

## Research Article

### Prevalence and Associated Risk Factors of HCV Infection Among Children in Lahore, Pakistan

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#### Abstract

**Background:** Pakistan has second highest prevalence of HCV in the world. The epidemiology and burden of HCV infection varies in people of different ages.

**Objective:** Present study was designed to measure the prevalence of HCV among children in selected public and private hospitals of Lahore.

**Methods:** Children in the study were screened for anti-HCV test through ELISA (third generation ELISA Kit and Qaigen kit) for detecting the viral load from June 2018 to May 2019.

**Results:** Children in the study were screened for anti-HCV test through ELISA (third generation ELISA Kit and Qaigen kit) for detecting the viral load. The average age of non-reactive and reactive children was  $7.28 \pm 3.36$  and  $5.50 \pm 3.8$  years respectively. Socio-economic status was found associated with anti-HCV. An association was found significant for birthplace, delivery assisted by, and type of milk given to the child.

**Conclusion:** This study shows that the prevalence of HCV is 3.85% in children in Lahore city of Pakistan, which is alarming situation for healthcare providers, researchers and policy makers.

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#### Introduction:

World Health Organization (WHO) has declared Hep (B) and (C) virus as a major public health issue with alarmingly high prevalence of 3.5%.<sup>1</sup> Literature has reported that prevalence of anti-HCV has jumped from >122 millions to an astonishing >257 millions over a short period of time.<sup>2</sup> The status of Hep (C) is not less than that of an epidemic as it has effected more than 10 million people around the world.<sup>3</sup> The literature reports its prevalence varying from 4.8% - 14% recently.<sup>3,4</sup> In pregnant women, its prevalence is 8% while in children it is between 0.5%-5%.<sup>5,6,7</sup> High HCV prevalence among pregnant women (10.84%)

was shown in a study conducted in Lahore, Pakistan.<sup>8</sup> Annual deaths due to HCV in Pakistan are approximately fifty thousand.<sup>9</sup>

The possibility of blood or blood products related transfusion of HCV could not be overlooked in Pakistan. One study conducted on blood donors in Lahore by Akhtar et.al, documented the prevalence 17.78% by Elisa method.<sup>10</sup> It is therefore mandatory to screen all the children that get born to mothers with the infection, or those who are transfused with contaminated or un-screened blood. Among the HCV infected children, 25% spontaneously clear the virus while 75% progress to end stage liver disease.<sup>11</sup> Vertical transmission has

become the leading cause of childhood HCV infection. Also, those children who have had a long term transfusion history are inevitably at higher risk of contracting the disease.

The aim of this study was to find the frequency of Hep (C) virus infection in children aged less than 12 years registered at selected hospitals (both private and public) in Lahore. The associated risk factors of HCV infection are also discussed, and the different genotypes of HCV through RT-PCR are determined as well as prevalent subtype was found during the study period.

## Methods

This study was designed to find the frequency of Hep (C) virus infection in children aged less than 12 years registered at the OPDs of Lahore General, Sir Ganga Ram, Mayo, Services and Jinnah Hospitals in domain of government hospitals, whereas, from two private hospitals including Farooq and Ghurki Trust Hospitals as well. This inclusion of sample from both public & private sector was done to ensure inclusiveness and prevent bias. The number of patients included from both setups included equal numbers of patients who were administered with Anti - HCV antibodies using the test called ELISA through 3rd Gen ELISA kit.<sup>12</sup>

For identification of several genotypes of Hep (C), RT (PCR) was used for storage of anti – HCV serum that were positive as well as Qaigen-kit was utilized for assessment of viral load. SPSS v. 16 was used for data entry and analysis. Mean and standard deviation was used for quantitative variables, while, frequency and percentage was used for qualitative variables. Chi square test was applied to see association, whereas, t-test was used to compare means of two independent groups. Odds Ratio was used for risk assessment keeping p-value of less than 5% as significant.

