

**COST AND OUTCOMES OF DIRECT ACTING ANTIVIRAL THERAPY IN CHRONIC
HEPATITIS C PATIENTS WITH GENOTYPE 3**Anum Hanif¹, Bazgha Ashfaq², Bushra Ali Sherazi³, Dr. Tahir Anwer⁴, Jawad Ashfaq⁵

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ABSTRACT

Context: Hepatitis is derived from Ancient Greek words hepa which means liver and itis which means inflammation. Hepatitis viruses have 5 different types each associated with a different etiology, distribution, mode of transmission and mortality risks. However, the virus of interest here being hepatitis C virus, which transmitted via blood. **Aims and Objectives:** The objectives of this study are to evaluate the prescription drugs cost of current treatment regimens available for HCV Genotype 3. **Design, setting and participants:** An observational and cross-sectional study was carried out in the community involving patients with diagnosed Hepatitis C. Data collection, analysis, and interpretation were stretch to a span of 6 months from August 2016 – January 2017. **Main outcome Measure:** Gender, age, monthly income, awareness and knowledge about HCV, knowledge about cause of HCV, knowledge about medication of HCV, blood profile in last three months, blood profile in last six months. **Results:** Most of the population in Pakistan belongs from the middle class 55% of the population for this sample size was belonging from middle class while 30% were very poor only 13% from upper middle class. **Conclusion:** In this, study the assessment of the treatment outcomes for different regimens of Direct Acting Antivirals (DAAs) in terms of patient compliance, relapse rate, improvement in liver architecture, the disability-free period the patient gets using a certain combination of drugs. The entire research directed to figure out the best treatment option for curing genotype 3 infection.

INTRODUCTION

Hepatitis is derived from Ancient Greek words hepa which means liver and itis which means inflammation. Hepatitis, therefore, is defined as the body's reaction, either self-limiting or progressive, in order to protect against the offensive foreign substance. Hepatitis C may follow one of the two patterns, either acute or chronic, however, in its latter version it may progress to fibrosis, cirrhosis or hepatocellular carcinoma. Hepatitis C is most commonly seen in the middle-aged people. According to the WHO statistics, approximately 3% of the entire population of the world (about 130-150 million people) suffer from chronic hepatitis C infection, and most of them, however; end up having hepatocellular carcinoma.^[1]

Hepatitis C has a geographic predilection for regions like Africa, East, and Central Asia. In specific continents, the only group of populations that have an exposure to its various risk factors has high concentration Hepatitis C infected cases. Regardless of its high prevalence rate, not every country in the world has schemes for early diagnosis, adequate treatment, and prevention. The protocols required for thorough screening are lacking. For particular nations, it's not even possible to screen the entire population against Hepatitis C, which causes the

immense lag in statistical data concerning the geographical distribution. Despite all these factors, hepatitis C, along with hepatitis B, is involved in 75% cases associated with the liver disease all over the world.^[2]

Hepatitis is characterized as liver inflammation, which is the local reaction of body, in this case restricted to liver, any foreign substance that invades the body. Hepatitis main have a number of causes however, hepatitis viruses being the most important of all. Hepatitis viruses have been classified into five basic types and given the names A, B, C, D and E. During the past few decades, hepatitis C virus owing to its increasing prevalence has drawn significant amount of attention.^[3] According to an estimate, approximately 70,000 people die every year due to causes associated with Hepatitis C. HCV is transmitted via blood, use of improperly screened blood for transfusion, inadequately sterilized surgical equipment, vertical transmission from mother to new born during delivery are some of the few factors responsible for its transmission. Virus exhibits two patterns of disease one is acute the other being chronic; is linked to progression into hepatic fibrosis, development of hepatocellular carcinoma or hepatic failure.^[4] HCV is found to have 6 different genotypes,

these 6 main types have been further classified into 15 subtypes, among these genotype 3 is the most attention demanding as it is responsible for majority of hepatitis C cases in Pakistan. Recent treatment plans are targeted at curing the illness by administration of antivirals and show a success rate of 90%. The pharmaceutical industry is giving their best for the development of treatment option that are more affordable for the patients and have high compliance.^[5]

