

## Chronic Hepatitis C Scenario among Patients Presenting to Liver Clinic at Holy Family Hospital Rawalpindi Pakistan (2006-2019)

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### Abstract

**Objectives:** To determine the demographic, clinical, hematological, histological and sonographic characteristics of chronic hepatitis C patients visiting Holy Family Hospital Rawalpindi Pakistan.

**Subjects & Methods:** A retrospective hospital data based study (2006-2019) was carried out by collecting data of Chronic Liver Disease (CLD) from liver clinic of Holy Family Hospital Rawalpindi. Data of total 9392 chronic hepatitis C patients confirmed by Polymerase Chain Reaction (PCR) was enrolled in this study through consecutive sampling. Data was collected pertinent to their demographic, clinical, hematological and histological attributes by structured questionnaire. Data was analyzed by SPSS version 25.0. Frequency of the patients belonging to each province was calculated. The mean age difference between males and females was statistically verified by independent sample t-test. Gender based differences in hematological parameters and biochemical variations with respect to severity of lesions were also statistically proven by independent sample t-test. Gender based variation in severity of grades of fibrosis was confirmed by chi-square test. P-value < 0.05 was taken as significant.

**Results:** Of the total 9392 chronic hepatitis C patients, 52% were females. Mean age of our study subjects was 38.3 ± 7.8 years. Maximum number (2341) of chronically infected hepatitis C patients was registered during 2019. About 7720 patients belonged to Punjab province. Mean age of the females statistically higher than those of males particularly during 2011, 2013, 2015, 2016, 2019 with P < 0.05. Sonographically majority of our patients were normal. Gender based differences in hematological attributes and biochemical parameters of patients with varying severity of lesions was statistically significant (P < 0.00). Fibrotic lesions with respect to gender were statistically insignificant (P > 0.05).

**Conclusion:** Hepatitis C among male populates of Pakistan is more fibrotic. Frequency of chronic hepatitis C is multiplying and expanding rapidly in Pakistan. There is need to increase awareness and screening of general public in order to arrest its rapid spread and provide treatment to the victims.

**Keywords:** Chronic Hepatitis c, Demographics, Polymerase Chain Reaction. Hematological Parameters, Fibrotic Lesions.

### Introduction

Hepatitis C virus is highly endemic in Pakistan. About 10 million inhabitants of Pakistan are known to be affected with Hepatitis C [1]. Thousands of new patients are adding annually due to un-

screened blood transfusion, scarcity of testing, ignorance of management options and inadequate application of preventive measures [2]. About 75% of the cases with acute liver infections are likely to have considerable progression to chronic Hepatitis C if

remain undiagnosed. Hepatitis C being contributing the considerable fraction of communicable diseases in Pakistan is tagged as a major public health problem [3]. Significant mortality and morbidity are attributed to this havoc [4]. Despite the availability of antiviral medications for hepatitis C, the attitude of the community towards diagnosis of this disease and seeking treatment for its cure is determined to be pitiable. Approximately 70% of hepatitis C cases are at risk of developing chronic hepatitis C and about 71 million across the globe are reported to have chronic hepatitis C infection [5]. Chronic hepatitis C is an ailment that should primarily be brought to spot light due to its association with hepatocellular carcinoma [6]. The hepatitis C burden among Pakistani population could not be reduced even by provision and accessibility to effective antiviral medication [7]. Chronic hepatitis C patients are sometimes asymptomatic although its mean incubation period is reported to be about 7 weeks [8]. All chronic hepatitis C patients should be promptly treated to attain sustained virological response [9]. No doubt, early diagnosis of Hepatitis C cases and their prompt treatment is of paramount significance in apt diminution of this disease load [10]. However, demographic analysis of chronic hepatitis C cases in the community is established to be the logical approach for identification of at risk population through screening [11]. This approach of secondary prevention is deemed necessary to arrest the progression of affected cases to chronic illness by adoption of suitable public health initiatives [12]. The present retrospective study is therefore intended to determine the demographic characteristics along with their clinical, hematological, histological and sonographic attributes of chronic hepatitis C patients who visited the liver clinic of Holy Family Hospital Rawalpindi during 2006-2019. This research would be quite significant in providing an overview pertinent to chronic Hepatitis C in Pakistan. Moreover, our policy makers would be able to take

appropriate measures for substantial reduction of disease burden nationally and to some extent globally.

