A Cost-Effectiveness Analysis of Different Antiviral Medicine Regimens in Patients with Chronic Hepatitis C Virus Genotype 3 Infection

By

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CERTIFICATE

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I dedicate this thesis to

My

Parents, Siblings

&

Husband.

Whom prayers and exceptional support

Enabled me to accomplish this.

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ABSTRACT

Pakistan is among the developing countries which are experiencing a rising burden of hepatitis C with the prevalence rate of 4.5 to 8% thus making it as a huge disease burden for the country. Besides the continuously increasing disease prevalence, the treatment is very costly. After 2011, there has been advancement in the treatment. The new drugs have been found to be more effective with increased cure rates and less cost. So this study is aimed at conducting the cost-effectiveness for hepatitis C treatments in patients with type 3 genotype. The costs and outcomes of providing treatment through intervention strategy is compared to the costs and outcomes of providing it through comparative strategy from provider perspective with the sample size of 697 patients. A decision analytic model i.e., Markov model is used for the analysis. The study has obtained the patient's and cost data through hospital records and meta-analysis for the year 2016-17. The study findings indicate that the intervention is more effective in term of both costs and effects in comparison to the comparator in terms of incremental cost-effectiveness ratio. And the life years gained through intervention strategy are 5.86 years more than the comparative strategy. So providing hepatitis C treatment through intervention is a good public health investment in the elimination of virus from the country.

Acronyms

CDC	Centre for Disease Control
CEA	Cost Effectiveness Analysis
DAA	Direct Acting Antivirals
HCV	Hepatitis C
HCC	Hepatocellular Carcinoma
RNA	Ribo Nucleic Acid
SVR	Sustained Virological Response
RVR	Rapid Virological Response
EVR	Early Virological Response
LYG's	Life Years Gained
QALY's	Quality Adjusted Life Years
WTP	Willingness to Pay Threshold

CHAPTER 1

INTRODUCTION

1.1 Background and Motivation:

Hepatitis C is a global health concern which is continuously on the rise. This disease is characterized by prevalence, chronicity and latency (Stein et al., 2002). It is an infectious as well as a communicable disease which is eliminated from a country by bringing its incidence to zero. This elimination goal is achieved through effective prevention and providing access to the treatment, thus wiping out the virus completely. According to "World Health Organization's first global health sector strategy on viral hepatitis (2016-2021)" that contributes to the achievement of the 2030 agenda for sustainable development, viral hepatitis is set to be reduced by 10% by 2021 and eliminated as a major threat to public health by 2030 (WHO, 2016).

The disease is caused by a virus belonging to the flaviviridae family of viruses. The virus is very small (50nm in size), enveloped, plus stranded Ribo Nucleic Acid (RNA) virus which was discovered in 1989 (CDC, 2014). This blood borne virus spreads through injectable drugs, unsafe blood transfusions and other healthcare practices. It can even transfer from a mother to a child through the fetus (WHO, 2017). This viral infection is asymptotic i.e., it remains active in patients causing harm to his liver without making him aware of the presence of virus (Riaz, 2016). Other than hepatitis C, there are four more types of viruses, A, B, D and E but hepatitis B and C are more prevalent and chronic while contributing to highest morbidity and mortality thus account for a huge disease burden in the country (NHSF, 2017-2021). Each type of virus is characterized and treated according to its own genotype which are 7 in number and will be explained later in this chapter.

Due to the huge disease burden, the virus constantly has a considerable impact on health system. If the hepatitis C infection is not treated timely, it progresses to more chronic stages such as cirrhosis and liver failure and can even lead to death. In Cirrhosis, liver functioning is affected due to the long-term damage which is caused due to the presence of scarred tissues. When liver is greatly damaged and it cannot perform its synthetic and metabolic functions anymore then this is categorized as liver failure. An estimated 71 million people are affected and 3.9 million people die each year worldwide. Cirrhosis and liver failure are responsible for high mortality (WHO, 2017). "If the number of people living with hepatitis remains at the

current high levels for the next 40-50 years, it is estimated that a cumulative 20 million deaths will occur between 2015 and 2030 (NHSF, 2017)."

If hepatitis C is treated at the initial stages of development then there is a lower chance that a person may develop advanced disease stages and thus it ultimately decreases mortality and related costs (Alavian et al., 2016). Over the last 5 years, owing to the high disease prevalence in different geographical regions, a relative explosion of new treatment options for hepatitis C infection is witnessed. Fortunately, with the advances in the field of health care, effective and affordable treatments are now available in Pakistan which ensure a much better cure rate. All the adult patients should be provided the treatment to eliminate the virus and to lower the risk of disease progression towards advanced stages. (Mohamed et al., 2015).

With the therapeutic advancements, a lot of antiviral drugs are available for treatment in the world. Among the currently available drugs, there are Interferon and Peg Interferon, Ribavirin, Direct Acting Antivirals (DAA's) which include Protease Inhibitor Antiviral Medications (Simeprevir), Polymerase Inhibitor and combination drugs, Sofosbuvir (Sovaldi), Ledipasvir and Sofosbuvir (Harvoni), Dasabvir, Ombitasvir, Paritaprevir and Ritonavir (Viekira Pak), Elbasvir and Grazoprevir (Zepatier), Ombitasvir, Paritaprevir and Ritonavir (Technivie), Daclatasvir (Daklinza) and Velpatasvir (Epclusa) (Cherney, 2015).

The most commonly used drugs in Pakistan for hepatitis C treatments are unipeg (pegylated interferon alpha-2a), uniferon (conventional interferon alpha-2b), sofosbuvir (sovaldi), ribazole (ribavirin) and mydacla (daclatasvir). Other than these, Rifaximin (Xafixan), Spironolactone (Aldactone), Silymarin (Silliver) and Aminolebam are commonly recommended as baseline treatment for liver scarring. Sofosbuvir, mydacla and sofosbuvir/velpatasvir (epclusa) are a new addition to the hepatitis C drugs family. These are the generic version of brand-name drugs. Since 1992, conventional interferon and ribavirin was used as a standard care with a cure rate of 40-50%. The treatment duration for this therapy is 24 or 48 weeks but from 2011, combination of sofosbuvir and ribavirin, sofosbuvir and daclatasvir with or without combination of ribavirin is being used. These combinations are beneficial for patients who are not eligible for interferon therapy or are intolerant with much better cure rate. The monotherapies are not recommended due to side effects (Abdel-Razek, 2014).

According to a research conducted at Agha Khan University, sofosbuvir along with the peg interferon and ribavirin gives almost 85% cure rate (Hamid, 2017). The cure rate for the

combination of velpatasvir, ribavirin and sofosbuvir is 91% (Catie, 2016). The cure rate of sofosbuvir and ribavirin is 93%, combination of daclatasvir, sofosbuvir and ribavirin is 100%, sofosbuvir and daclatasvir is 91%, sofosbuvir and ribavirin is 92%, ledispavir, sofosbuvir and ribavirin is 100% and combination of elbasvir, grazoprevir and ribavirin is 96% (Infohep, 2016). These cure rates are much better than the previously followed interferon based treatments which shows the effectiveness of new drug regimes.

But on one hand, where these new 'miraculous' treatments have reduced the risk of liver failure and subsequent development of cirrhosis along with improved survival rates, these are very expensive and of long duration because of the chronicity of the disease which makes the affordability difficult for the country with scare resources and disease prevalence among people with low socioeconomic status (Hamid, 2017). Table 1.1 shows the prices of different drugs which are used to treat hepatitis C based on their duration.

Table 1.1. Price of Drugs for hepatitis C Treatments.

Unipeg (Peg Interferon)	Rs. 4,500/vial
Uniferon (Conventional Interferon)	Rs. 398/vial
Sovaldi	Rs. 32,300/month
Sofosbuvir (generic version of Sovaldi)	Rs. 5,868/month
Mydacla (Daclatasvir)	Rs. 6,000/month
Clavir (Daclatasvir)	Rs. 4,550/month
Velpatasvir	Rs. 20,000/month
Ribazole (Ribavirin)	Rs. 34/10 tablets
Novia (Ribavirin)	Rs. 65/10 tablets

Ribavirin, sofosbuvir, daclatasvir and velpatasvir are more expensive but have better cure rates and minimal side effects as compared to peg interferon. Though government has subsidized these drugs but still they are much far behind the affording capacity of most of the population.

In the situation, where treatment options need to be selected among the variety of different antiviral drugs due to the limited resources, a cost effectiveness study is significant. As the cost-effectiveness analysis determines that how can a particular society maximize both the quality and quantity of life within the scare resources and this information is used by decision makers for the assessment and improvement in performance of health system (Muennig, 2008). A cost-effectiveness analysis (CEA) of a drug treatment provides

information on the costs and associated outcomes of the treatment. These cost and outcome ratios then rank the different treatments and indicates which treatment provide highest value for money and maximizes health for available resources. The one with the lowest cost per more clinical benefits gained is considered cost-effective (Mullins et al, 2002).

