

Leprosy and Hepatitis C co-infection: Epidemiological data from the Leprosarium, Srinagar, Kashmir, India

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Summary

Introduction: Leprosy early diagnosis and appropriate management remains a challenge, especially in low-source settings. Among other risk factors, viral co-infections' role in the pathogenesis and clinical outcomes are not fully explored.

Objectives: To investigate a possible outbreak and examine the co-occurrence of Hepatitis C virus (HCV) and Hepatitis B virus (HBV) in Indian leprosy patients followed at the Leprosarium, Srinagar, Kashmir, India.

Results: Out of the 187 blood samples, 79 patients followed at the leprosy hospital of Srinagar, Kashmir, India and 108 healthy controls dwellers of the leprosy colony. In total 36 patients with leprosy were found with hepatitis C seropositivity corresponding to a 45.5% (28.2% to 49.7% CI 95%). They were 26 males and 10 females, with a mean age 62.5 (\pm 11.8) years and 66.6 (\pm 10.9) years respectively. Further, all women had negative HBsAg and only one male had positive HBsAg test (1.2%).

Conclusion: HCV virus is highly prevalent in leprosy patients in Srinagar, Kashmir, India. Patients with leprosy should be monitored for hepatitis co-infections regardless of gender, age or clinical type. A tailored surveillance system is needed, particularly for the institutionalised patients.

Keywords: Leprosy, Hansen Disease, HCV, HBV, HbsAg, Risk Groups, NLEP, India

Introduction

Leprosy struck fear into human beings for thousands of years, well recognised in the oldest civilizations of China, Egypt and India and since ancient times has been regarded by the community as a contagious, mutilating and incurable disease.¹ Leprosy, caused by *Mycobacterium leprae*, can lead to scarring, deformities and disabilities.² A percentage of about 40% of patients may develop complications like neuropathy, with great impact on the quality of life of patients^{3,4} and unaffected family members⁵ along with important economic direct and indirect costs.^{3,6,7} There are still gaps in understanding the disease mechanisms² and multidrug therapy alone cannot prevent new cases.⁸

Leprosy control has improved significantly during the last decades,⁹ albeit new cases continue to occur, mainly in endemic countries in Africa, South America, and southeast Asia.^{3,10} In the United States, 90% of new cases are immigrants from developing countries¹⁰ and also in Europe incident cases emerge sporadically among refugees.¹¹ Despite progress, 250,000 new cases of leprosy are diagnosed every year globally.⁸ Notably, 60% of them are found in India.⁶ Leprosy in India was nationally eliminated by 2005 and the National Leprosy Eradication Programme (NLEP) integrated primary care services in diagnosis and treatment of the disease.¹²

The management of leprosy patients is itself challenging, especially in poor settings,¹³ and rigorous follow up of the patients is of paramount importance. Among various factors which play a role in the course of the disease, viral co-infections like HCV is not fully explored. It is suggested that the cellular deficits that immunologically characterise the disease, especially the lepromatous form, may lead to susceptibility to co morbid infections.^{14,15} Although, there is a degree of inconsistency in studies regarding different geographic areas or applied methodologies, growing evidence shows that viral co-infections add to the burden of disease.¹⁶ Still, current guidelines do not include routine screening of leprosy patients other than latent tuberculosis.¹⁰

On the other hand, Hepatitis C hepatitis (HCV), discovered in 1989,¹⁷ has nowadays an estimated worldwide prevalence of about 2.2–3% and it is considered a major source of liver disease.¹⁸ In India, the prevalence of HCV varies to the geographical area from 0.09 to 7.89%.^{18,19}

The co-infection of leprosy with hepatitis virus C (HCV) has been under research in the last decades but relevant studies in India are scarce. The objectives of our study are (i) to examine the extent of the co-infection of hepatitis C virus (HCV) in leprosy patients in Srinagar Kashmir, India, (ii) to examine whether any demographical characteristics were predictive of the co-infection and (iii) to design further actions and suggest healthy policy measures.

Methodology

POPULATION AND SETTINGS

The Leprosarium is situated along the banks of Dal Lake in Lal Bazar, Srinagar. It was established in 1891 by the British to look after leprosy patients who had been abandoned by their families. Nowadays, the 'Leper Home', as it is called, has 295 inmates with leprosy patients and their families living together. One hundred and two are enrolled with the Leprosarium as patients and 193 are members of their families. The last patient was admitted in 2000 and there have been no new cases since then in this hospital. All patients have completed their treatment but they are living in this leprosarium. A small hospital manned by one doctor and paramedics is available in the premises of the colony that takes care of the primary health needs of the patients and their families. These patients have been receiving secondary and tertiary care at SMHS and Associated Hospitals and SKIMS. The major surgeries are done in SMHS, JLN Hospital or SKIMS. All amputations are performed in Bone & Joint Hospital Barzulla, Srinagar.

