



# Consensus Statement of HCV Task Force of the Indian National Association for Study of the Liver (INASL). Part I: Status Report of HCV Infection in India

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Globally, around 150 million people are infected with hepatitis C virus (HCV). India contributes a large proportion of this HCV burden. The prevalence of HCV infection in India is estimated at between 0.5% and 1.5%. It is higher in the northeastern part, tribal populations and Punjab, areas which may represent HCV hotspots, and is lower in western and eastern parts of the country. The predominant modes of HCV transmission in India are blood transfusion and unsafe therapeutic injections. There is a need for large field studies to better understand HCV epidemiology and identify high-prevalence areas, and to identify and spread awareness about the modes of transmission of this infection in an attempt to prevent disease transmission. (J CLIN EXP HEPATOL 2014;4:106–116)

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Abbreviations used: CH-C: chronic hepatitis C; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HCV: hepatitis C virus; HIV: human immunodeficiency virus; INASL: Indian National Association for Study of the Liver; IV: intravenous; IVDU: intravenous/injecting drug user

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Hepatitis C virus (HCV) infection has an estimated global prevalence of 2%–3%, with approximately 122–185 million HCV-infected persons worldwide.<sup>1–7</sup> Based on prevalence of anti-HCV antibody, different areas of the world are categorized as ‘high’ prevalence (>3.5%), ‘moderate’ prevalence (1.5%–3.5%), or ‘low’ prevalence (<1.5%). Prevalence of HCV infection in India has been variously estimated as 0.9 and 1.9%.<sup>8,9</sup> Since India has one-fifth of the world’s population, with either of these estimates, it would account for a large proportion of the worldwide HCV burden. Thus, it is imperative to reliably determine the burden of HCV disease in India, to identify any hotspots of this infection in the country, and to

**Table 1** The ‘Grading of Recommendations Assessment, Development and Evaluation (GRADE)’ System for Grading Level of Evidence and Recommendations.

|                            | Grade        | Criteria  |
|----------------------------|--------------|---|
| Strength of recommendation | Strong [1]   | Factors influencing the strength of the recommendation included the quality of the evidence, presumed patient-important outcomes and cost   |
|                            | Weak [2]     | Variability in preferences and values, or more uncertainty. Recommendation is made with less certainty, higher cost or resource consumption |
| Quality of evidence        | High [A]     | Further research is unlikely to change confidence in the estimate of the clinical effect  |
|                            | Moderate [B] | Further research may change confidence in the estimate of the clinical effect   |
|                            | Low [C]      | Further research is very likely to impact confidence on the estimate of clinical effect   |
|                            | Very Low [D] | Very low quality — any estimate of effect is very uncertain   |

understand the risk factors associated with transmission of this infection. This would also allow appropriate choice and targeting of efforts to prevent the spread of this disease, and thereby reduce the burden of chronic liver disease in the country.

India does not have a national or regional registry for HCV infection. This review is therefore based on published reports from India as well as data collected by the Indian Association for Study of the Liver (INASL) Task Force on HCV; the latter include data collected from hepatologists, blood banks in northeastern India, thalassemia units and from an online data registry created specifically for this purpose.<sup>10</sup>

The available evidence and recommendations were graded based on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system for evaluating evidence.<sup>11</sup> In this system, quality of evidence is rated as A-D and the recommendations as 1 or 2 (Table 1).

## EPIDEMIOLOGY OF HEPATITIS C VIRUS IN INDIA

Population-based studies on prevalence of HCV infection in India are scarce. Most of the available data on the issue thus are based on blood bank screening, which may not be a reliable indicator of the true infection rate. The data from these studies show wide geographic variations, which may represent a true variation in prevalence due to differences in socio-economic status or cultural and healthcare practices in different regions, or variations in donor populations studied or test kits used for screening.

### Population Studies

The population-based studies have mostly been from rural and tribal populations, often from very restricted geographical areas. In addition, these are limited by use of flawed sampling techniques, and small sample sizes; thus, data from these studies are quite likely to be non-

representative of the true prevalence of HCV in the particular region or of the country.

