUS SEROPREVALNCE IN LIVER DISEASE PATIENTS AT SMS HOSPITAL AND ALLIED HOSPITALS

KEY WORDS: HCV, HBV, RAPID TEST, ELISA, HCC.

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ABSTRACT

Seroprevalence of Hepatitis C virus in Liver Disease patients at SMS Hospital and Allied Hospitals. Various hepatic disorders like Hepatitis,Fulminant hepatic failure,Sub acute fulminant hepatic failure,Chronic liver diseases,Livercirrhosis,Hepatocellular Carcinoma cause multi organ failure leading to death. The most important viral cause of hepatic disorders after HBV is HCV[18].

BACKGROUND: Various Hepatic disorders caused by HBV and HCV have become a major public health problem throughout the world. HCC is one of the ten most common cancers in the world and is the only cancer which can be prevented by vaccination[7]. HCV infection can be transmitted by blood transmission, injectable drugs, perinatally, improperly sterilized dialysis equipment, unprotected sex with infected partner specially MULTIPLE SEXUAL PARTENER groups detection and treatment and its prevention in community[25]

OBJECTIVES: To find out the seroprevalence of anti HCV antibodies in various categories of Liver Disease patients from different OPDS, wards and ICUs of SMS Hospital and J.K. Loan, MahilaChikitsalaya and Zanana Hospital Jaipur etc.This study is conducted to aid in early detection & treatment & its prevention incommunity.

METHODOLOGY: The study is conducted in the clinical microbiology laboratory of the S.M.S. Medical College & Hospital, Jaipur from period of 1st January, 2007 to 13th November 2007 to evaluate the prevalence of anti HCV Antibody in symptomatic and asymptomatic individuals of 500 confirmed Liver disease patients. RAPID Test and ELISA TEST was done at clinical microbiology laboratory S.M.S. Medical College & Hospital, Jaipur.

RESULT: Total no. of anti HCV antibody positive cases in our study were 4.2% in liver disease patients.All positive cases were above the age of 30 yrs.HCV positivity ratio among Male: Female was9.5:1(out of 311 males, 19 (6.10%) were positive and out of 189 females, 2 (1.05%) were positive for anti HCV antibodies in liver diseases patients).Highest prevalence of anti HCV antibodies was observed in the age group > 51 years (6.06%), followed by 5.43%, 2.58% in 31 – 40 years age groups and 41 – 50 years age groups respectively in liver diseases patients.Comparison of studies conducted by other researchers showed slight variations in prevalence of HCV infection.There is a scarcity of information on HCV prevalence particularly in developing countries like India, hence present study was conducted for early detection & prevention.

INTRODUCTION:

Since time immemorial mankind is suffering from various hepatic disorders like hepatitis, cirrhosis and hepatic carcinoma causing multi organ failure leading to death. The causes of hepatic disorders are broadly classified into: bacterial, chemical, parasitic, viral and drug induced. Various types of viruses cause liver infection or hepatitis. Among hepatic viruses A, B, C, D, E and G are responsible.Both hepatitis B virus and hepatitis C virus share common modes of transmission i.e., by blood and blood products mainly and also noticed in drug addicts. These viruses are highly infectious (About hundred times more than HIV virus). Globally, HCV has infected more than 170 million people and thus represents a viral pandemic 7 times more widespread than HIV infection.[2] In India approx 1.8-2.5% of the population is presently infected by HCV [11] and 20 million are suffering from HCV infection & its complications [24] Previously blood transfusion was a major mode of HCV transmission but now that donor blood is thoroughly screened, majority of cases are injectable drug users. HCV is also transmitted perinatally, by improperly sterilized dialysis equipment (68% of cases) and by unprotected sex with infected partners specially MSM group and with other STDs and even patients with HIV.[6] An estimated 20%cases of HCV infections will progress to cirrhosis [26] over 20-50yrs interval and others to hepatitis and hepatic carcinoma.

AIMS & OBJECTIVE:

To find out the Seroprevalence of hepatitis C virus among among Liver Disease patients.The epidemic proportion of HCV infection, the limited efficacy and expensive nature of approved therapeutics, the high cost of liver transplants and huge burden on health care system all point out to the need for extensive search for seroprevalance and prophylactic vaccine development and need new therapies to treat the disease and prevent its complications. Hence a study has been conducted to detect the seroprevalence of HCV among patients with Liver Disease patients to aid in early detection, treatment and prevention in the community.