### Subjects & Methods

A retrospective hospital CLD data based research was done by collecting data of 14 years (2006-2019) from liver clinic of Holy Family Hospital Rawalpindi Pakistan. Total 9392 chronic hepatitis C patients' data verified by PCR reports was included in this study through consecutive sampling. Data was gathered regarding clinical, hematological, histological and sonographic features of the patients. Histological scoring system of Ishak was used to grade and stage the liver disease [13]. As administrative units of Pakistan are comprised of four provinces (Punjab, Sindh, Balochistan & Khyber Pakhtunkhawa (KPK), two autonomous regions (Azad Jammu & Kashmir (AJK) and Gilgit-Baltistan (GB) and one federal area (Islamabad Capital Territory (ICT)), so the frequency of patients belonging to each province was computed [14]. Data was analyzed by SPSS version 25.0. The mean gender based age and hematological parameters were statistically confirmed by independent sample t-test. Moreover, difference in hepatological attributes between patients with early and adverse fibrous lesions was also verified by independent sample t-test. P-value < 0.05 was considered significant.

### Results

Of the total 9392 chronic hepatitis C patients visiting the Holy Family Hospital Rawalpindi during 14 years, 4508 (48%) were males while 4884 (52%) were females. Mean age of our study respondents was  $38.3 \pm 7.8$  years. Highest number of chronic hepatitis C patients was registered during 2019 as illustrated below in Figure 1.