No cost-effectiveness studies have been conducted in context of Pakistan for the estimation of the cost effectiveness of hepatitis C treatments. With reference to hepatitis C, there are several studies which have estimated prevalence, genotype distribution, efficacy, sustained virological response and end treatment response rate so to fill this gap, the present study focuses on estimating cost-effectiveness for hepatitis C treatments to obtain the outcome that is effective in terms of both cost and quality for appropriate policy making and implementation.

1.2 Global Prevalence of Hepatitis C:

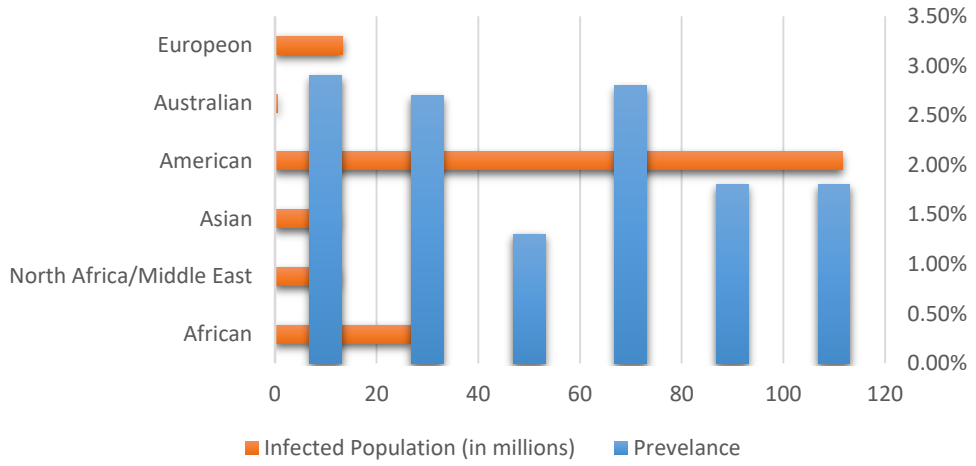
Hepatitis C is associated with high morbidity and mortality and is found worldwide. The prevalence of hepatitis C is mostly based on sero-prevalence studies (Shepard, 2005). Sero-prevalence indicates the amount of population which have active presence of the disease according to the blood serum samples. In 2015, 130-150 million people were affected globally which is reduced to an estimated 71 million people in 2017 and approximately, 3.9 million people die each year of this disease which is reduced from 5 million (as of 2015). This is due to the availability of effective treatment. The people who have active hepatitis C virus are more prone to the serious diseases like chronic liver disease, cirrhosis, and hepatocellular carcinoma (HCC) – a type of liver cancer. These advanced disease stages are responsible for high mortality rates (WHO, 2017).

Hepatitis C is spread worldwide with the different distribution in different regions of the world (WHO, 2010). In African continent, North Africa has the highest prevalence of 2.9% with 26.9 million cases. After North Africa, the disease is more common in central and Southern Africa with the prevalence of 6.0% & 0.9% respectively. In Asian Continent, the prevalence of disease is 2.8% with more than 60% cases worldwide. (Petruzziello, 2016).

In American Continent, the prevalence of hepatitis C is 1.3% with 12 million of estimated cases. (Petruzziello, 2016). In Australian Continent, the disease is more prevalent in New Zealand and Australia with the prevalence of 1.9% and 1.7% respectively. 1.7% in Australia with the estimated cases amounting to 0.5 million. In European continent, the occurrence of disease is estimated to be 1.8%, with more than 13 million of estimated cases

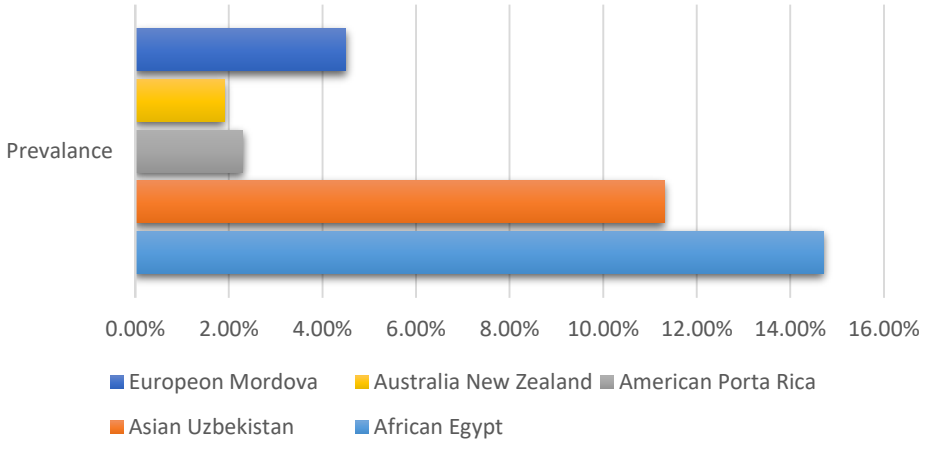
(Petruzziello et al., 2016). American, Australian and European continents have lower prevalence of hepatitis C as compared to the Asian and African Continents. (Lavanchy, 2009). Figure 1.1 shows the regional prevalence of hepatitis C with the infected population.

Fig 1.1. Regional Prevalance of hepatitis C



In African continent, Egypt has highest prevalence of 14.7% which is greater than any country in the world. In Asian continent, Uzbekistan has the highest prevalence of 11.3% among all countries. In American continent, Porta Rica has the highest prevalence of 2.3% among all the countries of the continent America. In Australian continent, New Zealand has a higher prevalence of 1.9%. In European continent, Moldova has the higher prevalence of 4.5% as shown in figure 1.2 below:

Fig 1.2. Countries with highest prevelance of hepatitis C in different regions of the world

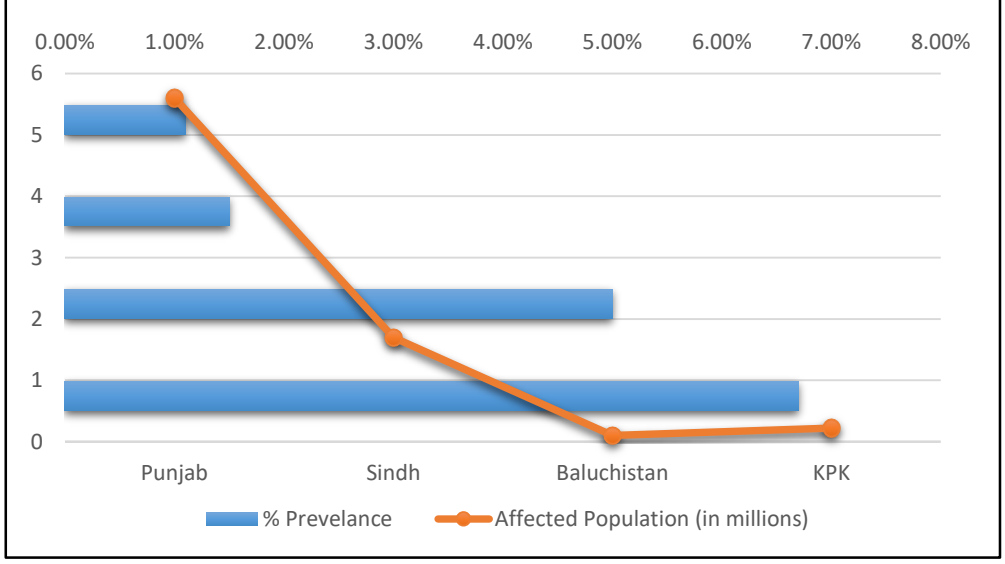


1.3 Prevalence of Hepatitis C in Pakistan:

In many developed countries like United States, Western and Northern Europe, Japan and Australia, they have lowered down the prevalence of hepatitis C to a much lesser extent but the developing counties are still facing the burden of this disease. Pakistan is one of them which is experiencing a continuous rise of hepatitis C after Egypt and Uzbekistan with the prevalence of around 6.8% with 6-10 million cases which was previously 4.9% according to National Hepatitis Survey, 2007-08 (Umer et al., 2016). The annually reported death rate is 1.4 million due to this chronic disease (WHO, 2016).

