ANALYSIS OF PRESCRIPTION TREND IN THE TREATMENT OF HEPATITIS C AND THE STUDY OF ASSOCIATION OF THIS THERAPY PLAN WITH THE AGE OF THE PATIENT.

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ABSTRACT

Objective: To check out the prescription trend for the hepatitis C i.e. to analyze the combination therapy. The association of therapy plan with the age of the patient was also studied.

Material and Methods: Prescriptions were collected from 97 patients diagnosed with hepatitis C from December 2016 to February 2017. Statistical calculations were carried out on these prescriptions to analyze the trend and to see the association of therapy plan with the age of the patient.

Results: In the prescription trend the combination of ribavirin 1200mg/day (400mg TID) and sofosbuvir 400mg/day was found to be the most frequent. Second frequent therapy was the combination of oral therapeutic agent (ribavirin 1200mg/day (400mg TID)) and an injectable (Peginterferonalfa 2a) whereas interferon alfa 2a were also used along with the ribavirin. There was no association found between age of the patient and the therapy plan.

Conclusion: Oral therapy for the hepatitis C treatment is the most frequent therapy plan in the Jinnah hospital where as the second frequent therapy plan was a combination of oral and the injectable. On the other hand there is no association of age of patient with the therapy plan followed for hepatitis C.

Key words: Ribavirin, prescription, sofosbuvir, therapy

INTRODUCTION

Viral hepatitis due to HBV & HCV is unfortunately highly endemic in Pakistan1-2. Hepatitis C virus (HCV) is a major public health problem affecting approximately 2-3% (130-170 million) of the world population3-4. According to a study conducted by Pakistan Medical and Research Council, prevalence of HCV infection in 2007-8 was 4.8% while that of HBV infection was 2.5%.

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A leading cause of considerable mortality and morbidity in the world is Hepatitis C caused by HCV5-6. Cirrhosis because of chronic hepatitis C is the prime factor for liver transplantation7. Untreated acute hepatitis may lead to chronic persistent hepatitis, which may further progress to cirrhosis, fulminant hepatic failure and/or cholestatic hepatitis8. However phenomena is more complex concerning other risk factors along with cofactors, complications, globally prevention and control activities etc. Other liver disorders must be investigated along with Hepatitis like sporadic porphyria, cutaneatarda, thyroid problems and cryoglobulinemia9. Another observed phenomena is the association of diabetes mellitus with hepatitis C i.e. Hepatitis C related autoimmune progression10,11.
It is critically important to improve Hepatitis C therapies. The existing medication like ribavirin and interferon-a can only create response to 50% of the infected people with genotype 1 infections.\textsuperscript{15,14} In developing countries like Pakistan the epidemiology and associated risk factors of hepatitis C are poorly understood, especially where self-medication and treatment by quacks is very common.\textsuperscript{15,16}

HCV is a major factor for glucose intolerance in patients suffering from liver cirrhosis. Patients suffering from diabetes type 2 have a trend to have cirrhosis, and another proportion may have some chronic or acute liver disease. This fact is supported by data explaining link between diabetes and HCV genotype 2a. It may be possible that hepatitis becomes an additional factor for the development of diabetes elsewhere any other liver disease solely.

The number of contributing factors discussed above may be due to the economic status of an individual in Pakistan. The poverty rate of Pakistan is 17.2\%, and nearly a quarter of the population is classified as poor\textsuperscript{17,18} and it is worrisome to note that 66% population of Pakistan is living in the rural areas.\textsuperscript{19,20} Considering the financial limitation in general public, only upper and middle class people can afford education and can use the private services. On the other hand, those who are unable to afford usually visit quacks or untrained medical professionals.

**MATERIAL AND METHODS**

The research was conducted to analyse the prescription trend for the treatment of hepatitis C in Jinnah hospital Lahore. 97 prescriptions were collected, from December, 2016 to Feb, 2017, of the patients who are diagnosed with the hepatitis C, and analysed individually. We checked out the drugs that are prescribed in the Jinnah hospital for the treatment of hepatitis C. The dose variability from patient to patient was studied as high as 16.3\%.