MATERIAL AND METHODS:

The study is conducted in the clinical microbiology laboratory of the S.M.S. Medical College & Hospital, Jaipur from period of 1st January, 2007 to 13th November 2007 to evaluate the prevalence of anti HCV Antibody in symptomatic and asymptomatic individuals of 500 confirmed Liver disease patients.Variuus categories were identified based on clinical evaluations & various investigations. The collected blood was allowed to clot & serum was separated. The sample were stored at 2-8°c & tested with in 7 days of collection. Patients' serum samples were subjected to following tests for detection of Anti-HCV antibodies.

A- Rapid test: - DOT immunoassay for detection of Anti-HCV antibodies.[20]

B- ELISA test :- For Detection of Anti-HCV antibodies[16]

HCV MICROELISA TEST: The 3rd generation HCV Microlisa is an in vitro qualitative enzyme linked immunosorbent assay for the detection of antibodies against HCV (anti-HCVs) in human serum or plasma. The kit is basically intended to screen blood donations to identify and eliminate the infected units of blood and for clinical diagnostic testing. This kit is

manufactured by J. Mitra& co. Pvt. Ltd. New Delhi, India.

Principle:- The 3rd generation HCV Microlisa is based on a highly sensitive technique, Enzyme Linked Immunosorbent Assay which detects antibodies against HCV in human serum and plasma. The HCV proteins are present in serum at levels well below the limits of detection. Thus, immunodiagnosis of HCV infection is based on detection of host generated antibodies (anti-HCVs) to viral proteins.The 3rd generation HCV Microlisa utilizes a combination of antigen with the sequence of both HCV structural and non-structural antigen i.e. CORE, E1, E2, NS3, NS4 and NS5. It has an obvious advantage over the available 2nd generation and 1st generation ELISA with improved sensitivity and specificity. The combinations of antigens for the structural and non-structural HCV proteins are coated onto the microwells. The microwells are then thoroughly washed with the diluted wash buffer to remove excess of unbound anti-HCV or other human IgGs which may interfere with the test. An enzyme conjugate, anti-human IgG conjugated with HRPO is added. At this stage the microwells hold only the bound antigen-anti HCV-enzyme conjugate complex. In the next step, the freshly prepared substrate solution is incubated with the complex in the microwells. The enzyme substrate reaction leads to development of a blue colour which is indicative of the Ag-Ab reaction which has occurred in the microwell. In the final step the stop solution is added and the yellow colour formed after addition of acid stop solution is read on microplate reader at an optical density of 450 nm.

- The results were read on Microplate spectrophotometer at 450 nm.
- Cut off value was calculated as per the manufacturer's guidance and the results were interpreted accordingly.

Cut off value = 0.1xPCx+0.1

PCx = Mean absorbance of positive control

- **Interpretation :-** According to their absorbance values, samples were interpreted as either reactive for HCV antibody (HCV positive) or non reactive for HCV antibody (HCV negative) if test specimens with absorbance value within 10% below the cutoff should be considered suspect for the presence of antibodies and should be retested in duplicate.
- Sample found to be reactive initially by HCV Microlisa test were again tested by visual rapid test which is HCV TRI-DOT test.

HCV TRI-DOT

The 4th Generation HCV TRI-DOT is a rapid, visual, sensitive and qualitative in vitro diagnostic test for the detection of antibodies to Hepatitis C Virus in human serum or plasma. The 4th Generation HCV TRI –DOT has been developed and designed with increased sensitivity for core and NS3 antibodies using a unique combination of modified HCV antigens. They are for the putative core (structural), protease/helicase NS3 (non-structural) NS4 (non-structural) and replicase NS5 (non-structural), regions of the virus in the form of two test dots "T_1" & "T_2" to provide a highly sensitive and specific diagnostic test. This Kit is manufactures by J. Mitra& Co. Pvt. Ltd. New Delhi, India.