In national hepatitis survey, 47 thousand persons were screened. In provincial level prevalence, Punjab showed a high prevalence rate of 6.7% which constitute 5.6 million people, followed by 5% in Sindh which constitutes 1.7 million, 1.5% in Baluchistan which constitute 0.1 million and 1.1% in Khyber Pakhtun Khwa which constitutes 0.22 million (National Hepatitis Survey Report, 2007-08). These prevalence rates in the provinces of Pakistan are represented in graphical form in figure 1.3 below:

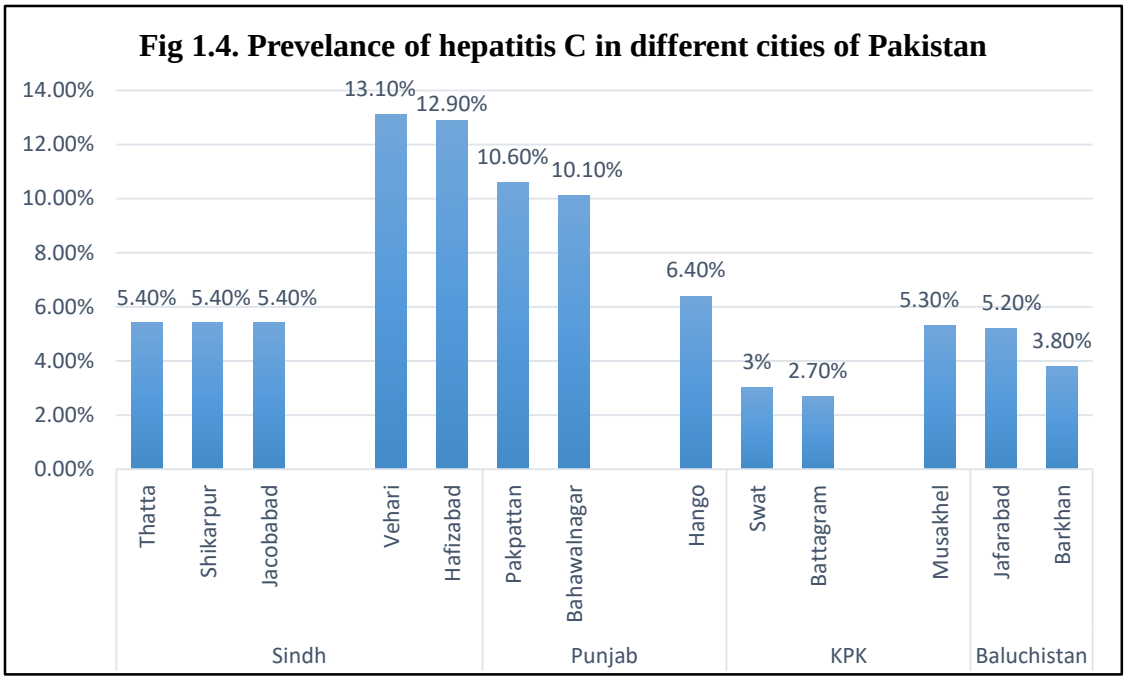
Fig 1.3. Prevelance of hepatitis C in provinces of Pakistan



In district wise prevalence; in Sindh, Ghotki had a higher prevalence of 12.7% followed by Sanghar with the prevalence of 7.8%, Dadu with the prevalence of 7.2%, Hyderabad with 5.7%, Thatta with 5.4%, Shikarpur and Jacobabad with 5.3% each. In Punjab, Vehari showed a high prevalence of 13.1%, followed by Hafizabad with the prevalence of 12.9%, Pakpattan with 10.6% and Bahawalnagar with 10.1%. In Khyber Pakhtunkhwa, Hango showed a high

prevalence of 6.4%, followed by Swat with 3% and Battagram with 2.7%. In Baluchistan, Musakhel showed a high prevalence of 5.3%, followed by Jafarabad with a prevalence of 5.2% and Barkhan with the prevalence of 3.8% (National Hepatitis Survey Report, 2007-08). These survey results are represented in the figure 1.4 below:

Fig 1.4. Prevelance of hepatitis C in different cities of Pakistan



Apart from the survey, there are several studies which have estimated prevalence of hepatitis C, according to which the prevalence of hepatitis C is more in Nausheroferoz district of Sindh (Aziz, 2010) and it is lesser in Gujranwala with the prevalence of 2.3 (Ilays, 2011). But most of this data is based on studies which are conducted only in Punjab, Sindh and KPK – the bigger provinces (Ahmed, 2010) which together make up for more than 80% of the population of Pakistan (Umer et al., 2016).

According to the study conducted in Swat district, the sero-frequency for hepatitis C is less in healthy population i.e. 3% as compared to the population with illness i.e. 8% (Rauf, 2011). As of 2010, the regions with the highest prevalence of hepatitis C are Thatta/Nausheroferoz (Rural area) with the prevalence of 25.1% (Janjua, 2009), Karachi (Peri-urban area) with the prevalence of 23.83% (Aziz, 2010) and Islamabad with the prevalence of 24.6% (Hashmi, 2010).

Besides the incorporation of advanced technology, developing countries like Pakistan are still facing acceleration in hepatitis C disease burden with high morbidity and mortality ratios. Because disease is highly prevalent in the population with low socio-economic status

for which it is difficult to afford expensive treatment. This alarming situation clearly leads to the importance of the fact that effective and affordable treatment is significant need of the hour.

1.4 Genotype Distribution:

Hepatitis C is categorized into seven genotypes and each genotype has several subtypes. Genotype is basically the part of genetic makeup of a cell and therefore of an organism or individual which determines a specific characteristics of that cell/organism/individual. Knowing genotype of the affected population is important because it helps in formulating the treatment strategy. Genotype distribution varies with persons and regions. Treatment strategy is different for each genotype thus making genotype an important factor in providing the right kind of treatment. So the decision makers have to formulate treatment strategies according to the regions based on the genotype for the effective removal of virus from the respective regions (Petruzziello et al., 2016).

1.4.1. Global Distribution:

While identifying worldwide genotype distribution, Genotype 1 is most prevalent in Europe, Australia, Asia and America which is estimated to account for overall 83.4 million cases with a prevalence rate of 46.2%. In Europe, genotype 1 is most occurring genotype in Northern and Western Europe with the prevalence of 64.4%. After Europe, it is more common in South America with the prevalence of 72%, North America with the prevalence of 66.3%, Australia with the prevalence of 55% and Asia with the prevalence of 46.6% (Petruzziello et al., 2016).

Genotype 2 is more common genotype in Africa. In Central Africa, its prevalence is 82.9% and in Western Africa, its prevalence is 62.9%. Genotype 3 is most occurring genotype in South Asia with the prevalence of 22.4%. According to an estimate, out of total cases of hepatitis C, 66.7% cases are associated with this genotype. This genotype is more common after genotype 1 due to the occurrence of 54.3 million cases which constitutes 30.1% globally. (Petruzziello et al., 2016).

Genotype 4 is most commonly occurring type in Middle Eastern countries especially Egypt which has a prevalence of 28.1%. Genotype 5 is most common type in South African region with the overall prevalence of 12.2%. Genotype 6 is more common in South East along with genotype 1 with the prevalence of 30.8% and 35.2% respectively. The prevalence of mixed genotypes is higher in Asia with the prevalence rate of 4.3%, followed by Africa with

the prevalence rate of 3.4%, America by 2.6% and Europe with the prevalence rate of 0.7% (Petruzziello et al., 2016). The overall global prevalence rates are represented in table 1.2 below:

Table 1.2. The global prevalence of genotypes for Hepatitis C.

Continents	G1 (%)	G2 (%)	G3 (%)	G4 (%)	G5 (%)	G6 (%)	Mixed Genotype (%)
Africa	26.3	23.7	6.3	28.1	12.2	-	3.4
Asia	46.6	18.6	22.4	1.0	0.1	7.0	4.3
America	74.5	10.2	10.6	1.7	0.1	0.3	2.6
Australia	55.0	6.5	36.0	1.2	-	1.3	-
Europe	64.4	5.5	25.5	3.7	0.1	0.1	0.7
North Africa/ Middle East	27.3	0.8	6.3	65.3	0.3	-	-

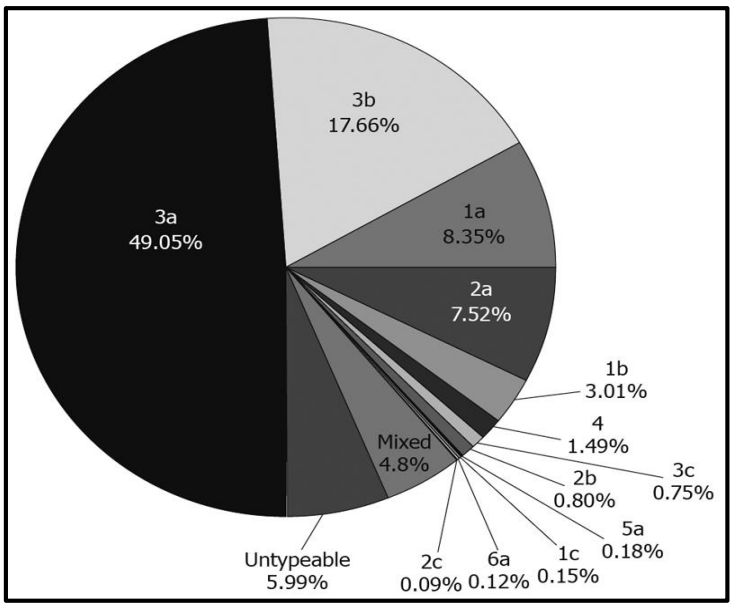
1.4.2. Pakistan Based Distribution:

On the whole, genotype 3 is the most prevalent genotype in Pakistan with the prevalence rate of 69.1%, followed by genotype 1 with the prevalence rate of 7.1%, genotype 2 with the prevalence rate of 4.2%, and genotype 4 with the prevalence rate of 2.2%. The prevalence of Genotype 5 & 6 is very low in Pakistan in Pakistan with the prevalence of approximately 0.2% each. The prevalence of mixed genotypes is 4.2%. Among subtypes, overall genotype 3a is most common with the prevalence rate of 61.4%, followed by genotype 3b with the prevalence rate of 7.6%, genotype 1a with the prevalence rate of 5.7%, genotype 2a with the prevalence rate of 3.7% and genotype 1b with the prevalence rate of 1.4%. There are several types of genotypes as well but their prevalence is less than 1% each. Umer et al., 2016).