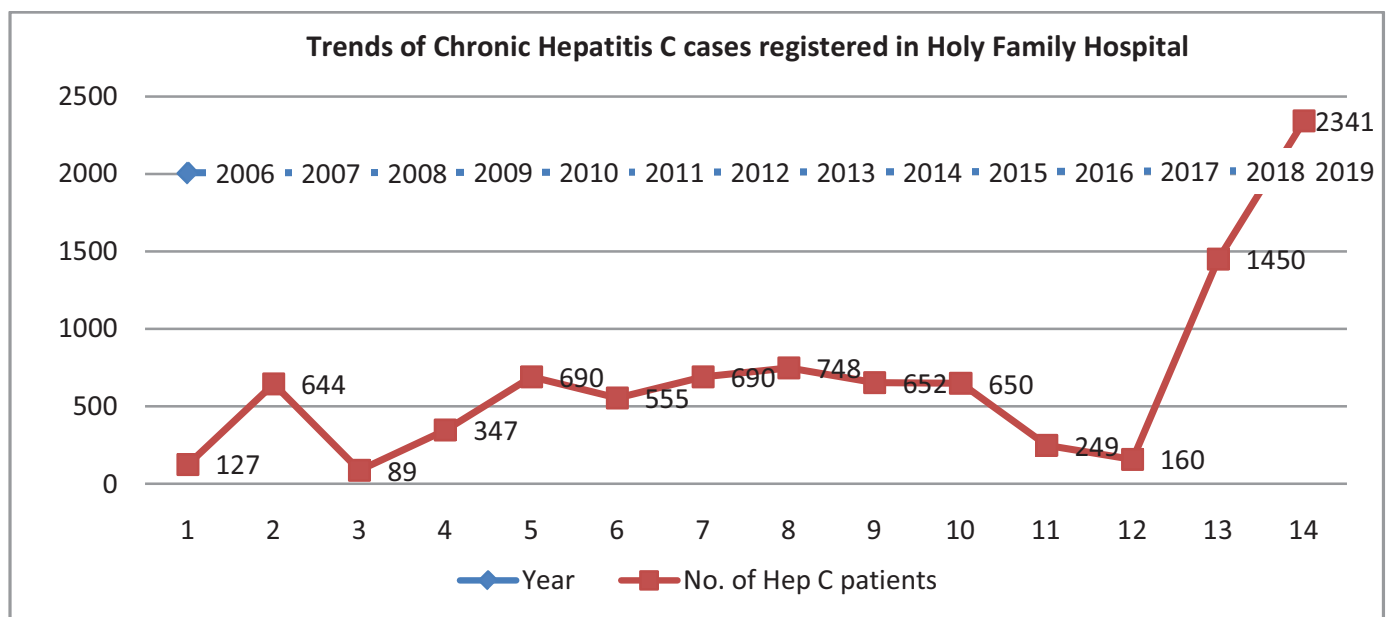


Figure 1

**Table 1:** Gender based comparison of mean age of chronic hepatitis C patients (2006-2019)

Year of getting diagnosed and treated at HFH	Overall Age (mean $\pm$ SD)	Age of Males (mean $\pm$ SD)	Age of Females (mean $\pm$ SD)	P value
2006	35.41 $\pm$ 8.2	35.30 $\pm$ 9.4	35.51 $\pm$ 7.1	0.89
2007	36.01 $\pm$ 9.2	35.50 $\pm$ 9.7	36.53 $\pm$ 8.7	0.16
2008	36.08 $\pm$ 9.4	36.90 $\pm$ 10.6	35.26 $\pm$ 8.3	0.43
2009	35.25 $\pm$ 8.7	34.40 $\pm$ 8.7	36.1 $\pm$ 8.7	0.07
2010	36.17 $\pm$ 8.3	35.75 $\pm$ 8.7	36.6 $\pm$ 7.9	0.18
2011	35.46 $\pm$ 5.3	34.49 $\pm$ 2.8	36.44 $\pm$ 7.9	*0.0002
2012	35.86 $\pm$ 8.8	35.46 $\pm$ 9.2	36.26 $\pm$ 8.5	0.24
2013	36.56 $\pm$ 7.3	35.57 $\pm$ 6.4	37.56 $\pm$ 8.3	*0.0004
2014	38.52 $\pm$ 6.9	37.77 $\pm$ 4.3	39.28 $\pm$ 9.6	0.01
2015	38.10 $\pm$ 6.7	36.75 $\pm$ 7.6	39.45 $\pm$ 5.9	*0.00001
2016	40.39 $\pm$ 6.8	39.17 $\pm$ 8.3	41.62 $\pm$ 5.4	*0.006
2017	41.23 $\pm$ 7.0	41.12 $\pm$ 6.9	41.34 $\pm$ 7.2	0.85
2018	45.35 $\pm$ 7.8	45.09 $\pm$ 8.6	45.61 $\pm$ 7.1	0.21
2019	45.75 $\pm$ 8.4	45.23 $\pm$ 9.2	46.27 $\pm$ 7.6	*0.003

**Table 2:** Province wise distribution of chronic Hepatitis C cases

Year	Punjab	Sindh	Balochistan	KPK	ICT	GB	AJK	Total
2006	116	0	0	3	6	0	2	127
2007	587	1	1	23	28	0	4	644
2008	83	2	0	3	1	0	0	89
2009	309	3	0	19	16	0	0	247
2010	590	1	1	59	39	0	0	690
2011	473	3	2	29	46	0	2	555
2012	574	5	1	43	65	1	1	690
2013	575	6	1	70	96	0	0	748
2014	510	8	0	59	73	1	1	652
2015	516	3	1	64	63	3	0	650
2016	207	0	0	24	15	3	0	249
2017	137	1	0	7	15	0	0	160
2018	1128	11	1	110	198	2	0	1450
2019	1915	6	0	94	320	2	4	2341
Total	7720	50	8	607	981	12	14	9392