## Results

Study showed very alarming results and found that a considerable number of patients had Hep (C), and were at high risk of impediment. Total number of children included in this study were 208, all below 12 years of age, who tested positive for Hep (C). Among all, 8(3.85%) proved to be reactive with anti – HCV test. The average age of children in reactive and the non reactive groups of children  $5.50 \pm 3.81$  years and  $7.28 \pm 3.36$  years as indi-

cated in Table-1. Among these, 5 males and 3 females were present. No statistical association was found between anti – HCV and father's occupation and the age. Study showed statistical association of socio-economic status with the status of anti – HCV (p-value < 0.05).

Table 2 shows no children caught the infection through

**Table 1:** Distribution of Hepatitis C Virus reactive & Non-reactive children less than 12 year of age according to Demographic characteristics from public & Private Hospitals of Lahore Metropolitan

| Demographic Characteristics  | Anti HCV Status |               | P-value | Odds Ratio | Confidence Interval      |
|------------------------------|-----------------|---------------|---------|------------|--------------------------|
|                              | Re-active       | Non-Reac-tive |         |            |                          |
| Gender                       | Male            | 5             | 121     | 0.901      | 1.088                    |
|                              | Female          | 3             | 79      |            |                          |
| Father's Occupational Status | Public Job      | 1             | 14      | 0.674      | 1.59                     |
|                              | Private Job     | 7             | 156     |            |                          |
|                              | Unemployed      | 0             | 30      |            |                          |
| Socio Economic Status        | 5000-10000      | 2             | 141     | 0.015      | 0.132                    |
|                              | 11000-20000     | 6             | 56      |            |                          |
|                              | 21000-30000     | 0             | 3       |            |                          |
|                              |                 |               |         | 0.268      | 6.310                    |
|                              |                 |               |         |            | 0.242, 164.57            |
|                              |                 |               |         |            | 0.025, 0.675             |
|                              |                 |               |         |            | 0.002 0.123 0.005, 3.083 |

treatment indicating some other infection source. One of the explanation about transmission of disease could be through the mother as no one received therapy of infection or went through any surgery of the sort. Statistically, there was no association of transfusion of blood, a foreign travel, any dental treatment, tattoo procedure, any vaccination, jaundice, or any injections with the status of anti – HCV. However, the place of birth of the children, weather the delivery was assisted by a midwife or medical doctor and the source of milk provided to the child were significantly associated (p-values < 0.05 for all). Also, there was no evidence of vertical transmission.

Additionally, as stated earlier out of 208, 8 children were found positive on reactive anti – HCV serum test. As there were no children who shared their utensils with other babies, no OR could be calculated and no p-value could be generated. When the children were categorized according to the type of Genotype, it was found that 1 patients had Type 2 while the sub-type that was found included 2a, and among 3 patients having Type 3, the sub-type was found as 3a, also among the 4 patients, as the viral load was not detectable i.e. < 500

**Table 2:** Summary of association between Hepatitis C and various risk factors among children in public & private hospitals of Lahore

| Indicators                                 | Response              | Anti HCV Status |              | P-value | Odds Ratio | Confidence Interval |
|--|-----------------------|-----------------|--------------|---------|------------|---------------------|
|  |                       | Reactive        | Non-Reactive |         |            |                     |
| Have Child Visited Abroad                  | Yes                   | 0               | 2            | 0.287   | 4.671      | 0.2077, 105         |
|  | No                    | 8               | 198          |         |            |                     |
| Place of Birth                             | Public Hospital       | 5               | 30           | 0.007   | 7.5        | 1.698,33.113        |
|  | Home                  | 3               | 135          |         |            |                     |
|  | Private Clinic        | 0               | 35           |         |            |                     |
| Delivery assisted by                       | Doctor                | 5               | 66           | 0.039   | 9.69       | 1.109,              |
|  | Midwife               | 1               | 128          | 0.083   | 0.076      | 84.718              |
|  | LHV                   | 1               | 1            | 0.414   | 0.3788     | 0.004,              |
|  | Relative              | 1               | 5            |         |            | 1.4006              |
|  |                       |                 |              |         |            | 0.036, 3.899        |
| Which kind of milk                         | Breast Feed           | 5               | 46           | 0.077   | 1.537      | 0.075,              |
|  | Formula Milk          | 0               | 6            | 0.025   | 5.362      | 31.169              |
|  | Breast + Formula Milk | 3               | 148          |         |            | 1.234, 23.302       |
| Has child ever been suffered from Jaundice | Yes                   | 0               | 1            | 0.146   | 7.824      | 0.2964-206.5        |
|  | No                    | 8               | 199          |         |            |                     |