After genotype 3, genotype 2 is most common, particularly in Sindh and KPK, with the prevalence rates of 11.3% and 17.3% respectively. Among subtypes, genotype 3a is more common in Punjab, Sindh and KPK with the prevalence rates of 67.7%, 53.9% and 46.9%

respectively. Genotype 2a is common in Sindh and KPK with the prevalence rates of 6.06% and 15.1% respectively (Umer et al., 2016). The overall prevalence of genotypes for hepatitis C is represented in figure 1.6 below:

Fig 1.6. Genotype Distribution in Pakistan



Source: Waheed, Y., Shafi, T., Safi, S.Z., & Qadri, I. (2009) Hepatitis C virus in Pakistan: A systematic Review of prevalence, genotypes and risk factors. *Word Journal of Gastroenterology: 15(45): 5647–5653*

1.5. Rationale of the Study:

The health sector of Pakistan always remained badly neglected and as a result of this, at present, Pakistan being a developing and middle income country is going through epidemiological and demographic transition. It is also facing double disease burden that is communicable and non-communicable diseases along with maternal, child health issues and other emerging health challenges (Nishtar, 2007). Despite these numerous problems, Pakistan is spending only 0.46% of Gross domestic Product (GDP) in health care sector as of 2016-17 which is even decreased from the past share of 0.76% as of 2015-2016. This share is too less than the World Health Organization's benchmark of at least 6% of GDP which is required to spend in health care sector to improve the quality of life. (Pakistan Economic Survey, 2016-17). This low budget is insufficient for growing population needs with a huge disease burden.

Though health sector of Pakistan has been able to cope many of the health problems through the past 10 but still there are a lot of diseases which are becoming increasingly prevalent and need much attention and investment. Hepatitis C is one of them. Around 4.8% of the population is suffering from this chronic illness which cost burden on individuals as well

as on the society by lowering the quality of life and life expectancy. With the advancement in the technology, treatments are available but they are very costly. Therefore, it is evident to focus on providing cost effective treatments in order to make treatment affordable and to lower the prevalence as the disease is more prevalent among people with low socioeconomic status.

Therefore, the present study is an attempt to evaluate the cost-effectiveness of treatment through new and advanced antiviral drug regimen and old & standard drug regimen by comparing the costs and effects of both the treatments. This cost-effectiveness analysis plays a significant role in selecting optimal treatment strategy. Therefore, the results of the study will help the policy makers to prioritize things in healthcare by providing a significant evidence.

1.6. Research Question:

This study is an attempt to address the following questions:

1. What is the total cost of providing hepatitis C treatments in the study site?
2. What is the effect of hepatitis C treatments on patients which are having treatment?
3. What is the cost effectiveness of hepatitis C treatments in terms of incremental cost effectiveness ratios?

1.7. Objectives:

The aim of the present study is to achieve the following objectives:

1. To estimate the associated direct and indirect costs incurred due to the treatment of hepatitis C.
2. To measure the years of life gained through the treatments of hepatitis C.
3. To measure the cost-effectiveness for the treatments of hepatitis C by evaluating incremental cost-effectiveness ratio.

1.8. Hypothesis:

Hypothesis of the proposed study are as follow:

Hypothesis I:

- **Ho** = Intervention is less costly in comparison to the comparator.
- **H1** = Intervention is more costly in comparison to the comparator.

Hypothesis II:

- **Ho** = Intervention yields more benefits in comparison to the comparator.
- **H1** = Intervention yields less benefits in comparison to the comparator.

Hypothesis III:

- **Ho** = Intervention is more cost-effective in comparison to the comparator.
- **H1** = Intervention is not cost effective in comparison to the comparator.

1.9. Organization of the Study:

The present study is comprised of five chapters. In the first chapter, there is introduction of the study which covers background, importance of the study in global as well as in context of Pakistan along with the research questions, objectives, hypothesis and rationale of the study. Second chapter covers the ample and detailed international and national level literature reviews related to the study. The third chapter explains data sources and methodological framework in detail. Results & findings of data analysis are represented in the fourth chapter. Fifth and the last chapter encompasses conclusion of the study and provides policy recommendations.

CHAPTER 2

LITERATURE REVIEW

2.1. Introduction:

This chapter is comprised of a brief examination of the literature on cost-effectiveness of different antiviral regimens for the treatment of hepatitis C. The literature has been reviewed to determine the current and previous understanding of cost effectiveness studies for hepatitis C treatments and to observe the present situation globally and nationally. An ample amount of literature suggests that cost-effectiveness analysis is significant especially when resources are scarce and disease burden is high because in this kind of situation, cost effectiveness analysis will help in suggesting that how to formulate treatment strategies for obtaining valuable health outcomes (Jamison, 2006).

This chapter is divided into four sections. First section contains a brief theoretical background about the study. The second section deals with the examination of available literature on cost-effectiveness of hepatitis C treatments in global context. Third section comprises of national level studies which are conducted related to the study. The fourth and last section deals with the conclusion of this chapter.

2.2. Theoretical Background:

In a country with scare resources and huge disease burden, it is essential that these resources should be distributed and used in such a way that they maximize the overall benefit. Here, economic evaluation plays a pivotal role as it is a technique that assist decision makers in resource distribution and for enhancing policy making by highlighting suitable substitute (Briggs, 2006). There are two types of economic evaluation i.e. partial and full economic evaluation. Partial evaluation examines either the costs or outcomes only. This includes cost of illness studies and they are conducted to measure the disease burden on the society. This burden is measured in terms of all types of costs. While the full economic evaluation examines both the costs and outcomes simultaneously. There are four commonly used methods of full economic evaluation in health care namely "cost-consequence analysis, cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis" (Drummond et al., 2005). All types of methods are used to measure both the costs and outcomes by modelling the cost to support strategic planning, decision making and cost reduction. All of these methods measure costs in

monetary units but the difference is of outcome measurement. Table 2.1 shows the differences in valuation of costs and outcomes among these different types of cost analyses.

Table 2.1. Different Types of Methods for Cost Analysis.

Analysis Type	Valuation of Costs	Valuation of Outcomes
Cost of Illness	$	None
Cost Consequence	$	Natural units
Cost Effectiveness	$	Natural units
Cost Utility	$	Utilities (e.g., QALYs)
Cost Benefit	$	$

(Drummond, M.F. & Sculpher, M.J. (2005). Methods for the Economic Evaluation of Health Care Programs. Oxford University Press).

The present study is evaluating the treatment strategies through cost-effectiveness analysis which determines the optimal option based on the comparison between relative costs and outcomes of the treatments. The cost refers to the cost of treatments which are measured in monetary units and outcome is referred to health gain which is measured in natural units such as years of life gained. This information about costs and outcomes enables the decision makers to make optimal choices within scare resources to formulate the public health policies for achieving better health outcomes (Jamison et al., 2006). Therefore the present study is conducting this analysis to evaluate the best possible treatment option for hepatitis C so that disease burden could be reduced within scare resources.

2.3. Literature Review based on Global Cost-effectiveness Studies:

With the prevalence of 71 million affected cases and a death rate of 3.9 million people worldwide, a lot of countries have been conducted cost-effectiveness studies to identify most suitable treatment strategies in terms of costs and quality in order to cope with this disease with the high mortality and morbidity rates. With this perspective, Stein et al., (2002) estimated the cost utility analysis of two treatments options for hepatitis C by comparing them for their relative costs and outcomes in United Kingdom. One was the combination of two drugs which are ribavirin and interferon and the other option was the single drug which is interferon. The study was conducted from UK secondary care perspective. Markov model which is a decision analytic model is used for the analysis. The outcomes of the study were Quality Adjusted Life Years (QALY's) and costs. The results showed that the first treatment option which was the combination of two drugs is effective as per both QALY's and costs.