MATERIALS AND METHOD

This study is targeted towards determining the treatment outcomes and cost imposed by hepatitis C drugs when given to chronic hepatitis patients having genotype 3 infections. Genotype 3 of HCV is very difficult to treat, therefore; it poses a greater financial burden when treatment regimens and healthcare is taken into consideration. Unfortunately, genotype 3 is one of the most prevalent types found in Pakistan. Hepatitis is essentially a disease of low socio-economic status moreover; unhygienic measures and poor sanitation pave the path for its spread. People of the lower class or the lower middle class are the favorite targets of this illness; this is due to the fact that limited health care options are available for this class. In such conditions, when earning a living is huge distress treatment costs for hardy infection like hepatitis become unbearable.

RESULTS

From 385 patients, 186 were male and 199 were female. Pakistan is low income country most of the population belongs from the middle class 55% of the population for

this sample size was belonging from middle class while 30% were very poor only 13% from upper middle class. From the total sample size of 385 patients 186 were male and 199 were female. The mean age of participants was 43 years. 85% of patients have knowledge about their disease while 15% don't know about HCV. The awareness in the patients suffering from HCV was 38.7% people know about the causes of disease and 61% community mostly from older age and uneducated people did not know about their disease causes. Nowadays treatment of HCV is with oral medications, use of interferon is reduced, 73% of patients from sample know about oral medications for HCV while 27% patients don't know about oral medications of HCV. 78% of Patients had a profile of regular blood tests after 3 months while only 21% had not. 88% of Patients had a profile of regular blood tests after 6 months while only 12% had not. 41% patients of HCV have received INF-based therapy while 57% did not received INF based therapy. 15% of patients said that treatment is affordable for them while 85% said treatment is unaffordable for them. 65 % patients complain about stomach pain, 16% were suffering from hypertension, general weakness and joints pain was 7.5% only 4% were suffering from only HCV with no other comorbidity. 11% of the patients from sample size is using Sof+Rib+Dac, 65.5% of patients using Sof +Rib, 13 % of patients are using Peg+INF+ Sof+Rib, 9.6% are using Dac+Sof. The average pharmaceutical cost of Sof +Rib, was calculated as 77,232 rupees for 24 weeks of the therapy and from the 385 of the population 252 patients are using this combination.

Variable	f (%)	
	Males	Female
Gender	186(48.3)	199(51.7%)
Age (in years)		
20-40 years	178 (46.2%)	
41-60 years	173 (44.9%)	
61-80 years	34 (8.8%)	
Monthly Income	5 (1.3%)	
<10,000		
10,000 - 30,000	113 (29.4%)	
30,000-50,000	214 (55.6%)	
More than 50,000	53 (13.8%)	

	Yes	No
Knowledge about oral medication of HCV	281	104
Perform blood test in last six month	388	47
Have you ever received INF Based therapy?	162	223
Affordability of HCV treatment	59	326

	Frequency	Percentage
Diabetes	29	7.5%
Hypertension	64	16.6%
General weakness+ joints pain	29	7.5%
Stomach pain	247	64.7%

Nil	16	4.2%
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Mostly used combinations for HCV G3

Combinations of DAA	f(%)
1. Sof + Dac + Rib	45(11.7%)
1. Sof + Rib	252(65.5%)
1. Peg-INF + Sof+ Rib	51(13.2%)
1. Sof + Dac	37(9.6%)

11% of the patients from sample size is using Sof+Rib+Dac, 65.5% of patients using Sof +Rib, 13 % of patients are using Peg+INF+ Sof+Rib, 9.6% are using Dac+Sof.