IU / mL, no identification of genotype was possible. Commonest sub-types found this study was the 3a genotype. The Table No: 3 shows the viral load in the sub-types of anti – HCV and its p-value. As given in the table, there was significant difference in average viral load in the sub-types of genotypes.

**Table 3:** Comparison of Predictive Values (Bishop Score vs. Cervical Length)

| Group                     | Genotype     | Number   | Mean           | Std. Deviation   | P-value |
|---------------------------|--------------|----------|----------------|------------------|---------|
| Children of age <12 years | 2a           | 1        | 28735.00       | -                | 0.000   |
|                           | 3a           | 3        | 15818.00       | 2315.763         |         |
|                           | Not Detected | 4        | 450.00         | 100.000          |         |
|                           | <b>Total</b> | <b>8</b> | <b>9748.63</b> | <b>10873.346</b> |         |

## Discussion

Literature indicates that Hep-C infection is increasing at an alarming level worldwide as well as in Pakistan. A study reported that in Pakistan, the prevalence of Hep-C was 3.4% (UI= 2.6-4.4).<sup>13</sup> Although this study reported upto 8% prevalence, children need regular screening as they are at higher risk to face Hep-C related complications. One study conducted in Baluchistan, Pakistan, the frequency of Hep-C was found as 2.8% in 6 to 12 years old children and it was found to be 18.3%

among children of 3 to 12 years olds.<sup>14</sup>

This study included a total of 208 patients, and we found the prevalence of 3.85 % among kids who got Hep-C infection which is considerably high in this age group. This study found that none of the children travelled in a foreign country whereas among them, 62.5% were given birth among public sector hospitals and they were given breast milk by mothers. Also, among all, 37.5 % were given birth in their houses and they were given both bottle and breast milk. Among them, none went through blood transfusion and also, none received a tattoo. More-over, none of them had a jaundice and all were vaccinated as well. Studies have reported that the mothers who delivered their babies at home, and those who received Rh factor vaccination had significantly higher risk of getting their babies infected. The frequency is relatively higher upto 55% among patients who had thalassemia and were transfused with blood.<sup>15</sup>

One study conducted in the USA upon the juvenile prisoners found prevalence of 2% Hep (C) while one in UK reported a prevalence of 2.9% in the child population<sup>16</sup> They also found that primary source of infection in them was through their mothers.<sup>17</sup> In our study as well, the major source of spreading the infection was through their mothers. One study done by Jafri et al. reported a prevalence of Hep (C) but major source of contracting

virus in their study was through injections<sup>(18)</sup>. Which is contrary to our study in which none got it through injections.

Moreover, one other study conducted in the USA reported prevalence of 0.4% among children. Among them, adult cases showed a decreasing trend but new cases among children were increasing. The major way of transferring the infection in their study was through their mother. Although the prevalence reported in their study was relatively lower compared to ours, but the source of infection was same as ours and should be considered as high priority in screening if mother gets infected during pregnancy.<sup>19</sup> Other literature also states that factors like hospitalization, surgical procedures, transfusions and injections are major causes of spreading infection.<sup>20,21</sup> However, in our study none of these factors were statistically significant and were not associated with spread of infection as well.