Principle:-4th generation HCV TRI-DOT has been developed and designed using modified HCV antigens representing the immunodominant regions of HCV antigen. HCV antigens are immobilized on a porous immunofiltration membrane. Sample and the reagents pass through the membrane and are absorbed into the underlying absorbent pad. As the patient's sample passes through the membrane, HCV antibodies if present in serum/plasma, bind to the immobilized antigens. In the subsequent washing step, unbound serum/plasma proteins are removed. In the next step, the protein-A conjugate is added which binds to the Fc portion of the HCV antibodies to give distinct pinkish purple dot against a white background at the test region ("T_1" &/or "$T"_2$) and the control has been devised to confirm the proper functioning of the device, reagent and correct procedural application.

- **Interpretation: -** Results are noted as per manufactures guidelines and results were interpreted accordingly. If test dots T_1, & T_2, either both dark and light in colour (pink), result should be considered reactive for antibody to HCV. If only control dot appear it indicates that the sample is non-reactive for anti-body to HCV.
- Sample found to be positive for HCV antibodies by both HCV microlisa test & HCV TRI-DOT method would be further tested for hepatitis B Surface antigen by ELISA test.

RESULT:

Total no. of anti HCV antibody positive cases in our study were 4.2% in Liver Disease patients.All positive cases were above the age of 30 yrs.HCV positivity ratio among Male: Female was9.5:1(out of 311 males, 19 (6.10%) were positive and out of 189 females, 2 (1.05%) were positive for anti HCV antibodies in liver diseases patients).Highest prevalence of anti HCV antibodies was observed in the age group > 51 years (6.06%), followed by 5.43%, 2.58% in 31 – 40 years age groups and 41 – 50 years age groups respectively in liver diseases patients. Comparison of studies conducted by other researchers showed slight variations in prevalence of HCV infection.

TABLE - 1
HCV Seroprevalence Among Liver Disease Patients

Various Liver disease patients	Total No. of sample tested	Total No. of HCV (+) cases
Liver disease patients* (AVH, FHF, SAFHF, CLD, LC, HCC)	500	21 (4.2%)

* AVH –Acute viral hepatitis, FHF – Fulminant hepatic failure, SAFHF – Sub acute fulminant hepatic failure, CLD – Chronic liver diseases, LC – Liver cirrhosis, HCC – Hepatocellular Carcinoma

The above table shows HCV seroprevalence among various Liver disease patients. In the present study a total no. of 500 samples were tested out of which 21 samples (4.2%) were positive for antibody to HCV.

TABLE - 2 Sexwise Distribution Of Anti Hcv Antibodies Among Liver Disease Patients

S. No.	Various Liver disease patients	Total No. of Sample tested	Male		Female		Total no. of HCV positive cases
			Total sample tested	HCV positive cases	Total sample	HCV positive cases	HCV positive cases
1.	Liver disease patients (AVH, FHF, SAFHF, CLD, LC HCC)	500	311	19 (6.10%)	189	2 (1.05%)	21/500 (4.2%)

The above table shows sex wise distribution of seropositivity of HCV antibody among various Liver disease patients.

This table clearly shows that out of 311 samples of males, 19 (6.10%) were positive whereas 189 sample of females, 2 (1.05%) were positive. This clearly shows HCV seroprevalence were more in males than females.

Table - 3 Age Wise And Sex Wise Distribution Of Hcv Seroprevalence In Liver Disease Patients

Age in year	Male		Female		Percentage (%)
	Total no. of tested	Total no. of HCV Positive	Total no. of tested	Total no. of HCV Positive	
0-10 year	13	0	11	0	0/24 (0%)
11-20 year	10	0	13	0	0/23 (0%)
21-30 year	12	0	9	0	0/21 (0%)
31-40 year	117	9 (7.69%)	67	1(1.49%)	10/184(5.43%)
41-50 year	62	3 (4.83%)	54	0	3/16 (2.58%)
>51 year	97	7 (7.21%)	35	1(2.85%)	8/132 (6.06%)
Total No. of Cases	311	19(6.10%)	189	2(1.05%)	21/500 (4.2%)

Table shows highest prevalence of anti HCV antibodies was observed in the age group > 51 years (6.06%), followed by 5.43%, 2.58% in 31 – 40 years age groups and 41 – 50 years age groups respectively in liver diseases patients.

Table also shows that out of 311 males, 19 (6.10%) were positive and out of 189 females, 2 (1.05%) were positive for anti HCV antibodies in liver diseases patients.