DISCUSSION

Hepatitis C is a burgeoning health problem in the modern world affecting an approximate amount of 130 to 150 million of the world population. Annually 70,000 people die of the diseases related to hepatitis C. patients infected by hepatitis C virus show a spectrum of symptomology, a small percentage i.e., 15-45 % recover from the disease without any treatment within 6 months. Treatment with combination therapy, provide above 80% cure rate according above results. However, there is considerable amount of population that demonstrates either acute or chronic symptoms of hepatitis C infection. Patients who are carriers of acute infection usually are asymptomatic. A 75-85% risk prevails that acute infection converted to chronic hepatitis C infection. Chronic hepatitis C itself is not very simple to treat because those involved may progress either to hepatocellular carcinoma or to liver cirrhosis. 15-30% of the chronic carriers develop liver cirrhosis over a period of 20 years.^[6]

Knowledge of HCV should be common among people, 61% people in the sample of 385 were not aware from reasons of HCV. Hepatitis C virus is a blood-borne virus that transmitted via contact with infectious blood, transfusions from donors to carriers of the virus, those undergoing dialysis, and patients having HIV infection along with HCV infection are sources of spread, use of inadequately sterilized equipment for medical and surgical purposes. HCV is one of the common issues to the fact that it has six genotypes further classified into 15 subtypes making it cumbersome to work out the treatment options. Each genotype has its own characteristics and an idiosyncratic response to the treatment regimens. The discovery of each genotype has called for an increased emphasis on the development of accurately targeted drugs customized for each genotype.^[7]

For the management of chronic hepatitis c treatment, between 2001 and 2011 traditional therapy was based on PEG-INF along with Ribavirin but now converted into totally oral based therapy which is more convenient. In December 2013, Sofosbuvir, a NS5B nucleotide polymerase inhibitor, was approved for use with PEG-INF and RBV for for 24 weeks in genotype 3.^[8]

Now the use of combination therapy is common for the treatment of HCV, sof+rib is most affective combination nowadays, During the past decade, the only treatment option for curing chronic hepatitis C infection was alpha interferon. As not much known regarding the various genotypes, the drug had its failures and successes. Being associated with very serious adverse consequences such as hemolytic anemia's, aplastic anemia, damage to the immune system, increased susceptibility to infections otherwise normally combated by a healthy body, interferon's were soon the less preferred choice and researchers began looking for drugs with lesser adverse reactions and more efficacy. Although it is still used in the medical setting interferon-alpha is associated with high relapse rate after discontinuation of treatment, demonstrated as raised SVR (sustained virologic response). After considerable interferon use, FDA approved ribavirin as a drug that could be in combination with interferon, it reduces the relapses of infection as well as improves treatment success rate. With the advent of direct-acting antivirals (DAAs) the whole scenario changed. As now newer options that are more targeted and fewer adverse reactions set out in the market.^[9]

CONCLUSION

In this, study the assessment of the treatment outcomes for different regimens of Direct Acting Antivirals (DAAs) in terms of patient compliance, relapse rate, improvement in liver architecture, the disability-free period the patient gets using a certain combination of drugs. Last but not the least the combinations used, were also assessed for their cost effectiveness and affordability. The entire research directed to figure out the best treatment option for curing genotype 3 infection. As per the analysis, it concluded that in 65% of the patients nowadays administer a combination of Sofosbuvir and Ribavirin. Whereas, only 11% use Sofosbuvir+ Ribavirin + Daclatasvir; 9% Sofosbuvir + Daclatasvir as a combination and 1% of the analyzed participants use pegylated Interferon+ Ribavirin + Sofosbuvir.

By far the combination of Sofosbuvir and Ribavirin is the new trend among the patients and the clinicians; very few still prescribe interferon as a treatment regimen. The increasing demand and compliance associated with Direct Acting Antiviral (DAAs) combination therapies are due successful results, easy mode of uptake and availability. Sustained virologic response (SVR) and rapid virologic response (RVR), are among the

diagnostic parameters that validate the success of drug by monitoring the viral load. Direct Acting Antivirals are favored because of their ability to exploit these parameters, thus, exhibiting astonishing results.

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