Ahmad et al<sup>22</sup> reported that among others the most significant factors for transmission of Hep-C include blood transfusion, barber shops and dental surgery. Similarly, in our study none of the children share any of the utensils with others. Estonia and Greece have reported decreases in subtype of genotype 1b and 2 and/or increases in subtype of genotype 3a over time.<sup>23,24,25</sup> Many studies conducted in Pakistan found that 3a and 1a genotypes of HCV infection were the most common.<sup>26,27</sup> Similarly, in our study the prevalent subtype of HCV genotype was 3a. Jimenez et al<sup>28</sup> showed that 22.4% of HCV infection cases with genotype 1 were categorized in the low HCV RNA viral load while in our study HCV RNA viral load with 3a genotype was prevalent in children <12 years of age. Saleh et al<sup>15</sup> found that children with HCV RNA positive mothers (0.44%) had a 1.7 times higher risk of getting HCV infection than those with HCV RNA negative mothers (0.26%).

### Conclusion:

This study concludes that the prevalence of HCV is 3.85% in children in Lahore city of Pakistan, which is alarming situation for healthcare providers, researchers and policy makers. Early screening and timely intervention can reduce the burden of Hep-C among children.

### References:

1. World Health Organization. Global Hepatitis Report. 2017. [Accessed on 14 February 2021]. Available online: <https://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/>.
2. Park SH, Plank LD, Suk KT, Park YE, Lee J, Choi JH, et al. Trends in the prevalence of chronic liver disease in the Korean adult population, 1998–2017. *Clin. Mol. Hepatol.* 2020;26(3):209-215.
3. Waheed Y, Shafi T, Safi SZ, Qadri I. Hepatitis C virus in Pakistan: A systematic review of prevalence, genotypes and risk factors. *World J Gastroenterol.* 2009;15(45):5647-5653.
4. Raja NS, Janjua KA. Epidemiology of hepatitis C virus infection in Pakistan. *J Microbiol Immunol Infect.* 2008;41(2):4-8.
5. Boucheron P, Lu Y, Yoshida K, Zhao T, Funk AL, Lunel-Fabiani F, et al. Accuracy of HBeAg to identify pregnant women at risk of transmitting hepatitis B virus to their neonates: A systematic review and meta-analysis. *Lancet Infect. Dis.* 2021;21(2):85–96.
6. Arshad A, Ashfaq UA. Epidemiology of Hepatitis C Infection in Pakistan: Current Estimate and Major Risk Factors. *Crit Rev Eukaryot Gene Expr.* 2017;27(1): 63-77.
7. Wen WH, Huang CW, Chie WC, Yeung CY, Zhao LL, Lin WT, et al. Quantitative maternal hepatitis B surface antigen predicts maternally transmitted hepatitis B virus infection. *Hepatology.* 2016;64(4):1451–1461.
8. Akhtar AM, Khan MA, Ijaz T, Maqbool A, Iqbal Z, Rehman A, et al. Hepatitis C Virus Infection in Pregnant Women in Lahore, Pakistan: An Analytical Cross-Sectional Study. *International Journal of Agriculture and Biology.* 2014;16(1):160-64.
9. World Health Organisation. Global burden of disease (GBD) for hepatitis C. *J Clin Pharmacol.* 2004; 44(1): 20-9.
10. Akhtar AM, Khan MA, Ijaz T, Iqbal Z, Rana MY, Maqbool A, et al. Seroprevalence and Determinants of Hepatitis-C Virus Infection in Blood Donors of Lahore, Pakistan. *Pakistan Journal of Zoology.* 2013; 45(3):1-7.
11. Danish FA, Koul SS, Subhani FR, Rabbani AE. Managing HCV Infection in Pediatric Age Group: Suggested Recommendations. *Saudi J Gastroenterol.* 2010;16(3): 230-5.
12. REBUZZINI G. Study of the hepatitis C virus NS3 helicase domain for application in a chemiluminescent immunoassay (Doctoral dissertation, Università degli