Approximately, hepatitis C has affected 2.7 million people in United States. Owing to the growing public health campaigns and advancement in health care, new treatments have been evolved which have a minimal incidence of liver damage. So to examine the clinical benefits and cost-effectiveness of newer treatments, Joshua et al., (2003) conducted a study to evaluate the treatment through standard peg-interferon alpha 2-b and treatment through the standard peg-interferon and ribavirin combination. Markov model was used to conduct the study. The patients with 40 years of age were selected for the study. Outcomes to be determined were life time costs, life expectancy, quality adjusted life years and incremental cost effectiveness ratio (ICER). The study suggested that the combination of peg interferon and ribavirin is optimal treatment strategy as compared to the standard peg interferon for patients of all genotypes except genotype 1 with the ICER of $10k to $28k per QALY.

The combination of Interferon alpha 2b and ribavirin yields highest SVR in treatment experienced patients but is costly. To estimate this, Siebert et al., (2003) compared the two treatment options to determine the optimal one. The treatment options are peg-interferon alpha 2-b and ribavirin and interferon alpha 2-b and ribavirin in Germany through societal perspective. Markov model is used for the analysis. The randomized clinical trials method was used for gathering data. Outcomes to be determined were costs and QALY's. According to the results, peg-interferon and ribavirin therapy is more cost-effective with the QALY's gained of 1.0 and cost of $6,600. This therapy also reduces the liver complications.

The global prevalence of HCV is estimated to be 2.2% and the prevalence in Europe is estimated to be 0.6 to 5.6% (GBD, 2004). The disease carries a huge burden due to the progression towards more advanced stages like cirrhosis and HCC. If the effective treatment is provided, it will restrict the disease from leading to worse complications. The new treatments are effective in terms of yielding a high SVR but are very costly. To estimate the effectiveness of boceprevir and telaprevir, Calogera et al., (2012) conducted a cost-effectiveness analysis in treatment naive patients for genotype 1 through a Markov decision model. Dual therapy (combination of peg interferon and ribavirin) is compared to the triple therapy (which is peg interferon, ribavirin, boceprevir and telaprevir). The patients with the 50 years of age were selected for the analysis. Costs, LYG & ICER were the outcomes. The results suggested that triple therapy is more cost effective than dual therapy of peg-interferon and ribavirin in treatment naive patients with genotype 1.

Due to the advancement in medicines, now only the sofosbuvir based regimes are affective for the treatment of hepatitis C. These drug regimens are effective but costly. In this context, Linas et al., (2012) conducted a study to evaluate the cost-effectiveness of sofosbuvir-based treatment regimens for type 2 and 3 in the United States. Three treatment strategies were analyzed in which sofosbuvir based therapies are compared with pegylated interferon and ribavirin and no therapy. The analysis was conducted through Monte Carlo simulation from payer perspective. The data was gathered through randomized trials, observational cohorts and surveys. Life time costs, QALY's and ICER were the outcomes. According to the results, sofosbuvir based treatment strategy is more effective for treatment experienced cirrhotic patients in comparison to non-cirrhotic patients which were treated for the first time because the cost of sofosbuvir based treatments for them exceed the willingness to pay threshold in United States.

Liu et al., (2012) conducted a cost-effectiveness study to evaluate the optimal treatment strategy among combination of pegylated interferon and ribavirin and the combination of standard therapy and a protease inhibitor for type 3 patients in United States. Markov model was used for the analysis over the life time horizon with the objective to determine costs, QALY's and ICER. Societal perspective was used and data was gathered through published literature and expert's opinion. The results showed combination of standard therapy and protease inhibitor is cost-effective with few complications and increase QALY's gained as compared to the peg-interferon and ribavirin combination.

Sean et al., (2012) conducted a cost-effectiveness analysis to evaluate the cost-effective treatment among the two treatment options which were; peg-interferon alpha 2a and ribavirin and conventional interferon alpha 2b and ribavirin through Markov model. The patients which received any of the treatments with fibrosis for 48 weeks and without fibrosis for 24 weeks were selected for the analysis. Life time costs, LY's, QALY's and ICER were the outcome. The results showed that the pegylated interferon alpha 2-a and ribavirin is optimal treatment strategy in terms of cost-effectiveness as compared to conventional interferon alpha 2-b and ribavirin with the incremental cost of €6,811 per LY's gained and €7,865 per QALY's gained respectively for all types of genotypes.

Hepatitis C has become a disease burden to United States with 2.7 million affected population. It has not increased death and disability rates but it also has imposed an economic burden to the society (Rein et al., 2012). As the disease is asymptotic so, half of the affected

populations never gets aware of the disease which leads the disease to move towards the advanced stages thus causes severe health problems. According to an estimate, among the affected population, only 12% of patients received treatment (Holmberg, 2013). The affective treatments are available but they are costly. To measure the cost-effectiveness of these treatments, Andrew et al. (2015) compared the two treatment scenarios in the patients. The treatment scenarios were; treatment at early stage and treatment at advanced stages of the disease. Markov model was used for the analysis to determine costs, QALY's and ICER as outcomes. The results showed that the early treatment is more affective because it leads to less costs and more outcomes.

Chhatwal et.al (2015) compared sofosbuvir–ledipasvir treatment strategy with the interferon-based therapies to evaluate the affective one. Markov model was used for the analysis with the perspective of third party payers. Data was collected from 120 people which were given the treatment for the first time and which were already treated. QALY's, ICER and 5-year healthcare spending were the outcomes to be determined. According to the results, sofosbuvir–ledipasvir strategy was cost-effective in both types of patients.

Najafzadeh et.al (2015) conducted a study to evaluate the cost-effectiveness of peg interferon and ribavirin and sofosbuvir and ribavirin for type 3 patients through societal perspective. Markov model was used for the analysis with the cohort of 10,000 patients to determine costs, QALY's and ICER as outcomes. According to the results, usual care (RBV+PEG) was the optimal strategy for patients with genotype 3 at a weekly willingness-to-pay threshold of $50,000. The study suggests that sofosbuvir based treatments are expensive but if their weekly cost is reduced to less than $5000 then these treatments van be considered as optimal strategy,

Moshyk (2015) conducted a study to determine the cost-effectiveness of sofosbuvir based treatments in Canada for hepatitis C treatment in type 3 patients through Canadian health-system perspective over a lifetime horizon. The treatment strategies were sofosbuvir and daclatasvir (DCV + SOF) and sofosbuvir and ribavirin (SOF + RBV). Markov model was used to estimate costs, QALY's and ICER as the outcomes. The new and already treated patients were selected for the study. According to the results, sofosbuvir and daclatasvir strategy is effective for both new and already treated patients with the QALY's of 12.37 and costs of $170,371 compared to the two other combinations. Therefore, the study suggests that for type 3 patients, sofosbuvir and daclatasvir combination is a cost effective treatment strategy.

To obtain an optimal treatment strategy for type 1, 2 and 3 patients in US, Zhang et.al (2015) conducted a study to evaluate the sofosbuvir based treatments in terms of costs and outcomes. For genotype 3, treatment strategies; sofosbuvir + ribavirin and peg interferon + ribavirin were selected for the initial phase and for other phase, treatment with sofosbuvir + ribavirin was selected. A Markov model was used to obtain costs and QALY's as outcomes. The results showed that for initial phase of treatment in type 3 patients, peg-interferon + ribavirin are more effective and for the other phase, sofosbuvir + ribavirin are more effective. Though sofosbuvir based treatment strategies are expensive but they are more effective because of high cure rate and lesser complications.

Hepatitis C has affected 187,000 people in Iran. So to add a step in overcoming this alarming situation, Alavian et al., (2016) conducted a study to evaluate the cost-effective option among the three treatment options which were; pegylated interferon and ribavirin, sofosbuvir and ribavirin and ledipasvir and sofosbuvir for type 1 patients through provider's perspective over the time horizon of 1 year. Markov model was used for the analysis with the data of 144 patients and the data was obtained through published studies and expert's opinions. The results showed that the treatment through peg interferon and sofosbuvir is more cost effective as compared to the other treatment options for type 1 patients with less costs and better outcomes.

For the reduction in this worldwide public health, new and advanced drugs were introduced named as direct acting antivirals which were interferon free so that disease cannot be move towards the more advanced stages like cirrhosis and cancer. But these drugs come with high costs. So in this perspective, Jona, et al., (2017) conducted a study to evaluate the cost-effective treatment strategy among the three strategies. The strategies are; combination of sofosbuvir and ledipasvir (SOF/LDV), combination of sofosbuvir and ledipasvir along with ribavirin and combination of peg interferon and ribavirin for type 1 genotype patients in Germany. Markov model was used for the analysis. Both types of patients were selected for the study i.e., the ones who were given the treatment for the first time and the ones who were already treated. The study was conducted through German healthcare perspective. A cohort of 10,000 patients was selected with the outcomes of costs, QALY's and ICER. The results showed that combination of sofosbuvir and ledipasvir is more effective as compared to the other strategies for both cirrhotic and non-cirrhotic patients treatment in terms of bot h the costs and outcomes.