In a good-quality field study, Chowdhury et al<sup>12</sup> assessed the prevalence of anti-HCV antibodies in 9 villages in Birbhum district of West Bengal. Of the 3579 individuals who were randomly selected from among 10,737 inhabitants of these villages, 2973 agreed to participate. Anti-HCV seroprevalence in these subjects was 0.87%, with the highest rate recorded in those aged >60 years.

In a study of 5258 subjects from Mullanpur, Punjab, with a mixed urban and rural population, Sood et al<sup>13</sup> reported anti-HCV prevalence of 5.2%, with the highest rate in the 40–60 year age group and significant clustering within families. In another study from the neighboring state of Haryana, Sachdeva et al<sup>14</sup> screened 1,50,000 residents of Fatehabad district for anti-HCV and found a population prevalence of 1%; in addition, they screened a select group of 7114 persons who were at a high risk of HCV (high risk behavior or high risk exposure), had history of prior jaundice or voluntarily came for screening. They found a seroprevalence of 21% [1505/7114].

Singh et al<sup>15</sup> screened 22666 trainees of Indian Armed Forces in 25 training centers selected by multistage random sampling, giving equal representation to all regions of India. They found an anti-HCV point prevalence of only 0.44%; they explained this low rate on exclusion of those who may be at risk for HCV infection from recruitment as military trainees.

In a study from rural Maharashtra ( $n = 1054$ ), Chadha et al<sup>16</sup> reported a prevalence rate of only 0.09%. In a recent HCV screening camp for general public in Puducherry, only 2 of 978 (0.2%) persons tested positive for HCV.<sup>17</sup> In Hyderabad, prevalence of HCV in similar gastroenterology camps ( $n = 704$ ) was 1.4%.<sup>18</sup>

### Studies in Tribal Populations

There are a few studies from tribal populations in India. In these, prevalence of anti-HCV antibody was found to be

**Table 2 Published Data on Anti-HCV Antibody Prevalence Among Patients with Thalassemia in India<sup>a</sup>.**

| Author                           | Year of publication | Geographic location | n   | % Anti-HCV positive |
|----------------------------------|---------------------|---------------------|-----|---------------------|
| Bhattacharya et al <sup>63</sup> | 1991                | Calcutta            | 73  | 14.3                |
| Amarapurkar et al <sup>64</sup>  | 1992                | Mumbai              | 40  | 17.5                |
| Williams et al <sup>65</sup>     | 1992                | Delhi               | 54  | 11.1                |
| Agarwal et al <sup>66</sup>      | 1993                | Mumbai              | 72  | 16.7                |
| Choudhry et al <sup>67</sup>     | 1995                | Delhi               | 102 | 30.3                |
| Irshad et al <sup>68</sup>       | 2002                | New Delhi           | 50  | 30                  |
| Marwaha et al <sup>69</sup>      | 2003                | Chandigarh          | 149 | 54.4                |
| Chakravarti et al <sup>70</sup>  | 1994                | Delhi               | 50  | 62                  |
| Mishra et al <sup>71</sup>       | 2004                | New Delhi           | 75  | 27                  |

<sup>a</sup>All data prior to mandatory HCV screening of blood, which started in June 2001.

7.89% in Lisu community in Changlang District of Arunachal Pradesh,<sup>19</sup> 2.02% in Lambada tribe in Andhra Pradesh,<sup>20</sup> and 1.0%-14.4% in seven central Indian tribes (viz. Baigas, Bharias, Saharias in Madhya Pradesh and Abujhmarias, Hill Kowas, Kamars and Birhors) in Chhattisgarh.<sup>21</sup> The prevalence was very high (14.4%) in the Bharia tribe. Cultural practices such as tattooing, traditional medical practices such as blood letting and scarification/branding, and closed community marriages may explain the higher prevalence of HCV infection in these groups.