- Studi di Milano-Bicocca).
13. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology*. 2013;57(4):1333-1342.
  14. Ahmed S, Ayub M, Naeem M, Nazir FH, Hussain A, Ghilzai D, et al. Thalassemia Patients from Baluchistan in Pakistan Are Infected with Multiple Hepatitis B or C Virus Strains. *Am J Trop Med Hyg*. 2021; 104(4): 1569–76.
  15. Saleh DA, Shebl FM, El-Kamary SS, Magder LS, Allam A, Abdel-Hamid M, et al. Incidence and risk factors for community-acquired hepatitis C infection from birth to 5 years of age in rural Egyptian children. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 2010;104(5):357–363.
  16. Saeed U, Waheed Y, Ashraf M, Waheed U, Anjum S, Afzal MS. Estimation of Hepatitis B Virus, Hepatitis C Virus, and Different Clinical Parameters in the Thalassemic Population of Capital Twin Cities of Pakistan. *Virology*. 2015;5(6):11-6.
  17. Feldman GM, Sorvillo F, Cole B, Lawrence WA, Mares R. Seroprevalence of hepatitis C among a juvenile detention population. *J Adol Health*. 2004; 25(1):505–508.
  18. Chatzipantazi P, Roy Km, Cameron So, Goldberg D, Welbury R, Bagg J. The feasibility and acceptability of collecting oral fluid from healthy children for anti-HCV testing. *Arch Dis Child*. 2004;89(9):185–187.
  19. Jafri W, Jafri N, Yakoob J, Islam M, Tirmizi Sfa, Jafar T, et al. Hepatitis B and C: prevalence and risk factors associated with seropositivity among children in Karachi, Pakistan. *BMC Infect Dis*. 2006;6(1):101.
  20. Rosenthal P. The HCV Advocate Medical Writers' Circle. The Hepatitis C Support Project a series of articles written by medical professionals about the management and treatment of hepatitis C. 2006.
  21. Kalil KA, Farghally HS, Hassanein KM, Abd-Elsayed AA, Hassanein FE. Hepatitis C virus infection among paediatric patients attending University of Assiut Hospital, Egypt. *EMHJ*. 2010;16(4):356-361.
  22. Ahmad W, Ijaz B, Javed FT, Jahan S, Shahid I, Khan FM, et al. HCV genotype distribution and possible transmission risks in Lahore, Pakistan. *World J Gastroenterol* 2010; 16(2):4321-4328.
  23. Sadoh AE, Sadoh WE. HIV co-infection with hepatitis B and C viruses among Nigerian children in an antiretroviral treatment programme. *SAJCH*. 2011;5(1):7-10.
  24. Tallo T, Norder H, Tefanova V, Krispin T, Schmidt J, Ilmoja M, et al. Genetic characterization of hepatitis C virus strains in Estonia: fluctuations in the predominating subtype with time. *J Med Virol*. 2007; 79(3): 374-382.
  25. Katsoulidou A, Sypsa V, Tassopoulos NC, Boletis J, Karafoulidou A, Ketikoglou I, et al. Molecular epidemiology of hepatitis C virus (HCV) in Greece: temporal trends in HCV genotype-specific incidence and molecular characterization of genotype 4 isolates. *J Viral Hepat*. 2006;13(1):19-27.
  26. Idrees M, Riazuddin S. Frequency distribution of hepatitis C virus genotypes in different geographical regions of Pakistan and their possible routes of transmission. *BMC infectious diseases*. 2008 Dec;8(1):1-9.
  27. Ali MM, Aslam R, Hussain F, Ali N. Molecular Identification Of Hepatitis C Virus In Different Districts Of Punjab, Pakistan: A Preliminary Study. *Pakistan Journal of Science*. 2015 Jun 1;67(2):222.
  28. Jimenez-Mendez R, Uribe-Salas F, López-Guillen P, Cisneros-Garza L, Castañeda-Hernandez G. Distribution of HCV genotypes and HCV RNA viral load in different regions of Mexico. *Annals of hepatology*. 2010 Jan 1;9(1):33-9.