The Directorate of Health Services (DHS) in Kashmir observed in January 2015 a clustering of six cases of chronic Hepatitis C in the Colony. These cases had come to the attention of the health authorities during routine testing by surgeons at JLN Hospital. In response, a survey of all the household contacts of the diseased subjects was undertaken.

SURVEY AND SCREENING

Teams from DHS Kashmir visited and surveyed the inmates four times during January and February 2015 (on 15-01-2015, 23-01-2015, 05-02-2015 and 06-02-2015). To identify the source of infection and mode of transmission in the community, the team, along with health workers from the department, organised a house-to-house survey of the villagers. A structured questionnaire²⁰ was used to determine the use of injections, blood transfusion and surgical procedures in leprosy patients and the unaffected contacts in the past 10 years.

LABORATORY INVESTIGATIONS

Blood samples were taken from all the subjects who were screened by the one step card test for anti HCV (SD Bioline Rapid Immunochromatographic test for antibody IgG). Those samples found positive were further tested by the third generation ELISA (ERBA LISA Enzyme Linked Immunosorbent assay for detection of IgG) for detection of antibodies to Hepatitis C virus in human serum and plasma at JLN Hospital, Srinagar. In addition, all subjects were tested by one step HbsAg antigen test. The samples were further analysed for genotyping and viral load and genotype 3a was detected.

STATISTICAL ANALYSIS

The statistical analysis was performed using Chi Square for categorical variables, and t-test for continuous variables. The data were expressed as mean \pm standard deviation (SD). Frequencies are expressed as percentages. The criterion for significance was 0.05. All analysis was performed by using Statistical Package SPSS 22v.

Table 1. Composition of patients and healthy contacts in the Colony and HCV seropositivity percentages

	(N) (%)
Total population	295 (100%)
Leprosy patients	102 (34.5%)
Healthy contacts	193 (65.5%)
Total samples collected	187 (63.4%)
Samples from leprosy patients	79 (77.4%)
Samples from healthy controls	108 (55%)
HCV positive	36 (19.2%)
HCV positive in leprosy patients	36/79 (45.5%)
Healthy contacts with HCV	0 (0%)

APPROVAL OF THE STUDY

All patients and controls signed a written informed consent before the interviews and the sampling for laboratory examination. The study was under the approval of the Directorate of Health Services, Kashmir, India.

Results

Out of 295 dwellers of the colony, 187 samples were taken (63.3% response rate) and tested for Hepatitis C and Hepatitis B. We found 36 patients with leprosy that had Hepatitis C seropositivity. This corresponds to 45.5% (28.2% to 49.7% CI 95%) of the leprosy patients of the study area. No Hepatitis C case was found in healthy controls (Table 1, Figure 1).

Statistically significant differences were observed between the genders of HCV seropositive patients (P value = 0.04). The mean age of males and females were age 62.5 (± 11.8) years and 66.6 (± 10.9) years ($P = 0.34$), and they all came from the same geographical area and belonged to Kashmiri muslim ethnicity. Additionally, only one male had a positive HbsAg test (3.8%). Table 2, and Figures 2 and 3 present the HCV and HbsAg seropositivity variation in leprosy patients among genders.

A single transmission route was not apparent in the majority of cases (Table 3).

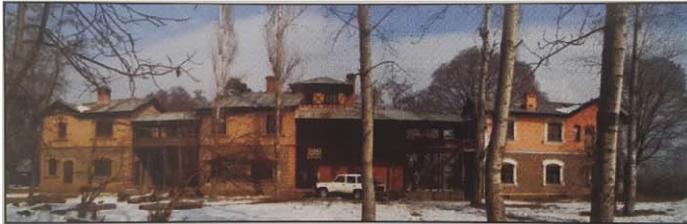
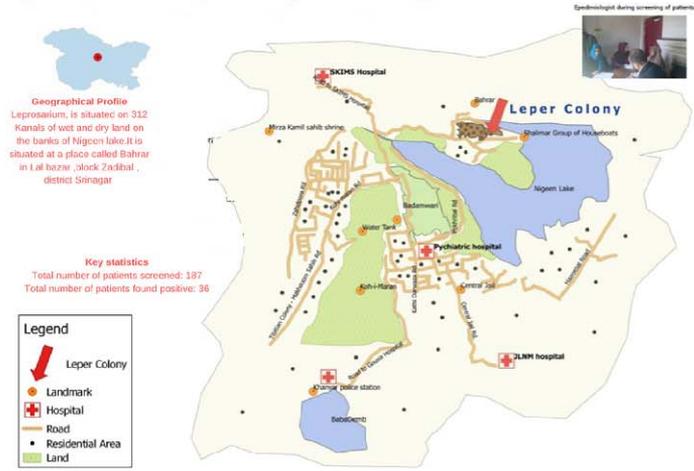
PREVENTION MEASURES

The following steps were made towards prevention of secondary spread: (a) a large scale health education programme was launched in the Leprosarium to increase awareness among people regarding the HCV and how to prevent it; (b) targeted counseling was done to seropositive patients to prevent the spread of disease to their contacts, and (c) we strongly recommend vaccination against Hepatitis B in this population, as there is no vaccine yet against Hepatitis C.