### Blood Bank Data

Blood bank data form the largest source of data on prevalence of HCV in India. In these data, anti-HCV prevalence was 0.29%-1.85% in northern states, 0.08%-1.4% in southern states, 0.27%-1.17% in northeastern states and 0.31-1.09% in eastern states. In contrast, data from the western Indian states show a lower prevalence of 0-0.9% except for a few reports with higher prevalence.<sup>22-57</sup> In a study from an armed forces blood bank, representing 39,646 blood donors from all over the country, the prevalence was 0.51%.<sup>58</sup> The prevalence rate is higher in professional blood donors than in voluntary donors.

There is a common perception that there is a high seroprevalence of HCV in the northeast, especially since a high prevalence has been seen in intravenous drug users (IV-DUs), HIV and in the Lisu tribe. However, blood bank data from the northeast show seroprevalence rates ranging from 0% to 1.97%, with most blood banks reporting a rate around 1.5% (Kamal Chetri, personal communication). This prevalence rate is only somewhat higher than that in the rest of the country. Similarly, in Punjab, in contrast to the high prevalence rate reported in a population-based study by Sood et al,<sup>13</sup> blood bank data shows a lower prevalence. These low HCV prevalence rates in blood donors in Punjab as well as the northeast may be related to the fact that blood donors are a select group that differs systematically from the general population, because persons with

history of liver disease, known HCV infection, or even risk factors for HCV infection may either not volunteer for blood donation or may fail the strict prescreening by blood banks. Use of different anti-HCV test kits with variable sensitivities and specificities may also contribute to variations in HCV seroprevalence.

### Pregnant Women

Prevalence of HCV antibodies in pregnant women has ranged from 0.6% to 1.4%.<sup>59-61</sup>

### Consensus Statement

1. *Data on HCV prevalence from India is limited with few population-based studies and is mostly based on blood bank data. The estimated prevalence of HCV in India is between 0.5 and 1.5% with higher prevalence in the northeast, in tribal populations and in Punjab and a lower prevalence in Western India and Eastern India (Strength-2, Level of evidence-C)*
2. *Larger epidemiological studies from India are required to identify high-risk areas where concentrated efforts are required to prevent disease transmission (Strength-1, Level of evidence A)*

### RISK FACTORS AND TRANSMISSION IN HIGH-RISK PERSONS

Parenteral transmission is the most important route of transmission of HCV. This most commonly occurs through transfusion of infected blood or blood products, intravenous drug use, unsafe therapeutic injections, occupational (needle-stick) injuries or nosocomial transmission during healthcare related procedures such as surgery, hemodialysis and organ transplantation. Injection drug use, which is the predominant mode of transmission of HCV infection in several developed countries, is not as widespread in India being encountered in only a few

**Table 3 Unpublished Data on Anti-HCV Antibody Prevalence in Patients with Thalassemia Major (Collected by INASL Task Force on HCV<sup>10</sup>).**

| Center                          | Number studied | Anti-HCV positive, number (%) |
|---------------------------------|----------------|-------------------------------|
| Mumbai<br>(12 day care centers) | 953            | 118 (12.4)                    |
| Chennai                         | 206            | 31 (15.0)                     |
| Hyderabad                       | 1500           | 8 (0.5)                       |
| Lucknow                         | 242            | 28/242 (11.6)                 |
| Ludhiana                        | 192            | 58 (30.2)                     |
| Total                           | 3159           | 243 (7.7)                     |

limited pockets. The predominant modes of transmission of HCV in India thus are likely to be unsafe therapeutic injections and blood transfusion.