Out of 97 prescriptions, 48.5\% of all the patients studied were males whereas 51.5\% were females. At the same time, for the age analysis, the number of contributing factors discussed above may be due to the economic status of an individual in Pakistan. The poverty rate of Pakistan is 17.2\%, and nearly a quarter of the population is classified as poor\textsuperscript{17,18} and it is worrisome to note that 66% population of Pakistan is living in the rural areas.\textsuperscript{19,20} Considering the financial limitation in general public, only upper and middle class people can afford education and can use the private services. On the other hand, those who are unable to afford usually visit quacks or untrained medical professionals.

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The most common and frequent therapy plan is complete oral therapy consisting of ribavirin 1200mg/day (400mg TID) and sofosbuvir 400mg/day. The second frequent therapy plan was to treat hepatitis C with the ribavirin 1200mg/day (400mg TID) along with peginterferonalpha 2a (Injections). The details of other therapies are shown in the table 2.

The 2 variables (age and the drug(s) prescribed), here in this research, were studied simultaneously to check out the dependence of therapy plan on the age, results are shown in the table 3. H1: The therapy plan for the hepatitis C is associated with the age of the patient. H0: The therapy plan for the hepatitis C is not associated with the age of the patient. Results revealed that both the variables are significant at 0.5\%. The value of Pearson chi square calculated was 28.994 where df = 21, as shown in the table 4. As the test value (28.994) is less than the table value (41.401) so the null hypothesis (H0) will be accepted. So this test proved that the therapy plan is not associated with the age of the patient.

**RESULTS.**

The treatment of hepatitis C may be carried out with number of combination therapies. We made 23 combinations of all the drugs that can be prescribed in case of hepatitis C. out of 23, according to Figure 1, 8 combinations were practiced in jinnah hospital Lahore. The most common and frequent therapy plan is complete oral therapy consisting of ribavirin 1200mg/day (400mg TID) and sofosbuvir 400mg/day. The second frequent therapy plan was to treat hepatitis C with the ribavirin 1200mg/day (400mg TID) along with peginterferonalpha 2a (Injections). The details of other therapies are shown in the table 2.

![Figure1. Drug (s) Prescribed for the treatment of Hepatitis-c](image)

**DISCUSSION.**

HBV causes 563,000 deaths and HCV cause 366,000 death annually. The objective of this research was to check out the prescription trend for the hepatitis C i.e. to analyse the combination therapy. The association of therapy plan with the age of the patient was also studied. HBV and HCV infections are highly endemic in Pakistan. The HBV prevalence across Pakistan has been reported to be 1.11\%, 3\%, 3.2\% and 4%\textsuperscript{21,23}. HCV prevalence has been estimated to be 3.3\%, 2.2\% and as high as 16.3\%\textsuperscript{24}.

Prescription trend studies are a tool for assessing the prescribing, dispensing and distribution of medi-
## Table 1: Frequency of Gender of the Patient

<table>
<thead>
<tr>
<th>Valid</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>47</td>
<td>48.5</td>
<td>48.5</td>
<td>48.5</td>
</tr>
<tr>
<td>Female</td>
<td>50</td>
<td>51.5</td>
<td>51.5</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

## Table 2: Frequency of Age of the Patient

<table>
<thead>
<tr>
<th>Valid</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-20 Years</td>
<td>1</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>21-40 Years</td>
<td>60</td>
<td>61.9</td>
<td>61.9</td>
<td>62.9</td>
</tr>
<tr>
<td>41-60 Years</td>
<td>33</td>
<td>34.0</td>
<td>34.0</td>
<td>96.9</td>
</tr>
<tr>
<td>&gt;60 Years</td>
<td>3</td>
<td>3.1</td>
<td>3.1</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