**Table 3:** Sonographic findings among chronic hepatitis C patients (n = 5244)

Findings on Abdominal Ultrasonography	Females	Males	Total
Normal study	2634	2454	5088 (97%)
Cholelithiasis	43	47	90 (1.72%)
Cirrhosis/ CLD	22	23	45 (0.86%)
Interior abdominal wall defect	01	0	01 (.02%)
Abdominal hernia	01	0	01 (.02%)
Acid Peptic Disease	0	02	02 (.04%)
Ascites	0	01	01 (.02%)
Bilateral end stage renal disease	0	02	02 (.04%)
Dilated hydronephrosis	0	01	01 (.02%)
Bilateral nephrocalcinosis	0	01	01 (.02%)
Bilateral renal calculi / cysts	03	07	10 (0.2%)
Fatty liver	0	02	02 (.04%)
Total	2704	2540	5244 (100%)

**Table 4:** Hematological profile of Chronic Hepatitis C patients

Hematological profile	Females (mean ± SD)	Males (mean ± SD)	P-value
Hemoglobin (gm/dl)	10.46 ± 1.62	12.03 ± 2.7	< 0.000
WBCs (×109/L)	6.22 ± 2.33	6.48 ± 1.08	< 0.000
Platelets ((×109/L)	173.27 ± 4.8	167.34 ± 6.02	< 0.000

**Table 5:** Grading & staging of chronic hepatitis C on liver biopsy as per Ishak score

Ishak grading & staging	Scores		P- value
	Males (n = 525)	Females (n = 228)	
Grades	13.2 ± 1.8	9.6 ± 2.2	< 0.00
Stages	5.4 ± 2.4	3.7 ± 1.4	< 0.00

Biopsy grading as per Ishak showed moderate piecemeal necrosis, zone 3 necrosis in most areas, focal lytic necrosis, apoptosis and focal inflammation in more than 10 foci with moderate to marked portal inflammation. Liver biopsy grading as per Ishak grading system among males is revealing marked portal bridging with occasional nodules that is suggestive of incomplete cirrhosis. On the

other hand, liver biopsy among females is reflecting fibrous expansion of most portal areas with minimal portal to portal bridging. However, this difference was determined to be statistically insignificant while difference in biochemical attributes was statistically significant as depicted below in Table 6.

**Table 6:** Biochemical attributes of patients with varying pattern of hepatic Fibrosis (n = 834)

Attributes	None – some portal fibrosis (0-1) (n = 382)	Most portal fibrosis – incomplete cirrhosis (2-5) (n = 452)	P- value
Males (n = 396)	299 (75.5%)	97 (24.5%)	* >0.05
Females (n = 438)	355 (81%)	83 (19%)	
AST (IU/L)	43.02 ± 4.73	45.26 ± 5.2	<0.00
ALT (IU/L)	56.3 ± 5.8	53.33 ± 3.08	<0.00
ALP	156.36 ± 6.2	149.41 ± 6.37	<0.00
Bilirubin (mg/dl)	3.7 ± 0.9	5.6 ± 1.7	<0.00
Albumin	3.32 ± 4.4	2.6 ± 0.83	<0.00

**Note:** \* means statistically insignificant

## Discussion

Hepatitis C constitutes substantial global burden of disease. About 6% of Pakistani inhabitants are suffering from its devastating effects [15]. Chronic liver disease is attributed to Hepatitis C infection primarily due to its diverse natural history varying from negligible to severe complications [16]. Detection of hepatitis C cases in the society would be considerably beneficial in reducing associated complication and death toll by subjecting them to antiviral therapy [17]. Mean age of chronic hepatitis C cases in our study from 2006 – 2015 was reported to be 35.41 – 38.52 years. However, this age composition pertinent to hepatitis C patients in our country was found to be drastically different during 2015-2019 with increased propensity among 40-45 years old population. Moreover, unlike 4342 cases reported during first 9 years (2006-2014), about 4850 chronic hepatitis C cases were registered in liver clinic of Holy Family Hospital during the last 5 years. Contrary to the present study, national disease surveillance for hepatitis C cases in United States not only revealed three fold rises in acute hepatitis C cases from 2009-2018 but also showed bimodal distribution of chronic hepatitis C cases with greatest frequency among 20-39 and 50-69 years old people [18]. The discrepancy in mean age of our respondents from those of United States might be due to cultural diversity that should be scrutinized for better comprehension of this variation.