### Transfusion of Blood and Blood Products

This route accounts for most of the HCV transmission in India. Compulsory screening of blood in the blood banks in India started only in the year 2001, i.e. later than in the developed world. A survey of blood transfusion practices showed that screening for transfusion-transmitted infections is unsatisfactory, often poorly regulated, and enforcement of existing guidelines is poor.<sup>62</sup>

Patients with thalassemia who receive blood transfusions every 1–4 weeks are at high risk of acquiring HCV infection. Several prevalence studies of hepatitis C in thalassemic patients, most of which included patients who received transfusions prior to 2001, have reported prevalence rates of 11.1%–62% (Table 2).<sup>63–72</sup> Despite mandatory screening since 2001, transfusion related HCV transmission has not been eradicated. Makroo et al<sup>73</sup> studied 462 patients in Delhi and found HCV infection in 107 (23.1%); 24.3% of those who tested positive for anti-HCV antibodies had been transfused after 2001, when mandatory testing for anti-HCV in transfused blood was implemented. Other recent studies in multi-transfused thalassemia patients have shown HCV prevalence rates of 2%<sup>74</sup> to 15%.<sup>75</sup> This disparity may reflect differences in the nature of blood donor pool (voluntary, replacement or remunerated), prevalence of HCV infection among donors, type of test kits used for blood-bank screening, nature of care of thalassemia patients, association of high transfusion rate with better survival.<sup>76</sup>

The INASL task force collected data from 5 centers around the country (THINK Foundation in collaboration with Children's Liver Foundation in Mumbai, Thalassemia and Sickle society, Hyderabad; DMC Hospital, Ludhiana; SGPGI, Lucknow; and the Thalassemia Welfare Association, Chennai). Of the 3159 patients for whom data were avail-

able, 243 (7.7%) had anti-HCV antibodies with rates varying from 0.5 to 30% in different centers. This was 5–15 times higher than the rate in the general population. In Hyderabad, the prevalence rate was lower than that in the general population (Table 3). In a subset of patients where data on time of start of transfusions were available, the prevalence rate has declined from 22.5% among those who received transfusions prior to 2001, when mandatory testing for anti-HCV was introduced in blood banks, to 13.6% among those who received transfusions only thereafter.<sup>10</sup>

International guidelines suggest that thalassemia patients who received blood transfusion before 1992 should be tested for anti-HCV antibodies and that thalassemia patients with elevated serum aminotransferase levels for more than 6 months should be tested for anti-HCV, as in done for general population.<sup>77</sup>

The Task Force felt that thalassemia patients in India should be tested for anti-HCV annually, until prevalence of HCV infection in this group comes down (Level 2B).

A high prevalence rate of HCV infection has also been reported in persons with hemophilia.<sup>78</sup>

### Unsafe Injection Practices

Worldwide, unsafe injections are estimated to cause nearly two million new HCV infections annually.<sup>79</sup> In India, injections overprescribed and unsafe injection practices are common.<sup>80,81</sup> Injections are often used unnecessarily for common self-limiting illnesses, with illiterate patients often demanding injections believing these to be more efficacious than the oral route. The annual frequency of injections is estimated as 2.9 per person, almost double of that in developed countries.

Of the nearly 3.0 billion injections are administered annually in India, 1.89 billion are estimated to be unsafe due to inadequate sterilization, use of faulty techniques or unsatisfactory injection waste disposal.<sup>82</sup> Unsafe therapeutic injection practices include the use of reusable glass syringes, contaminated multi-dose vials or saline bags from reinsertions of used needles and syringes, the use of one needle or syringe to administer intravenous medication to multiple patients, and the use of one spring loaded finger stick device to monitor blood sugar levels in multiple patients. In one study, 31% of patients who had received multiple injections for Kala Azar were found to have HCV infection.<sup>83</sup>

It has been estimated that 38% of HCV infections in India may be attributable to unsafe medical injections.<sup>84</sup>

### Transmission by Intravenous Drug Abuse

India has an estimated 1.1 million injection drug users (IV-DUs).<sup>85</sup> A community-based surveillance study of IVDUs in Kolkata showed an increase of anti-HCV seroprevalence from 17% to 80% over a 7-year period despite an ongoing needle-exchange programme.<sup>86</sup>