To evaluate the cost-effectiveness of all new recommended therapies for the treatment of hepatitis C genotypes 1 and 4, Mattingly et al., (2017) conducted a study to evaluate the cost-effectiveness of all the new drugs which are used for the treatment of hepatitis C for type 1 and 4 genotypes by using a Markov model. Third-party payer's perspective was used over a time period of 5, 10 and 50 years. Data was obtained through clinical trials and observational analysis and pharmacies. Costs and QALY's were the outcomes. According to the results, for type 1, QALY's range from 18.08 to 18.40 and costs range from $88 107 to $184 636. For type 4, QALY's range from 18.23 to 18.43 QALYs and costs range from $87 063 to $127 637. Among all the drugs, combination of grazoprevir and elbasvir and combination of sofosbuvir and velpatasvir are effective treatment options for type 1 and 4 patients. So conclusively, the combination of Grazoprevir and elbasvir is more effective in terms of both costs and outcomes among all the drugs for type 1 and 4 patients.

After 2011, direct acting antivirals agents (DAA) were introduced which were interferon free drugs with more effectiveness but higher cost. To assess this, William et al., (2017) conducted a study to evaluate which drug is more cost-effective for the treatment of HCV type 1, 2, 3 and 4 in Canada. The patients who were given the treatment for the first time and the patients who were already treated were selected for the study. Markov model was used for this purpose and data was gathered through published sources and expert opinion. The treatment regimens included: pegylated interferon and ribavirin, sofosbuvir, sofosbuvir and daclatasvir, sofosbuvir and ledipasvir, boceprevir, telaprevir, simeprevir, ombitasvir, paritaprevir, ritonavir and dasabuvir. According to the results, for type 1 population, among the direct acting antiviral agents, at least 1 direct acting antiviral agent is more cost effective in comparison to the interferon based treatments. The cost-effective drug varied by population. For type 2,3 and 4 population, the direct-acting antiviral drugs are not cost-effective as compared to interferon therapies for the patients which were given the treatment for the first time but for the patients which were already given the treatments, these drugs are effective,. However, there were direct-acting antiviral therapies that appeared to be attractive when compared with no treatment for the treatment-experienced.

2.4. Literature Review based on National Cost-effectiveness Studies:

Chronic HCV is a global as well as national public health problem for Pakistan. New treatments are considered to be more effective. To conduct the effectiveness and safety of these treatments, Kokhar (2002) conducted a study for measuring the effectiveness of interferon and

ribavirin for hepatitis C treatment. 100 patients were selected to be the part of analysis. Outcomes was End of the treatment sustained viral response. The results showed that 72.7% males and 88.3% females achieved a SVR of 79.5%. So this combination therapy can be considered effective with a good SVR rate.

Iqbal (2011) estimated the efficacy and effectiveness of conventional interferon and ribavirin in combination for the treatment of hepatitis C treatments. Descriptive methodology was used with a sample size of 340 and the data was collected from District Headquarter Hospital, Dir, Pakistan. Outcomes were End of treatment sustained viral response. The time period taken was from 2009-2011. The results showed that conventional interferon and ribavirin generate a better response rate and only minimal side effects are noticed with this combination. So the study suggested that this combination is an effective treatment option for non-affording HCV patient.

Due to the high disease prevalence in the country, "prime minister's program for prevention and control of viral hepatitis infection" was launched for 5 years from 2005-2010 nationwide for those patients who cannot afford the expensive treatment. Qureshi et al., (2013) evaluated the response of treatments in national hepatitis program. Data for HCV was taken through the 12 sites out of total 61 sites and analyzed through a special program. According to the results, out of total 7572 patients in 12 sites, 3440 patients (45.4%) have been treated through interferon therapy and they completed their treatment. ETR was observed in 1686 patients (49%).

Qureshi (2015) conducted a study to evaluate the optimal treatment option for hepatitis C treatment (type 3). The outcomes were to determine the efficacy and side effects of treatments using descriptive statistics. 220 patients were selected for the study which were given the treatment for the first time in KRL hospital. Conventional interferon was used as the drug for the treatment for the 6 months. The results showed that 169 patients achieved end of treatment response (ETR) and 126 achieved sustained virological response (SVR). But the side effects like leukopenia, gastrointestinal and miscellaneous systemic complaints were observed. So the study suggested that the conventional interferon is not required to be used in place of pegylated interferon without another combination.

Pakistan is on second number among the countries which possess higher viremia rate of HCV infection. A study conducted in Europe indicated that the HCV infected people (type 3), who received treatment based on the combination of sofosbuvir and ribavirin have a RVR

of 99% and SVR of 85% respectively. To determine the viral response of patients with sofosbuvir based treatment, Akhtar (2016) conducted a quasi-experimental study. 502 patients with type 3 genotype who were treated with interferon based treatments for the first time and more than one time. The treatment duration was 6 months. According to the results, 91% patients are completely cured after the 4 months of treatment and 96.5% patients cured after the complete treatment. 85.5% showed SVR after 3 months. This rate was observed higher in females as compared to males. So the study indicated that sofosbuvir based treatment is effective irrespective of the previous treatment or complications in patients with HCV type genotypic patients.

Umer (2016) conducted a study in which meta-analysis has been done to estimate the sustained virological response of interferon free direct acting antivirals for HCV. The direct acting antivirals which were included in different studies were sofosbuvir, ledipasvir, daclatasvir, simeprevir, dasabuvir, ombitasvir, paritaprevir and ritonavir. In this meta-analysis, one of the study conducted by Sulkowski et al., (2014) estimated the SVR of the combination of sofosbuvir and daclatasvir as a treatment for patients with HCV. In this study, phase II trial has been done on patients with type 1, 2, and 3 genotype. The results showed that this combination yielded a SVR of 98% after 24 weeks of treatment irrespective of the genotype.

Hashmi (2017) conducted an experimental study to determine the effectiveness of sofosbuvir and ribavirin in children which were treated for the first time. 35 patients (within the age of 5 to 18 years) with active virus were selected for the study. The outcomes were most prevalent genotype, SVR, RVR and EVR. All the patients were using sofosbuvir and ribavirin for 6 months as a treatment. The response rates were determined through PCR at different stages of the treatment. The most common HCV genotype was type 3 with the prevalence rate of 77.15% followed by type 1 with 17.14% and genotype 2 with the prevalence rate of 5.71%. 37 patients achieved RVR and other 5% achieved EVR. 34 patients achieved SVR. The virus got inactive in all the patients after the treatment. So the treatment indicate that sofosbuvir and ribavirin is an effective option for type 1 and 3 patients because of better response and no complications.

A study conducted by Raza et al., (2017) conducted a study which measured the impact of early and rapid response rates on sustained virological response in HCV patients (genotype 3). 1,471 patients were the part of analysis and Interferon alpha 2-b & ribavirin for 3 months were the treatments whose effects were measured. The results showed that, of the total patients involved in the analysis, after treatment, 43% patients showed low viral burden retrieving early

response rate while 56.6% maintained a high viral load. The rapid response is higher with 85.9% as compared to the early response rate. So the study indicated that the treated patients who showed that higher rapid virological response rate leads their sustained virological response towards the better remission which can be treated with standard treatment in short duration.

Despite the availability of revolutionary treatments for HCV, these treatments are not widely available in developing countries. Hanif et al., (2017) conducted a study to evaluate the outcomes of sofosbuvir and ribavirin which are the only direct acting antivirals available in Pakistan for HCV patients which are recipients of renal transplant. 37 patients with renal transplant which were using this combination of treatment were the part of the study. Out of these, 25 people were given the treatment for the first time & 5 were already treated. The outcomes were Rapid virological response (RVR), Early Virological Response (EVR), End of Treatment Response (ETR) and Sustained Virological Response (SVR). SPSS was used to perform the analysis. According to the results, 33 patients achieved RVR of 89.2%. All the 37 patients achieved EVR, RVR and ETR after 3 months of treatment. So the study suggests that sofosbuvir and ribavirin is effective option for treatment if used in comparison with no complications for HCV patients with renal transplant irrespective of the genotype.

2.5. Conclusion:

The literature concluded that there are several studies worldwide which highlighted the significance of conducting a cost-effectiveness analysis for hepatitis C treatments. But in national perspective, only one study has been found which has evaluated the treatments through cost-effectiveness approach. The focus of most of the research was on estimating prevalence, genotype distribution, efficacy, sustained virological response and end treatment response rate.

So the present study included those studies which are somehow closely related to this study. Most of the studies included focused on estimating efficacy of the treatments which somehow relates to the determination of outcomes of this study. Pakistan is a developing country with the rising disease burden of hepatitis C. Due to the advancement in medical technology, several new medicines are available but most of the population especially in developing countries still can’t afford these medicines. To cater with this situation with low resources and high disease burden, cost-effectiveness study becomes very significant in order to have successful elimination of the virus. It will also be helpful in developing efficient policies that will help in tackling enormous challenges that a country faces in terms of high disease burden and cost. Hence this study is an attempt to narrow down this gap.