Age Wise And Sex Wise Distribution Of Hcv Sero prevalence In Liver Disease Patients

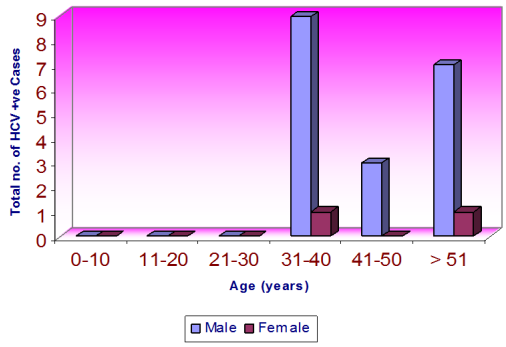
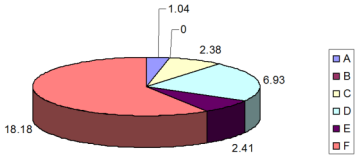


Table - 4 Sex Wise And Total No. Of Cases Wise Hcv Seroprevalence In Various Types Liver Disease

Type of liver Disease	Male		Female		Percentage (%)
	Total no. of tested	Total no. of HCV Positive	Total no. of tested	Total no. of HCV Positive	
Acute Viral Hepatitis	64	1 (1.56 %)	32	0	1/96 (1.04%)
Fulminant Hepatic Failure	17	0	11	0	0/28 (0%)
Sub acute Fulminant Hepatic Failure	23	1 (4.34%)	19	0	1/42 (2.38%)
Chronic Liver Disease	114	12 (10.52 %)	88	2 (2.27 %)	14/202 (6.93%)
Liver Cirrhosis	84	3 (3.57 %)	37	0	3/121 (2.41%)
Hepatocellular Carcinoma	9	2 (22.22 %)	2	0	2/11 (18.18%)
Total No of Tested	311	19 (6.10 %)	189	2 (1.05 %)	21/500 (4.2%)

Table shows highest prevalence of anti HCV antibodies was observed in hepatocellular carcinoma patients (18.18%), followed by 6.93%, 2.41%, 2.38% and 1.04% in chronic liver disease, liver cirrhosis, sub acute fulminant hepatic failure and acute viral hepatitis patients respectively.

Table also shows highest prevalence of anti HCV antibodies in hepatocellular carcinoma 22.22%, followed by 10.52%, 4.34% and 1.56% in CLD, SAFHF, LC and AVH in male patients respectively. HCV prevalence was seen only in chronic liver disease 2.27% in female patients.



A = Acute Viral Hepatitis
B = Fulminant Hepatic failure
C = Sub acute fulminant Hepatic failure
D = Chronic Liver disease
E = Liver Cirrhosis
F = Hepatic Cellular Carcinoma

Sex Wise And Total No. Of Cases Wise Hcv Seroprevalence In Various Types Liver Disease

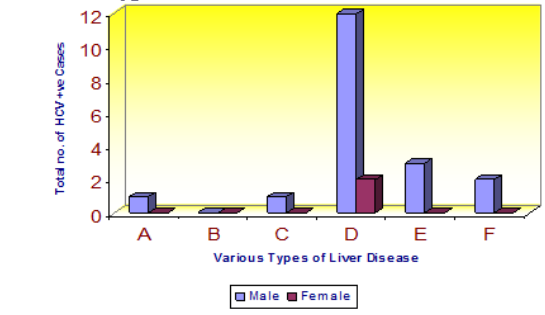


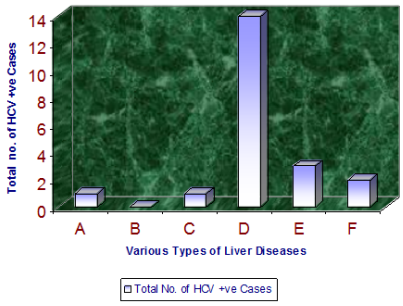
Table – 5 HCV Seroprevalence Among The Various Types Of Liver Diseases

Type of Liver diseases and the HCV Positive patients	Total No. of HCV positive cases	Percentage
Acute Viral Hepatitis	1	1/21(4.76%)
Fulminant Hepatic failure	-	0/21(0%)
Sub acute fulminant Hepatic failure	1	1/21(4.76%)
Chronic Liver disease	14	14/21(66.6%)
Liver Cirrhosis	3	3/21(14.28%)
Hepatic Cellular Carcinoma	2	2/21(9.52%)
Total No. of cases	21	21/500(4.2%)

Out of 21 HCV positive sample of liver disease patients 14 (66.6%) had chronic liver diseases, 3 (14.28%) had cirrhosis of liver, 2 (.52%) had hepatocellular carcinoma, 1 (4.76%) had acute viral hepatitis and 1 (4.76%) had sub acute fulminant hepatic failure. No case of Sub acute fulminant hepatic failure was present.