Discussion

In this paper, we present the results of a HCV coinfection survey in well-demarcated, isolated population of leprosy patients living in an institution for the past 30 years. Our main result is

Hepatitis B and C investigation at Leprosarium, Srinagar, Kashmir, India



Leprosarium, Kashmir, India



Leprosy patients in the Leprosarium showing various types of deformities

Figure 1. Map of affected zone of HCV, Leprosarium, Srinagar, Kashmir, India.

Table 2. HCV and HbsAg seropositivity variation in leprosy patients among genders

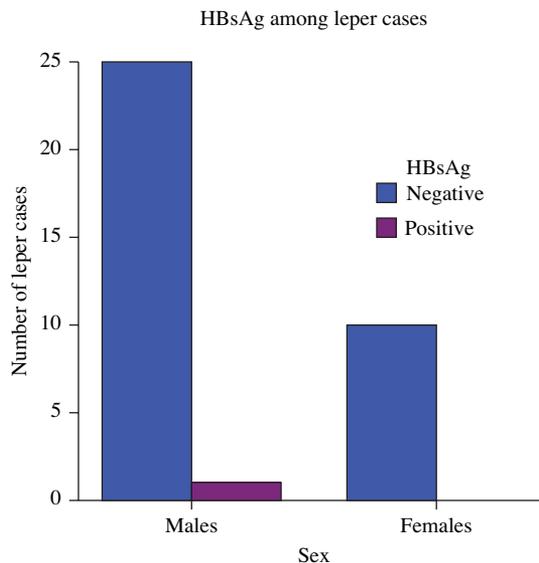
Tests	Gender N (%)		P-value
	Males	Females	
HCV Positive	26 (63.4%)	10 (26.3%)	0.04 ^a
HbsAg Positive	1 (26%)	0 (0)	0.04 ^a

A Chi-Square test (two-tailed, $\alpha = 0.05$).

that leprosy patients are at a substantial higher risk of HCV infection in contrast with their health counterparts. We report the occurrence of HCV infection in this cohort of leprosy patients at an astonishing percentage of 45.5% (28.2% to 49.7% CI 95%).

As far as the interpretation of this high co-occurrence of HCV, as there is no test which that can actually differentiate between acute and chronic HCV infections, theoretically it could be an outbreak among the leprosy patients or it an infection acquired decades back due to blood transfusions and then amplified in the community. But some assumptions could be made to explore the situation. First, we must not lose sight of the fact that these inmates have multiple morbidities and need care at various hospitals in the state. The fact that no healthy person staying in the area had the virus shows that probably is from procedures that mostly affect patients. Frequent exposure to unsafe injections and surgical practices in the hospitals, dental clinics and within families would greatly amplify the risk of getting infected.

During our visit to the leprosarium we found that disposable syringes and sterile dressing material are being used, but the exact sterilisation status i.e whether glass syringes were boiled or blood and blood products were tested during previous years remains largely unknown. The inmates could have got the infection almost anywhere: at dental clinics, in the

**Figure 2.** Frequency of HbsAg among leprosy patients per gender ($P = 0.04$).

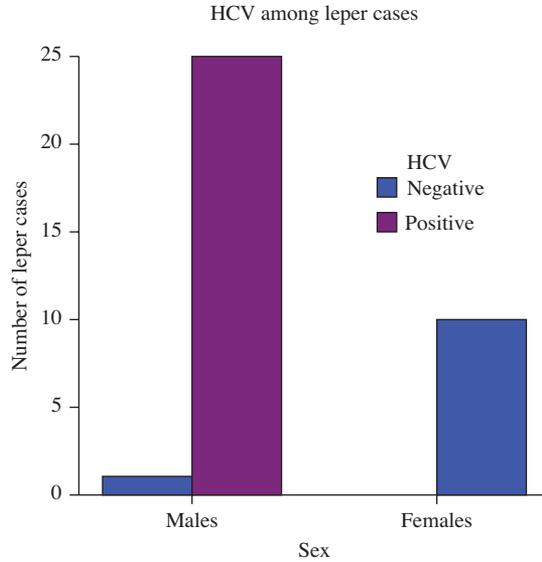


Figure 3. Frequency of HCV among leper patients per gender ($P = 0.04$).

hospitals, through blood transfusions or through unsafe injections because of their higher exposure to surgeries. The use of disposable syringes, mandatory screening of blood and blood products is a recent phenomenon in the state. Since leprosy is a dermatological condition, these patients require repeated dressings of wounds. The long-term use of unsterilised reusable syringes and instruments is a key to spread of blood borne infections. Further, the amplification of the infection among leprosy patients within the closed community is possible because of shared space, shared instruments and syringes.