CHAPTER 3

DATA SOURCES AND METHODOLOGY

3.1. Introduction:

This chapter discusses the data sources and methodological framework which is employed for measuring the cost-effectiveness for hepatitis C treatments. This chapter is divided in to four sections. The first section of this chapter includes the framework of this study which explains the important factors that will aid in carrying out the current study. The second section deals with cost components used in this study. The third section encompasses the details about methodological framework which is employed for the accomplishment of the three objectives of the study. The analysis is performed under the framework of decision analytic modeling. This sections describes that how this evaluation will be conducted. The fourth section describes the data sources which are used for the purpose of evaluation of cost-effectiveness of hepatitis C treatments.

3.2. Framework of the Study:

This section describes the study framework which includes the detailed description of the study settings, target population, time period and analytical horizon of the study, treatments to be evaluated, study perspective and approach.

3.2.1. Study Settings:

As hepatitis C can infect people at any age, the treatment starts after the diagnosis and generally followed by a period of 3 or 6 months depending upon the severity, stage and genotype of the disease. This study has considered HCV infected people with type 3 genotype only due to the higher prevalence in Pakistan. So for genotype 3, combination of sofosbuvir and daclatasvir (intervention) are generally used for 3 or 6 months depending upon the type of treatment in “treatment naive patients” (the patients which are getting treatment for the first time) with the course of 28 tablets per month. And treatment through peg interferon and ribavirin (the comparator) is provided for 6 months in the form of injectable, 3 times a week with a total of 72 injections and oral dose of ribavirin with a course of 60 tablets per month.

3.2.2. Target Population:

The group of population which is intended to receive an intervention is called the target population (WHO, 2008). In this study, target population is a cohort of people which are diagnosed with hepatitis C and are recommended to use intervention strategy of treatments. A cohort is a group of people with common characteristics, here the common characteristic is the active hepatitis C virus infection.

3.2.3. Time Period and Analytical Horizon:

The analytical horizon corresponds to the period over which costs and outcomes of health care intervention take place. For measuring the accurate costs and effects of intervention, a long period is required (Drummond et al., 1997). The costs and effects observed and measured for the present study span over a time period of one year therefore, the analytical horizon of the study is one year i.e. 2016-2017 The analysis has been carried out retrospectively. In a retrospective cohort study, research is conducted after the occurrence of outcome (the disease) and exposure to the treatment.

3.2.4. Treatments to be evaluated:

When it comes to evaluation, there is involved a choice between competing alternatives between competing alternatives. This requires two options for comparison; an 'intervention' and a 'comparator'. The term intervention is used for a new treatment, diagnostic test or a new prevention strategy to tackle a disease or overcome a health problem while comparator refers to the option against which the intervention is compared (Drummond et al., 1997). Few relevant comparators that can be considered include

i) Current practice
ii) Best available alternative or feasible low-cost alternative
iii) Do nothing; (a) without new intervention (b) without any care (Muennig, 2008).

For the present evaluation exercise, the intervention and its comparators are mentioned below:

Intervention: The present study is implying an intervention named as drug A which is a combination drug (combination of two drugs).

Drug A: Sofosbuvir + Daclatasvir.

Comparator: This includes treatment under standard care which is also a combination drug.

Drug B: Peg Interferon + Ribavirin.

Drug B (peg interferon and ribavirin) was the preferred regimen for hepatitis C treatments before the arrival of new and more effective drugs like sofosbuvir and daclatasvir. Peg interferon is used in the form of injectable. Ribavirin, sofosbuvir and daclatasvir are used in oral form. The treatment duration for drug B (interferon and ribavirin) is 6 months or 24 weeks and there are several adverse effects which are associated with this drug regimen (reported in 40% of clinical studies) like "injection site inflammation/reaction, fatigue, headache, rigors, fevers, nausea, myalgia, and anxiety or emotional lability/irritability". The treatment duration of drug B (combination of sofosbuvir and daclatasvir) is also 6 months or 24 weeks with the response rate of 91%. Based on this, interferon free oral treatments are more preferred against the standard care regimen. Based on this, the present study is evaluating the interferon regimens against the new and oral regimens which are considered as intervention strategies. The difference of effects between the treatments will yield the incremental effects of intervention strategies.

3.2.5. Study Perspective:

For any economic evaluation, the study perspective should be known. There are several perspectives for carrying out economic evaluations. The choice of the perspective is important as it affects the components of costs as well as effects to be considered. Three types of perspectives are used in economic evaluations which are payer, provider and societal perspective.

- The **payer's perspective** assesses the cost and health outcomes for a particular individual or organization which is getting services against payment.

- The **provider perspective** assesses the cost and health outcome for a particular individual or organization which is providing services and bearing expenses by own self.

- The **societal perspective** assesses the costs and health outcomes for the entire population which includes both the payer and provider perspectives.

The broadest and recommended perspective is the societal perspective. It is a comprehensive perspective and incorporates all costs and effects related to an intervention (Drummond et al., 1997). However, owing to data limitations and difficulty to capture costs and effects in such a broad way, we are employing provider perspective for our analysis.

The provider in this study refers to the public health care hospitals only which are providing the free of cost treatments for hepatitis C. The choice of the public health system perspective is justified because in developing countries like Pakistan, the health sector is often faced with scarcity of resources so in order to maximize the resource use through efficient allocation, costs and outcomes of different treatments option should be known to implement the most optimal strategy for treatment within scare resources.

3.2.6. Study Approach:

Cost studies can be conducted through the following two approaches:

i) Incidence based approach.
ii) Prevalence based approach.

- **Incidence Based Approach:**

Incidence based approach is a traditional approach which is used by most analyst for conducting evaluation studies i.e., the studies based on cost-effectiveness, cost-benefit, cost-consequences and cost-utility analysis. The focus of this approach is to determine the costs and outcomes of the treatments for the complete duration of disease.

- **Prevalence based Approach:**

Prevalence based approach is usually employed for the partial evaluation studies i.e. cost of illness studies. The focus of this approach is to determine the annual costs and outcomes of the treatment.

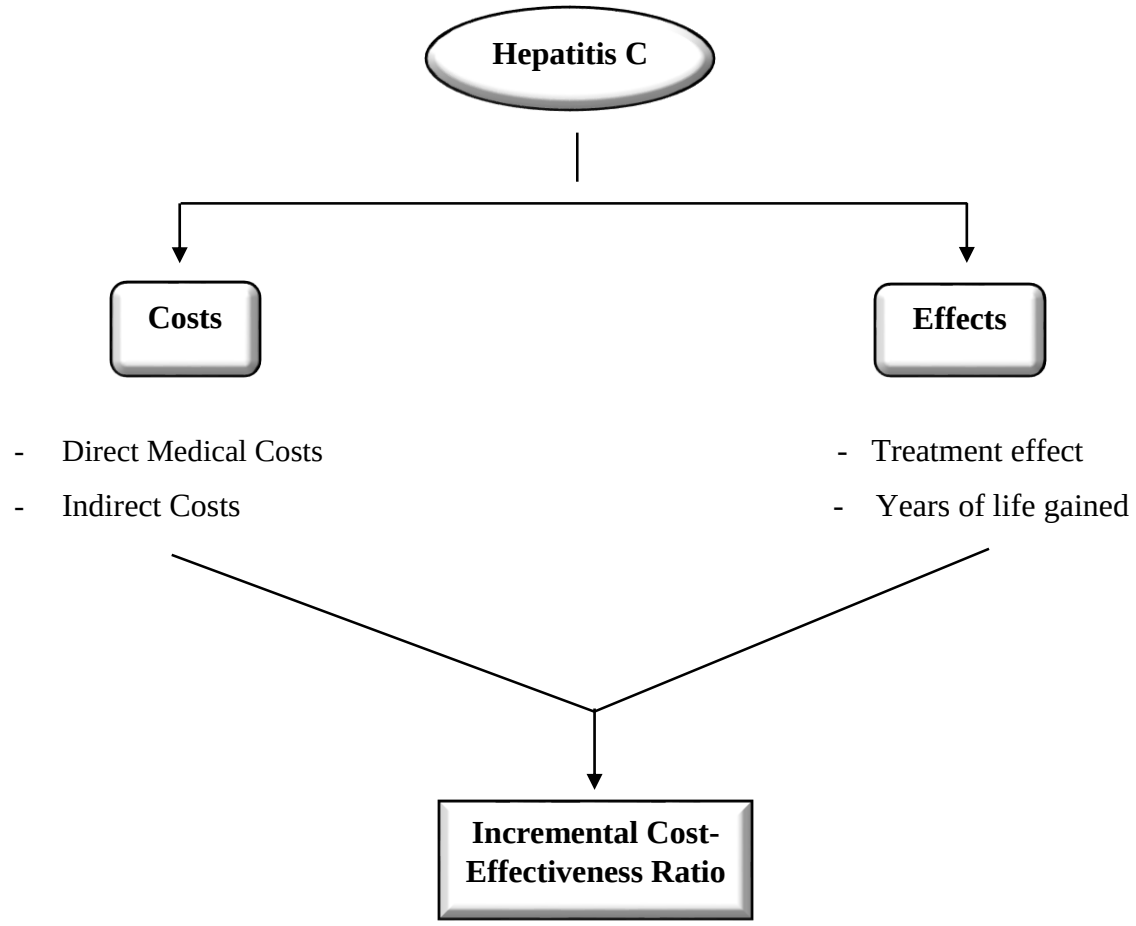
The present study is employing incidence based approach as it is evaluating the new treatment against the standard treatment through incremental cost-effectiveness ratio.

