REPORT

Study is about the prevalence of the HCV disease and survival of HCV patients with associated factors in the population of district Multan

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Abstract: To find out the significant factors associated with HCV disease and evaluate the impact of these factors on the survival patternof HCV patients in district Multan. The study was conducted in Nishter Hospital of Multan district from 1st January 2011 to 1stOctober 2012. To see a significant difference between the survival rates of patients with associated factors, non-parametric Cox- proportional hazard model with their graphical results were used. All the patients above 11 years old of both sexes were included in the study. All those who were surviving with HCV diseasewere studied with their associated factors such as age, family history (FH) barber/parlor services, blood group (BG) types weight loss (WL), Gender and drug use were collected from Nishter Hospital Multan. Results indicated that age, blood group types and gender are the most significant factors in the patients who are surviving with HCV disease. It was also observed that survival rate of female patients is high as compare to male patients.

Keywords: Cox model, HCV, Factors, Survival pattern.

INTRODUCTION

The main causative agents for hepatitis are Viruses and Hepatotrophic viruses are responsible for causing hepatitis all over the world. Hepatitis is considered as a general term and is defined as the inflammation of the liver, which is caused by several mechanisms and also includes the infectious agents. Hepatitis can be caused by different viruses such as A, B, C, D and E. (Boston and Mahmood, 2010). The virus that is responsible for most transfusion-associated non-A and non-B was identified in 1989 and named as HCV (WHO, 2002). HCV disease caused by a virus which is a small i.e. 40 to 60mm in diameter enveloped single strandedRibonucleic Acid Virus (RAV) of the family Flaviviridae and genus Hepacivirus (Ghany *et al.,* 2009). HCV is a major causative agent for chronic liver diseases. HCV also named as type C Hepatitis, parent rally transmitted Non-A Non-B hepatitis (PT-NANB), Non-B transfusion-associated hepatitis, Post transfusion non-A non-B hepatitis and hepatitis C (HC) (WHO, 2002). There are six genotypes of HCV and have more than 50 sub genotypes (Roger, 2004). To define the epidemiology of the HCV disease the identification of the HCV genotype is very important. Genotype 1a, 1b and 3a is particularly common in Europe and United State (Ghany *et al.,* 2009). Genotypes 4 and 5 are distributed in Africa and genotype 6 is distributed in Asia and in Pakistan most common HCV genotype is 3a (Muzaffar *et al.,* 2008).

Worldwide the estimated prevalence of HCV is about 2.2% of the whole population and highest prevalence of HCV is in Egypt approximately 15 to 20% (Reker and Islam, 2014). The estimated prevalence of HCV is 3% in Pakistan while in Punjab HCV prevalence is 4.3% (Ghias *et al*., 2010). In developed countries the factors associated with the transmission of HCV are intravenous drug use, haemodialysis, blood transfusion, needle-stick injuries, tattooing, prenatal infections and sexual intercourse. While in developing countries the use of therapeutic injections from reused needles and improper sterilization of medical equipment's are the main source of blood transfusion disease (Bosan *et al.,* 2010). Alcohol and drug users, blood donors, and the persons who are transplanted with an organ are also the source for this virus (Jones, 2001). The persons who have a direct exposure to the blood are at high risk of HCV infection. Medical health workers, having a sex to a partner who had a family history of HCV, having a sex with multiple partners, low living standard, dental services, surgeries, ear piercing, and barber and parlour services are also main source for the HCV disease (Alter *et al.,* 1998). Hepatitis C Virus has some association with ABO blood groups and their rhesus factors. By testing the association of different blood groups types with Hepatitis C Virus, it was concluded that patients with blood group type O were more resistant to viral hepatitis (Naeini *et al.,* 2010).

Various researchers studied the HCV associated factors in Pakistan with different statistical investigation but mostly used chi-square and logistic regression. These includes Ghias and Pervaiz (2009), Waheed *et al* (2009), Ghias *et al* (2010) and Gorar *et al*. (2014). So in this study, we studies the HCV factors with survival time using cox-regression method. That is new way related to the

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Population of Pakistan and especial to the Population of Multan.

MATERIALS AND METHODS

A total of 540 patients for our research study were collected from Nishter Hospital, Multan. Only the patients belonging to the district Multan of both sexes (male, female) were considered in this study based on the time period from 1st January 2011 to 1st October 2012. The data was collected for the analysis of the prevalence rate of HCV disease with associated factors in the male and female. Cox-proportional hazard model is used to analyze the relationship between the survival time and the one or more predictors. Cox proportional hazard model formula is:

$$h(t, X) = h_0(t)e^{\sum_{i=1}^{p}\beta_i X_i}$$

Dependent variable: Survival Time (days)
Survival status (SS): 0 for censor: 1 for event (failure)
Factors (levels) are: age in years, gender (male, female), FH (no, yes), barber/Parlor (no, yes), WL (no, yes), drug use (no, yes), and BG (A+, A-, AB+, AB-, B+, B-, O+ and O-**).** Note that initial level for each factor use as a base line for comparison of survival pattern of HCV patients.