## Table 3: Drug(s) Prescribed for the Treatment of Hepatitis-C

<table>
<thead>
<tr>
<th>Valid</th>
<th>Drug(s) prescribed for the Treatment of Hepatitis-C</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir 400mg + Ribavirin 1200mg</td>
<td>54</td>
<td>55.7</td>
<td>55.7</td>
<td>55.7</td>
<td></td>
</tr>
<tr>
<td>Peginterferonalfa 2a + Ribavirin 1200mg</td>
<td>12</td>
<td>12.4</td>
<td>12.4</td>
<td>68.0</td>
<td></td>
</tr>
<tr>
<td>Classical Interferon + Ribavirin 1200mg</td>
<td>7</td>
<td>7.2</td>
<td>7.2</td>
<td>75.3</td>
<td></td>
</tr>
<tr>
<td>Peginterferonalfa 2a + Sofosbuvir 400mg + Ribavirin 1000mg</td>
<td>4</td>
<td>4.1</td>
<td>4.1</td>
<td>79.4</td>
<td></td>
</tr>
<tr>
<td>Peginterferonalfa 2a + Sofosbuvir 400mg + Ribavirin 1300mg</td>
<td>5</td>
<td>5.2</td>
<td>5.2</td>
<td>84.5</td>
<td></td>
</tr>
<tr>
<td>Ribavirin 1400mg</td>
<td>1</td>
<td>1.0</td>
<td>1.0</td>
<td>85.6</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir 400mg + Ribavirin 800mg</td>
<td>10</td>
<td>10.3</td>
<td>10.3</td>
<td>95.9</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir 400mg + Ribavirin 1000mg</td>
<td>4</td>
<td>4.1</td>
<td>4.1</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Table 4: Age of the patient*Drug(s) prescribed for the treatment of Hepatitis-C

<table>
<thead>
<tr>
<th>Count</th>
<th>Sofosbuvir 400mg + Ribavirin 1200mg</th>
<th>Peginterferonalfa 2a + Ribavirin 1200mg</th>
<th>Classical Interferon + Ribavirin 1200mg</th>
<th>Peginterferonalfa 2a + Sofosbuvir 400mg + Ribavirin 1000mg</th>
<th>Peginterferonalfa 2a + Sofosbuvir 400mg + Ribavirin 1300mg</th>
<th>Ribavirin 1400mg</th>
<th>Sofosbuvir 400mg + Ribavirin 800mg</th>
<th>Sofosbuvir 400mg + Ribavirin 1000mg</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-20 Years</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>21-40 Years</td>
<td>33</td>
<td>8</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>60</td>
</tr>
<tr>
<td>41-60 Years</td>
<td>19</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>1</td>
<td>33</td>
</tr>
<tr>
<td>&gt;60 Years</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>12</td>
<td>7</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>10</td>
<td>4</td>
<td>97</td>
</tr>
</tbody>
</table>

## Table 5: Chi-Square Tests

<table>
<thead>
<tr>
<th>Value</th>
<th>df</th>
<th>Asymp. Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>28.994a</td>
<td>21</td>
</tr>
<tr>
<td>Likelihood Ratio</td>
<td>25.426</td>
<td>21</td>
</tr>
<tr>
<td>N of Valid Cases</td>
<td>97</td>
<td></td>
</tr>
</tbody>
</table>

a. 28 cells (87.5%) have expected count less than 5. The minimum expected count is .01.
cines. The present study has been done to know the prescription pattern of Hepatitis C and its association with the age. The treatment of hepatitis C may be carried out with number of combination therapies. We made 23 combinations of all the drugs that can be prescribed in case of hepatitis C. Out of 23, 8 combinations were practiced in Jinnah Hospital Lahore. In the prescription trend the combination of ribavirin 1200mg/day (400mg TID) and sofosbuvir 400mg/day prescribed to 55.7% of the patients was found to be the most frequent. Second frequent therapy was the combination of oral therapeutic agent (ribavirin 1200mg/day (400mg TID)) and an injectable (Peginterferonalfa 2a) which was prescribed to 12.4% of the patients whereas interferon alfa 2a were also used along with the ribavirin. Our study showed that combination therapy was mostly being prescribed for the treatment of hepatitis C patients than monotherapy in which we observed only Ribavirin 1400mg was used along in 1% patients. Oral therapy for the hepatitis C treatment is the most frequent therapy plan. Where as the second frequent therapy plan was a combination of oral and the injectable. It was also concluded from the statistical values.

CONCLUSION

Oral therapy for the hepatitis C treatment is the most frequent therapy plan in the Jinnah hospital whereas the second frequent therapy plan was a combination of oral and the injectable. On the other hand there is no association of age of patient with the therapy plan followed for hepatitis C in the Jinnah hospital Lahore. It directly means that the therapy plan is independent of the age of the patients and it will be chosen according to the condition of the patient and the disease.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Yousaf H: Conception and design, Acquisition of data, final approval of the version to be published.

Mehmood Y: Drafting the manuscript.

Ashraf MI: Analysis and interpretation of data, final approval of the version to be published.

Raza SA: Critical revision.

Hassas SS: drafting the manuscript.

Bilal A: Bibliography.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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