Among leprosy patients, a high prevalence of HCV infection has been reported by different authors around the world. In a study in southern Brazil¹⁵ anti-HCV antibodies found positive in a percentage of 3.52% (seven out of 199) patients with leprosy and in 0.15% of the controls corresponding to an odds ratio (OR) = 24.79; (95% CI = 3.03–202.74; $P = 0.0002$). It is also notable that the risk of HCV infection observed in institutionalised patients was increased (OR = 14.95; 95% CI = 1.76–127.03; $P = 0.004$) as well as in the lepromatous form of the disease (OR = 7.67; 95% CI = 0.43–136.62; $P = ns$) versus other

Table 3. Risk Factors associated with acquiring Hepatitis C among leprosy patients

Risk Factor	Leprosy patients sampled N = 79	Leprosy patients HCV Positive N = 36	Leprosy patients HCV negative N = 43	Healthy Contacts N = 108
Surgery	28	16	12	30
Blood transfusion	4	2	2	6
Injections in past IM/IV	54	28	24	53
Dental procedures	50	32	25	60
Promiscuous sexual activity	0	0	0	0
IV drug abuse	0	0	0	0

forms. Authors conclude that interactions of leprosy and hepatitis C should be monitored, especially in case of institutionalization.¹⁵

The prevalence of anti-HCV was also examined in 1309 leprosy patients and a control group of 1469 subjects from six sub-Saharan African countries and the Yemen.²¹ HCV seropositivity was 7.1% in leprosy patients which was significantly higher than in the control group (2.6%) and increased with age in both. No statistically significant differences were reported between anti-HCV seropositivity and the various clinical types of leprosy.²¹

To our knowledge the previous studies regarding hepatitis C coinfection with leprosy in India are limited and non updated. One study conducted in Pune and Bombay metropolitan areas were patients from different risk groups were tested for anti-HCV. Leprosy patients had almost 0.7 per cent HCV seropositivity.¹³

India has an estimated burden of 8.6 million HCV carriers of whom about one third will develop hepatocellular carcinoma.^{22–24} Twenty percent of chronic liver disease in the country is due to hepatitis.^{25,26} The predominant genotype in India is three and it is transmitted mainly through blood transfusions, suboptimal injection practices, and other health-related procedures.^{27,28} Leprosy being a dermatological disease with many secondary infections, patients' skin and wounds were cared for with reusable syringes, needles bandages and surgical instruments and there were many chances for staff and patients to come into contact with blood without adequate sterilisation. A similar situation can be seen here in the leprosarium in Kashmir where the community lives in isolation and numerous injections, surgical procedures and dressings carried out over the last 20–30 years with sub-optimal sterilisation provided numerous opportunities for infection. A recent outbreak in the same area showed a 38.8% of HCV in the general population villages and dental procedures were a statistically significant risk factor.²⁰

Although our research has the limitation of a small power sample size to draw solid conclusions, it has also several strengths. It gives an updated insight for the co-occurrence of the two diseases leprosy and hepatitis in a Leprosarium in India. First, this can further enlighten the current needs of patients' neglected diseases like leprosy. The inmates of the colony are poor and socially the most ostracised population. These patients have extreme forms of leprosy with disfigurement and amputations and have been abandoned by their families. Public Health Care providers are bound to provide some relief to patients who require treatment and this is of paramount importance when the patients are under privileged. In addition, the goal of therapy is not only to prevent complications and death from HCV infection but also prevent further spread of infection.²⁸

Conclusion

Leprosy patients of both genders can be at high risk for HCV virus especially in poor and industrialised settings. Routine screening of patients with leprosy for hepatitis co-infection regardless of gender, age or clinical type should be considered. Secondary and tertiary prevention is needed in order to improve survival of HCV affected patients.

Reconstruction of leprosaria could transform them into reference centres up to the unmet needs of patients (i.e. for rehabilitation) but also up to the standards of the healthcare community so that they can be used as reference centres for rigorous training and high quality research on leprosy.

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4. Mr. Imtiaz Amin (State DM)
5. Ms. Irfana Bhat (State DEO)

List of abbreviations

HCV Hepatitis C virus

HBV, HbsAg Hepatitis B surface Antigen

NLEP National Leprosy Eradication Programme

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