About 82.2% of the chronic hepatitis C patients visiting liver clinic in our study belonged to Punjab province followed by 10.4% from Islamabad Capital Territory (ICT) and 6.5% from KPK. Another national research carried out by Mahmud S et al concluded that estimated figure of chronically infected hepatitis C patients was about 4.2 million in Punjab province. Moreover, people with liver related disorders and those injecting intravenous drugs were frequently afflicted with this catastrophe [19]. The current study is done among confirmed chronic HCV patients who visited, registered and comprehensively treated for 6 months' duration at liver clinic of Holy Family Hospital Rawalpindi during 2006-2019. The trend of cases shown in Figure 1 reflects the highest count during 2018 and 2019. Even the systematic review of Hepatitis C case globally revealed that Pakistan was the second largest hepatitis C prevalent country [20]. Despite the launch of WHO strategy for elimination of viral hepatitis by 2021 with meticulous prioritization of hepatitis B and C and elimination of all sorts of viral hepatitis as a major public health menace by 2030, the scenario in Pakistan is still very distressing. Motivating the strategic planners for their rigorous efforts in this regard is highly necessitated to achieve the WHO specified 2030 targets [21].

In our study, of the total 9392 chronically infected hepatitis C cases, the females (58%) were comparatively greater. Moreover, mean age of the females in current research was found to be statistically higher than those of males particularly during 2011, 2013, 2015, 2016, 2019, revealing that males in our society are infected in early age than those of females. However, mean age of our study subjects was  $38.3 \pm 7.8$  years. Another national study done by Farooq

M et al during 2018 to screen the general population of Lahore revealed mean age of hepatitis C patients around 36.15 years. In addition, hepatitis C was found to be statistically significantly associated with advanced age [22]. In contrast to my research, males in the screening of Lahori population revealed higher frequency of infected among male as compared to females. Higher frequency of females detected with chronic hepatitis C in our study might be due to their regular screening during antenatal care. However, there is possibility of variation in gender based distribution of hepatitis C cases but this could better be elucidated by determining the risk factors contributing to this disparity. However, a massive research on provincial level with prime focus on the risk factors could better be able to rule out the prevalence of hepatitis C region wise in our country.

Our study showed statistically significant difference ( $P < 0.00$ ) in hepatic enzymes between two groups of chronic hepatitis C patients (Table 6). In contrast to our results, a research done in Jazan region of Saudi Arabia illustrated statistically significant escalation in liver enzymes of patients suffering from hepatitis C [23]. However, likewise Abdullah SM et al serum albumin of our chronic hepatitis C patients was at reduced level. Liver biopsy has been considered one of the imperative diagnostics in staging and grading the liver disease among chronic hepatitis C patients prior to treatment [24]. Gender based liver biopsy findings of our hepatitis C patients demonstrate more complexity of disease among males in comparison with those of females. Contrary to our research that is based on 14 years' extensive data and done by using Ishak grading and staging, a study was carried out in Pakistan over a span of one year (2004-2005) to determine histological changes among chronic hepatitis C patients by employing METAVIR scoring system. This research revealed that about 44% of study participants had equal to or greater than grade 2 fibrosis [25]. The current study is depicting extensive fibrosis among our patients. This difference might be due to inclusion of massive population and long span of our research. However, other contingent factors should also be studied thoroughly to verify this difference.

## Conclusion & Recommendations

Gender based difference in fibrotic lesion among chronic hepatitis C cases is statistically insignificant. Due to rapid growth of this havoc among both genders, strategic planners and health authorities should ensure universal coverage of Hepatitis C awareness and treatment facilities across the nation for the substantial reduction of its prevalence in the country.

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