Hazard ratio and z-score also computed to compare the survival pattern of male and female using female as base line**.** Hazard ratio (HR) is used to compares the survival pattern from the base line (initial level of any factor) to other levels of factors and HR is computed by the following formula;

$$HR = e^{-\hat{\beta}}$$

The interpretation of *HR* are as given below;
If *HR*<1, this means that survival rate on any level is smaller than that of baseline of the given factor. If *HR*=1, this means that survival rate at any level and baseline of given factor is identical. If *HR>1*, this indicated that the survival rate of any level is higher than that of baseline of the given factor.
Wald statistics (Z) is calculated by the formula as given below;

$$Z = \frac{\hat{\beta}}{SE(\hat{\beta})}.$$

Data Analysis
The data was analyzed by using the software Minitab 16 and stat graphics. Cox proportional regression model is used to explore the relationship between the factors associated with HCV disease and the survival time of patients. The model for Cox- proportional regression is

$$h(t/x) = h(t/0)\times \exp\begin{bmatrix} \beta_1 Age + \beta_2 Barber\_Parlor + \beta_3 Drug\,use + \beta_4 FH + \beta_5 WL + \beta_6 BG = (A+) \\ + \beta_7 BG = (A-) + \beta_8 BG = (AB+) + \beta_9 BG = (AB-) + \beta_{10} BG = (B+) \\ + \beta_{11} BG = (B-) + \beta_{12} BG = (O+) + \beta_{13} BG = (O-) + \beta_{14} G = M \end{bmatrix}$$

Hazard ratios and z-score also calculated to compare their survival rate under different associated factors such as WL, age, gender, FH, barber, parlor services, drug users and BG types.

RESULTS

Table 1 shows the results of fitting a failure-time regression model to describe the relationship between survival time and the seven independent variables (age, barber/ parlor, drug use, family history, weight loss and blood group, gender). The hazard functions at a selected combination of our input factors **x** is a multiple of the baseline hazard function as shown below:

$$h(t/x) = h(t/0)\times \exp(0.0080 \times Age + 0.5655 \times Barber\_Parlor + 0.2640 \times Drug\,Use - 0.0299 \times Family\,History + 0.161459 \times Weight\,Loss - 0.2300 Blood\,G\,A+ = -0.2365 \times Blood\,G = A- - 0.6441 \times Blood\,G = AB+ - 0.6288 \times Blood\,G = AB- - .0.7371 \times Blood\,G = B+ - 0.1388 \times Blood\,G = B- - 0.3561 \times Blood\,G = O+ - 0.5071 \times Blood\,G = O- - 0.1887 \times Gender = M$$

Notice that the highest P-value for the likelihood ratio tests is 1 as indicated in table 2; belonging to WL indicates that this factor for Hepatitis C Virus disease is insignificant. Similarly for the factor FH the likelihood ratio tests is 0.05 indicates that the role of the family history is insignificant for the Hepatitis C Virus disease. The P-value greater or equal to 0.05 indicates that the term is not statistically significant at the 95.0% or higher confidence level. And for gender, barber-parlor drug use, blood group the P-value is less than 0.05 indicate that the role of gender, barber-parlor, drug use, weight loss and blood group are significant to explain the Cox proportional hazard model for survival of HCV patients.

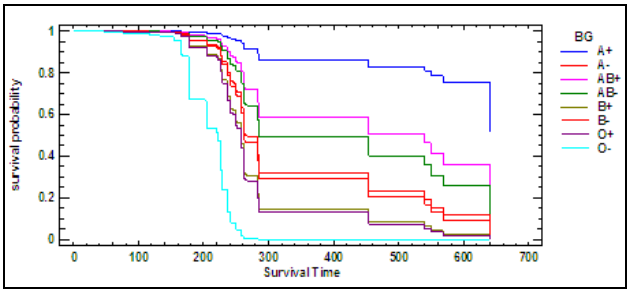

Fig. 1: Survival Pattern by Blood Groups

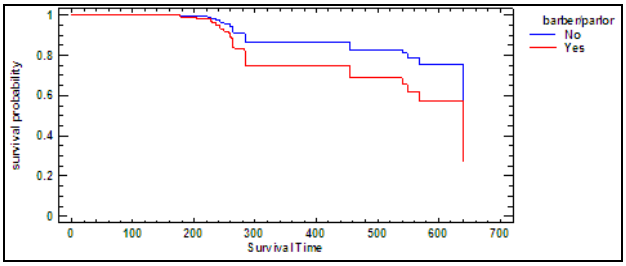

Fig. 2: Survival Pattern by barber/parlor

Table 1: Summary of COX proportional hazards model for the survival time of HCV patients