Out of total 500 sample of liver disease patient. There is total 21 sample (4.2%) were positive.

HCV Seroprevalence Among The Various Types Of Liver Diseases



A = Acute Viral Hepatitis
B = Fulminant Hepatic failure
C = Sub acute fulminant Hepatic failure
D = Chronic Liver disease
E = Liver Cirrhosis
F = Hepatic Cellular Carcinoma

DISCUSSION:

Hepatic disorders caused by HCV have become a major public health problem throughout the world affecting millions of people. It is the cause of considerable morbidity & mortality in humans both from acute infections & its chronic sequalae.HCC is one of the ten most common cancers worldwide & is the only cancer which can be prevented by vaccination. Mortality due to HCV infection is increasing at alarming rate, therefore detection of seroprevalence of HCV in hepatic disorders is very essential[18].

Table-6 Comparative Study On Hcv Seroprevalnce In Liver Disease Patients

S. No.	Author and Year	AVH %	FHF %	SAHF %	CLD %	LC %	HCC %
1	Yapi et al 1991 (Singapur) [50]	2	-	-	20	33	-
2	Singh et al 1991 (India) [45]	37.5	12.5	-	-	9	-
3	Mehta et al 1992 (India) [30]	27	38.4	-	39	-	-
4	Acharya et al 1992 [3]	0	-	-	10.5	-	-
5	Sumathy et al 1993 (Southern India) [43]	2.5	-	-	23.9	19	-
6	Narang et al 1994 (North India) [32]	3	-	-	18	2.9	20
7	V.A. Arankalle et al 1995 (Western India) [46]	0.21	-	-	5.29	-	-
8	Irshad et al 1995 (Delhi) [27]	12.5	43.6	41.6	48.5	8.8	0
9	Jaiswal et al 1996 (Central India) [47]	4.85	6.25	23.80	21.87	31.57	-
10	Gosavi et al 1997 (Mumbai) [17]	11.7	-	-	83	-	-
11	Berry et al 1998 (Delhi) [1]	-	-	-	23.5	50	33.3
12	S.Shantha et al 2002 [39]	-	-	-	16.2	12	15.8
13	Ashish Kumar et al 2004 [9]	46.75	-	-	-	12.98	-
14	Present Study 2007 (Jaipur)	1.04	-	2.38	6.93	2.47	18.18

Our findings are in accordance with various authors as above.

- The prevalence of HCV among patients of Acute Viral Hepatitis varies widely in different centres. In our region it was 1.04% while it varies in different geographic areas - 0.2% in Western India, 2.5% South India, nil, 12.5% and 37.5% in Delhi, 4.85 in Central India, 11.7% in Mumbai, 46.75% in Uttranchal, and 2% in Singapur.
- The role of HCV in the development of fulminant hepatic failure (FHF) is not well established except for reports from Japan and Taiwan where HCV is highly endemic. Reports from North India have shown anti HCV in 36 to 43.6% patients of FHF patients had anti HCV. In the present study none of FHF patients had anti HCV.
- The prevalence of HCV among sub acute fulminant hepatic failure (SAFHF) in our region was 2.38% while it varied from 23.80% in Delhi to 41.6% in Central India.
- In several parts of world the frequency of HCV in chronic liver diseases (CLD) patients has increased sharply. In the present study, it was 6.93% while it varies from 5.29% in Western India, to 10.51% and 18% in Delhi, to 23.9% in South India, to 83% in Mumbai, to 16.2% in Chennai and to 20% in Singapur.
- Surprisingly Anti HCV positivity among liver cirrhosis (LC) patients was low 2.4 percent in present study, while it was 33%, 19%, 31.57%, 12% and 12.98% in Singapur, South India, Central India, Chennai and Uttranchal respectively.
- The prevalence among Heptocellular Carcinoma (HCC) patients similar to other report. In our region it was 18.18% while it was 20%, 33.3%, 16.9%, 15.8% in North India, Delhi, Patna and Chennai respectively.