Though prevalence of HCV infection among IVDUs in most Indian states is 30%–50%, a higher prevalence has been reported from the northeastern states.<sup>87–100</sup> States that share a border with Myanmar, i.e. Manipur, Nagaland and Mizoram, have a large number of IVDUs.<sup>101</sup> Prevalence of HCV infection among IVDUs varies between these states, with a lower prevalence rate in Nagaland (5.4–29.9%)<sup>91,94</sup> than in Manipur (56%–98%)<sup>91,93,95</sup> and Mizoram (71%).<sup>96</sup> These differences may be related to number and type of drugs used (higher with heroin and multiple drugs), frequency of injections, degree of syringe sharing, practice of injecting at dealer's place, and duration of injection drug use. In Manipur, majority of IVDUs injected heroin whereas the main injection drug used in Nagaland was dextropropoxyphene.<sup>91</sup>

### **Perinatal Transmission**

Nearly 25% of infants born to HCV RNA-positive pregnant women have been reported to develop HCV infection.<sup>59,61</sup>

### **Sexual Transmission**

Transmission from an infected person to family member may occur through sexual, vertical or horizontal routes, and may be more frequent between spouses than between the non-sexual contacts. Although acquisition of HCV by sexual route is not as efficient as the parenteral route, sexual transmission of HCV from female sex workers may pose a risk to the community. Barua et al<sup>102</sup> found HCV infection in 9.6% of 426 female sex workers in Dimapur district of Nagaland. The higher HCV positivity in this group may have been contributed by the accompanying HIV infection. Sexual transmission of HCV infection is more efficient in presence of ulcerative sexually-transmitted infections and homosexual practices.<sup>103</sup> However, in a survey of men who have sex with men in eight cities in Tamil Nadu, HCV infection was uncommon (1/721).<sup>104</sup> Sexual transmission of HCV has been shown to be infrequent (0.68%) in sexually transmitted disease clinics in Pune, Maharashtra.<sup>105</sup> Solomon et al<sup>106</sup> also found that heterosexual transmission of HCV is infrequent (0.5%).

### **HIV Infection**

The prevalence of HCV in HIV-infected persons has ranged between 1.3 and 4.72%. In southern India, prevalence of HCV infection among HIV-infected persons is higher than that in northern India.<sup>107–112</sup> HCV-HIV co-infection is commoner in patients with low CD4 counts (<200/ $\mu$ L)<sup>109</sup>

### **Occupational Exposure in Healthcare Workers**

Healthcare workers are at increased risk of acquiring HCV infection. The prevalence of HCV infection in healthcare workers has ranged from 0% to 4%, and is higher among staff working in hemodialysis units.<sup>113–116</sup>

### **Dialysis and Renal Transplantation**

In patients undergoing hemodialysis and/or kidney transplantation, HCV infection is a leading cause of liver disease, and is a significant risk factor for graft loss and excess mortality. HCV infection is also associated with various forms of glomerular injury, such as cryoglobulinemic glomerulonephritis, membranoproliferative glomerulonephritis, focal-segmental glomerulosclerosis and membranous glomerulonephritis.<sup>117</sup>

Patients receiving dialysis have been found to have a high risk of HCV infection, with anti-HCV antibody prevalence of 4.3%–46%.<sup>118–124</sup> Occult HCV infection has been reported to range from 79.16 to 90%.<sup>125,126</sup>

The prevalence of HCV infection in renal transplant recipients in India has been reported to be 26.2%–55.9%.<sup>127,128</sup> ‘Holiday Hemodialysis’ resulting in imported HCV has been reported in UK citizens returning from a holiday in the Indian subcontinent.<sup>129</sup>

## **PREVENTION OF HCV INFECTION**

Treatment of HCV is costly, associated with significant adverse events, and has limited efficacy, making prevention particularly important. Currently, no vaccine against HCV infection is available. High-risk individuals include IVDUs, persons who receive blood transfusions, acupuncture, tattooing, unsafe injection practices, etc. HCV transmission in hospitalized patients may follow blood transfusions, medical procedures, unsafe medical practices and needle-stick injuries. Reuse of single-use accessories is common due to cost constraints. It is important to ensure adequate sterilization of such accessories.