Parameter	Estimate $\hat{\beta}$	$SE(\hat{\beta})$	Hazard raito (HR)	Lower 95% CI for HR	Upper 95% CI for HR	Z-score	P-value
Age	0.0081	0.0032	1.0081	1.0018	1.0117	2.5312	0.9943
Barber/parlor (n=530)	0.5931	0.2851	1.8095	1.0349	1.9350	2.0803	0.9813
Druguse (n=229)	0.2640	0.0770	1.3021	1.1197	1.6250	3.4285	0.9997
FH (n=192)	-0.0299	0.0820	0.9970	0.8264	0.6680	1.6044	0.9457
WL (462)	0.1797	0.1120	1.1961	0.9610	1.1070	1.6044	0.9457
BG =A-(n=76)	-0.2300	0.1605	0.7945	0.5801	0.2732	-1.4330	0.0759
BG=AB+(n=73)	-0.6441	0.1454	0.5251	0.3949	0.0850	-4.4298	0.0000
BG=AB-(n=45)	-0.6288	0.2363	0.5332	0.3356	0.0627	-2.6610	0.0039
BG=B+(n=39)	-0.7357	0.1504	0.4791	0.3568	0.0636	-4.8916	0.0000
BG=B-(n=153)	-0.1383	0.1680	0.8708	0.6265	0.3483	-0.8232	0.2052
BG=O+(n=17)	-0.3561	0.1215	0.7004	0.5520	0.2185	-2.9308	0.0017
BG=O-(n=86)	-0.5071	0.1749	0.6022	0.4275	0.1138	-2.8993	0.0019
Gender=M (n=285)	-0.1887	0.0771	0.8280	0.7119	0.4254	-2.4474	0.0072

Graphical representation of the survival time of HCV patients under different factors are shown in fig 1and fig 2. From table 1, we observe that the use of drug has no significant impact on the survival time of active hepatitis c virus (HCV) patients as HR close to 1. The prevalence of HCV does not depend on the family history of the patients. As there is no clear significant difference between the survival times of HCV patients as HR is approximately close to one as indicated in table 1for who have family history and who do not have family history. The loss of weight due to the disease has no impact on the survival time of the Hepatitis C Virus patients. Table 1 shows that the survival rate of male patients is low as compare to Female patients because HR is less than 1. The survival time of the active Hepatitis C virus patients having different blood group types is shown in fig. 1 from which it is clear that the patients who have blood group type A+ have a high survival rate than those who have A- blood group and blood group O- has lowest survival chances as other blood groups with HCV. From fig. 2, we have found that the patients who take a service of barber/parlor have low survival chances as compared to those patients of active HCV who do not use the service of barber/parlor.

Table 2: Likelihood ratio test for Hepatitis C Virus Patients data

Factor	Chi-Squared	Df	P-Value
Age	19.461	1	0.04
Barber_parlor	34.514	1	0.02
Druguse	54.241	1	0.00
FH	-2.7507	1	0.05
WL	-0.6917	1	1.00
BG	23.3715	7	0.00
Gender	5.773	1	0.00

DISCUSSION

In this study, we explore different behavioral factors which are affecting the HCV patients and their survival time in the population of district Multan. We observed through the likelihood ratio test that age affect the situation of HCV. Another factor which is the cause of HCV, is the use of barber/parlor whose positive effect have been observed. This indicated that increase the use of barber/parlor results more chances to occur HCV. Similarly the excessive use of drug may also effect the survival time of HCV patients. Various blood groups have different effect on the survival time of HCV patients. On comparison of survival chances of HCV patients by blood group it has been observed that HCV patient with blood group A has more survival chances as other blood groups. While blood group O- HCV patients has lowest survival rate as other blood groups. Gender wise discrimination has also been observed regarding HCV survival time. While family history and weight loss does not indicated occurrence of HCV in the population of district Multan. So the barber/parlor use and blood groups are the significant factors which are effecting the survival time of HCV patients.

CONCLUSION

In this research we studied the survival pattern of HCV patients under different factors. It was concluded from the above results that the ratio of male patients suffering from HCV disease is high as compared to female in those patients who are surviving with HCV. We have observed that various factors affect the survival chances of HCV patients. Various associated factors studied separately shows that the blood group types, barber/parlor, family history, drug used and age are the factors that are

associated with the happening of this disease. In our study, we have found that age, blood groups, barber/parlor, drug use and gender are the significant factors of HCV while weight loose and family history are the insignificant factors. The survival chances of HCV are mostly affected by blood groups and barber/parlor use. The educational and socio economic level in the Multan district is low and majority of patients come in Nishter Hospital, Multan have a poor background. It is necessary to include all socio-economic level in the study of the prevalence of HCV disease to find out the accurate estimate about the disease

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