SUMMARY AND CONCLUSION:

The present study was conducted in the Department of Microbiology & Immunology; SMS Medical College Jaipur The object was assessing the seroprevalence of anti HCV antibodies in Liver Disease patients in SMS and Allied Hospital.

- The patients included in the study were of OPD and IPD from all associated hospitals of SMS Medical College reporting for diagnosis of anti HCV antibodies in Department of Microbiology from 1st January, 2007 to 30th November, 2007. The samples were collected and processed as per routine recommended methods of technical guidelines.
- In all, 500 patients were screened. The observations were made with reference to age sex, constitutional symptoms, various risk groups and investigations.
- The seroprevalence of HCV has declined since the screening of blood for donation in blood banks for anti HCV antibodies became mandatory in 1991 in some parts of the world and in India since 1997.
- HCV infection prevalence varies with geographical distribution and social characteristic of population groups.
- We observed Total no. of anti HCV antibody positive cases in our study were 4.2% in Liver Disease patients. All positive cases were above the age of 30 yrs.HCV positivity ratio among Male: Female was9.5:1(out of 311 males, 19 (6.10%) were positive and out of 189 females, 2 (1.05%) were positive for anti HCV antibodies in liver diseases patients).Highest prevalence of anti HCV antibodies was observed in the age group > 51 years (6.06%), followed by 5.43%, 2.58% in 31 – 40 years age groups and 41 – 50 years age groups respectively in liver diseases patients. HCV infection prevalence varies with geographical distribution and social characteristic of population groups
- We observed highest prevalence of anti HCV antibodies was observed in hepatocellular carcinoma patients (18.18%), followed by 6.93%, 2.41%, 2.38% and 1.04% in chronic liver disease, liver cirrhosis, sub acute fulminant hepatic failure and acute viral hepatitis patients respectively. We also observed highest prevalence of anti HCV antibodies in hepatocellular carcinoma 22.22%, followed by 10.52%, 4.34% and 1.56% in CLD, SAFHF, LC and AVH in male patients respectively. HCV prevalence was seen only in chronic liver disease 2.27% in female patients.
- Our study is a step ahead in this direction with the purpose of providing authentic scientific data based on the affected population attending our hospital.

- HCV infection is the most important cause of chronic hepatitis in several countries of the world. But at present no vaccine is available for it. Because of the increasing prevalence rate, this is necessary that medical personnel and health care workers must be educated and trained about the danger and consequences of HCV infection. All anti HCV antibody positive patients must be considered highly infectious and must be prohibited from donating blood, organ, tissues or semen. Therefore, routine screening of all the blood donors should be done in Blood Bank.
- We conclude that HCV directly affects epidemiology, morbidity, mortality, socioeconomic and preventive aspects. Infection with HCV is a growing health problem assuming epidemic proportion specially effecting young adults causing morbidity and mortality resulting in loss of man power thus badly affecting the economy of countries.There is a scarcity of information on HCV prevalence particularly in developing countries like India, the present study and other similar studies by early detection of viral prevalence for in assessment of disease burden in community, in controlling the complications of viral infections like CAH, cirrhosis and malignancies and for effective implication of preventing and curative strategies. Routinely Ag-Ab detection tests and viral assays are done.It is very important that the priority for HCV control is concentrated on early detection and effective treatment of both HCV and HBV of which may offer the greater chance of prolonging the life of those suffering from HCV infection. It is suggested that education of public at large to increase the general awareness towards the transfusion transmitted diseases and how to prevent them. Innovative diagnostic techniques that are more efficient, rapid and cost effective should be made available for both rural and urban population to identify cases as early as possible& to prevent and control the spread of this deadly virus. It is time we acted and took appropriate steps to generate public awareness about different aspects of the disease and preventive measures till we get a definite answer to the problem through an effective vaccine. This calls for stringent screening measures for blood borne viruses at departmental laboratories and blood banks for all sera/blood processed. Health care workers, especially unsuspecting surgeons and nurse are at high risk of contracting such diseases from unscreened patients, reiterating the need for universal precautions to be followed at all times.

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