### **Avoiding Unsafe Injection Practices**

Healthcare workers should be educated about the need to avoid unnecessary injections and to adopt safe injection practices to prevent the spread of HCV and other blood-borne infections. Safe injection practices include the use of aseptic technique, not to reuse syringes or fluid infusion sets for multiple patients, and use of proper precautions when single-dose vials are used.

### **Prevention in IVDUs**

IVDUs need to be educated about mechanisms of HCV transmission and to avoid sharing of needles and syringes. In one study from Kolkata, needle exchange program among IVDUs was shown not to be beneficial.<sup>86</sup> One meta-analysis on the subject found insufficient evidence that interventions such as provision of sterile injecting equipment are effective in reducing transmission.<sup>130</sup> There should therefore be a greater stress on education of persons with IVDU about transmission of infection and to avoid sharing of needles and syringes.

## Provision of Safe Blood and Blood Products

Transmission of HCV infection in India does occur, though it has declined with introduction of mandatory testing of blood for anti-HCV since 2001. The quality of test kits used for anti-HCV testing may be a reason for concern, since some test kits used in limited-resource countries including India has been found to be unsatisfactory.<sup>131,132</sup>

Use of nucleic acid testing (NAT) has been evaluated for preventing transmission of HCV as well as other blood borne pathogens (human immunodeficiency virus-1 and hepatitis B virus) in Indian blood donors has been proposed. It has been estimated that NAT could interdict 3272 infections annually among nearly 5 million annual donations.<sup>133,134</sup> This strategy however, while making blood transfusions safer, would add considerably to the cost of blood screening. It is therefore not routinely recommended. A more important issue is curbing the unnecessary use of blood transfusions, where these are not clearly indicated.

## Other Preventive Measures

Spread of HCV through body piercing, acupuncture and tattooing, etc. needs to be addressed by health education about preventive measures.

Transmission of HCV infection in hemodialysis units and other healthcare settings can be reduced by following universal precautions.

## Consensus Statement

3. *Unsafe therapeutic injections and transfusion of unsafe blood are the predominant mode of transmission of HCV in India (Strength-2, Level of evidence-C)*
4. *IVDUs have a higher prevalence of anti-HCV than general population (Strength-2, Level of evidence-B)*
5. *An awareness campaign of safe injection practices is required to prevent the spread of HCV (Strength-1, Level of evidence-A)*
6. *Blood transfusion related HCV transmission can be addressed by avoiding unnecessary blood transfusions, audit of blood banks and standardization of the kits being used (Strength-1, Level of evidence-C)*
7. *The following should be screened for HCV infection:*
  - a. *All persons who received blood transfusions before 2001, when mandatory HCV testing in blood banks was introduced (Strength-1, Level of evidence-A)*
  - b. *Unexplained chronic liver disease (Strength-1, Level of evidence-C)*
  - c. *High risk behavior*
    - i. *IV drug use (Strength-1, Level of evidence-A)*
    - ii. *HIV infected individuals (Strength-1, Level of evidence-A)*
  - d. *High risk exposure*

- i. *Hemodialysis (Strength-1, Level of evidence-A)*
- ii. *Organ transplant recipients (Strength-1, Level of evidence-A)*
- iii. *Healthcare workers in instances of exposure to needlesticks, sharps or mucosal exposure to blood (Strength-1, Level of evidence-A)*
- iv. *Thalassemics (annually) (Strength-2, Level of evidence-B)*
- e. *Children borne to HCV positive mothers (Strength-1, Level of evidence-D)*

## GENOTYPES DISTRIBUTION OF HCV IN INDIA

Genotype of HCV is a major predictor of response to anti-viral therapy. In published studies genotype 3 is the commonest genotype in India, accounting for 54%–80% of cases.<sup>135–143</sup> Within genotype 3, subtype 3a has been the most frequent in most studies, but a recent report found subtype 3b to be the most prevalent.<sup>144</sup> Studies from northern, eastern and western India have uniformly shown predominance of genotype 3; however, in southern India, both genotype 1 and 3 HCV are prevalent.<sup>110,145</sup> Genotype 4 HCV has been identified in some cases from southern and western India.<sup>139,141,146</sup> Genotype 6 HCV infection has been reported from eastern and northeastern parts of India.<sup>147,148</sup> In a study of 75 isolates from the northeastern part of India with a predominant tribal population, genotype 4 was reported to be to be the commonest genotype (31%) with genotype 6 accounting for 13.6% of cases.<sup>148</sup> Two cases of genotype 5a have also been reported.<sup>10,149</sup>

Overall, genotype 3 is the most prevalent HCV genotype in India.

## Consensus statement

8. *Genotype 3 is the most common HCV genotype in India, followed by genotype 1. Genotype 1 has been reported more commonly from southern India than from other parts of the country and there are increasing reports of genotype 4 from India (Strength-1, Level of evidence-B)*

## NATURAL HISTORY OF HCV IN INDIA

Majority of acute HCV infections are asymptomatic. Persistent HCV infection occurs in 50%–90% of those with acute infection. Mortality associated with CH-C infection results mainly from the development of liver cirrhosis and its complications.<sup>150</sup> The predominant genotype in India is genotype 3. In a Swiss study, genotype 3 HCV infection was associated with accelerated fibrosis progression compared to infection with other HCV genotypes.<sup>151</sup>

Comparison of natural history of HCV infection in United Kingdom among persons originating from the Indian subcontinent with a group of White patients showed

that Asian patients were more likely to be older, female, infected with genotype 3 and to not consume alcohol. The Asian patients had a significantly higher fibrosis score at the time of first biopsy ( $3.0 \pm 2.3$  vs.  $1.8 \pm 2.0$ ,  $P < 0.001$ ) and higher necro-inflammation and steatosis scores. In those patients where duration of infection could be estimated, fibrosis progression was similar for both groups ( $0.25 \pm 0.31$  vs.  $0.16 \pm 0.54$  Ishak points/year,  $P = 0.068$ ). The higher fibrosis scores on biopsy seen in Asian patients was explained by the longer duration of infection and the older age.<sup>152</sup> The major acceleration of the disease process occurs after 40 years of age and severe fibrosis/cirrhosis has been seen in 74.24% of patients above 40 years of age as compared to 33.3% of patients below 40 years ( $P = 0.001$ ).<sup>137</sup>

Data on natural history on HCV infection, and its progression to cirrhosis, in India are very scanty. A study from India showed that the median time to develop cirrhosis was 20 years, and progression to cirrhosis was faster (16 vs. 20 years) in those who acquired infection after the age of 35.<sup>153</sup> Hissar et al<sup>154</sup> reported a median rate of fibrosis progression in Indian patients with chronic HCV infection of 0.25 (0.0–1.5) fibrosis units per year, suggesting that it would take 16 years for cirrhosis to develop. A higher histological activity index and longer duration of infection were shown to be associated with a significant risk of advanced liver disease. They found that the rate of fibrosis progression was slower in individuals younger than 30 years and higher in older patients. The median duration of progression to cirrhosis was faster (12.1 vs. 6.7 years) in those who acquired infection after the age of 30. There was no significant difference in hepatic fibrosis progression in HCV genotype 3 and non-genotype 3.

## CONCLUSIONS

The data on prevalence of HCV infection and routes of its transmission in India is highly inadequate. Based on limited available data, the prevalence of HCV appears to be between 0.5% and 1.5%. The prevalence appears to be higher in the northeast, in tribal populations and in Punjab, and lower in Western India and Eastern India. Blood transfusion and unsafe therapeutic injections appear to be the predominant modes of transmission. Genotype 3 HCV is the most prevalent viral genotype. Data on natural history of HCV from India are extremely inadequate. There is a need for larger epidemiological studies on HCV infection and disease in India, to help obtain a better estimate of HCV disease burden, and to identify high-prevalence areas and predominant routes of transmission. These studies would help identify the most effective methods for preventing further transmission of this disease and to better target these measures to areas where these could be the most effective.

## CONFLICTS OF INTEREST

All authors have none to declare.

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