3.2.7. Diagrammatical Representation of Study Framework:

The pictorial description of this study is represented in the form of figure 3.1 below which represents the objectives of the study in detail. This study is based on the framework of decision analytic modelling which provides an approach through Markov model to estimate the costs and years of life gained through the different treatment strategies. Costs and outcomes are an important part of any cost-effectiveness study as they yield the main outcome which explains that which intervention is more effective. After measuring the costs and outcomes of these treatment, the optimal strategy is selected based on the incremental cost-effectiveness

ratio which is obtained by the costs and outcomes difference of the treatment strategies (Drummond et al, 2005). This cost-effectiveness ratio which is a dependent variable because it requires cost and outcomes values to give the final result is significant for the countries with the scare resources and huge disease burden because it helps in prioritizing the resources in order to utilize the best out of scare resources.

Fig. 3.1. Diagrammatic representation of framework for cost-effectiveness study of hepatitis C



Based on the framework of Decision Analytical Modeling
Drummond, M.F. & Sculpher, M.J. (2005). Methods for the Economic Evaluation of Health Care Programs. Oxford University Press.

As the objective of this study is to evaluate the cost-effectiveness hepatitis C treatments. This purpose will be achieved by achieving the two main outcomes which are costs and effects. As the study is conducted through provider's perspective so the direct medical costs represents the direct medical expenditure incurred on the patients by the provider and the indirect costs

represent the administrational costs borne by the hospital in providing the treatments (Intervention and comparative strategy) to the patients. The effect yields the treatment effect and life years gained as a result of the treatment through both treatment strategies. The values for these costs and effects will help in getting incremental cost-effective ratio which is the main outcome. The incremental cost-effectiveness ratio will then suggest the optimal treatment strategy in terms of both costs and quality for the treatment of hepatitis C (Chhatwal, 2015).

3.3 Methodological Framework:

The present study is using the framework of decision analytical modeling for the evaluation of cost-effectiveness. This modelling technique is used worldwide for the estimation of cost-effectiveness of treatments and health care programs for the diseases with long-term health effects high chances of reoccurrence (Sato, 2010). The decision analytic models embrace a variety of mathematical techniques but the two main forms which are used in economic evaluation are decision trees and state transition models (Karnon, 2003). In this study, as the costs and outcomes of hepatitis C are to be estimated over a tome horizon of one year i.e. 2016-2017. Therefore, state transition model i.e. Markov model is applied due to its feasibility to deal with randomly changing health states and illustrating long-term outcomes associated with different decision.

3.3.1. Markov Model:

"A Markov model is defined as a stochastic model which is used to model randomly changing systems where it is assumed that future states depend only on the current state not on the events that occurred before it" (Chhatwal, 2016). This model was formulated by a Russian mathematician named as Andrey Andreyevich Markov (famously knows as Andrey Markov). The use of epidemiological and economic evaluation is rapidly increasing by the investigators in health economics due to its ability to measure both the costs and the outcomes (Sato, 2010). "The model is useful when decision problem involve risks that is continuous over time, when the timings of events are important and events may happen more than once" (Sonnenberg et al, 1993).

These models are particularly suitable for modelling chronic diseases in context of health care because they enable to construct flexible applications to reflect disease progression using constant, time dependent and discrete processes. For any given disease, Markov model

is capable of being in more than one health state, can make the possible transition paths between those states and the rate parameters of those transitions (Edward, 1992).

3.3.1.1. Health States:

In this model, it is assumed that patients can be in one of the many health states at a certain time. These states are known as Markov states (Briggs, 2006). These health states are basically the description of disease which are shown by simplifying it into a series of states, representing clinical and economic outcomes. These Markov states are mutually exclusive because the patient can only be in one state of disease at one point. (Sato, 2010). The Markov model for this study incorporates four health states which are mentioned below:

i) State A is defined as Hepatitis C.
ii) State B is defined as Cirrhosis.
iii) State C is defined as DCLD.
iv) State D is defined as Death.

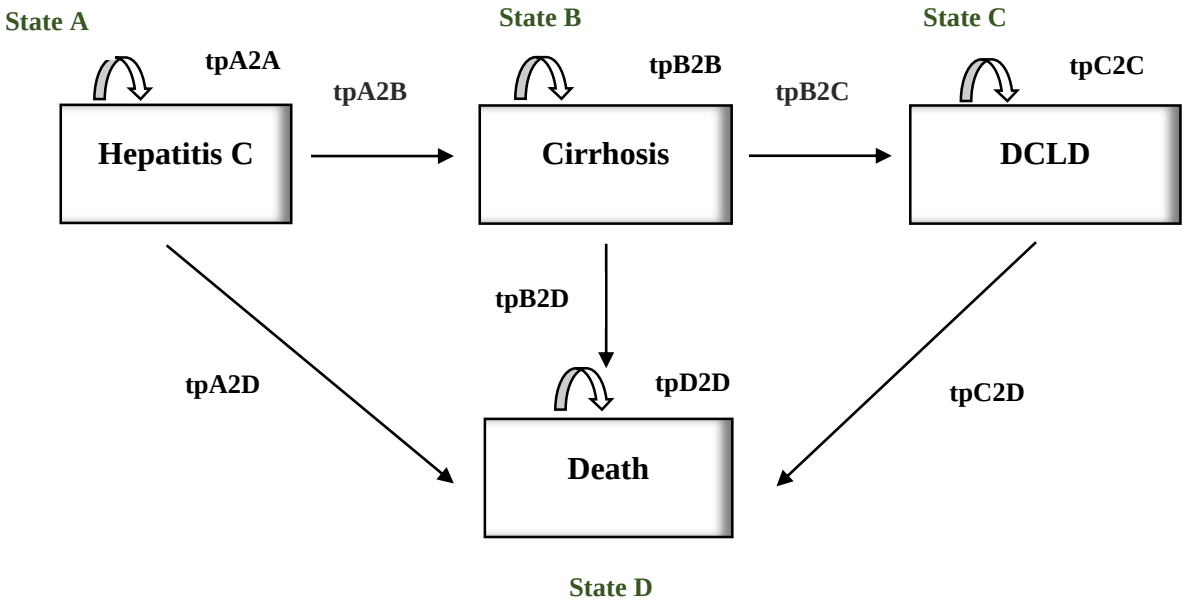
Hepatitis C is a blood bone virus which affects liver. Cirrhosis is a stage of hepatitis C where scarring of liver makes it difficult for the liver to perform routinely functions for the body. DCLD is decompensated chronic liver diseases which is an end stage liver disease with irreversible damage and poor prognosis. Death is the cessation of human organs which is the worst scenario in case of this disease.

3.3.1.2. Transition States:

As in Markov model, at one point of time, patient can only be in one state of the disease and can move towards the advanced stages of diseases after a certain time which can be termed as intervals or cycles (Briggs, 2006). These movements from one stage of the disease to the other are categorized as transitions and they are calculated in the form of likelihood or probabilities in order to know the rate of movement from one state to another. All the patients will start in state A which is the initial state. Patients can move forward, i.e. they can move from A to B, A to C or A to D (and the same for B to C and B to D and C to D) or they may stay in the same state (i.e. if they are in state A, they may stay in A in the next cycle or move to B). Patients cannot go back to the previous states in this model (for example, they cannot go from C to B, D to A or B or C) because the disease can either be cured or move towards advanced stages.

In this model, the health states for hepatitis C with the transition between these states are represented in the below state transition diagram:

Fig. 3.2. Schematic Representation of Markov State Diagram.



Based on Markov Modelling Approach

In the above diagram, it is shown that how these states link to each other. The possible transitions between these four health states (chronic hepatitis C, cirrhosis, DCLD, and death) are indicated by linear arrows and the possibility of remaining in a same health state in each cycle are indicated by loops. All the patients are initially infected with hepatitis C. They may remain with hepatitis C (i.e. cured) or may move towards further advance disease stages like cirrhosis, DCLD or death with the passage of time. When the people are moved to cirrhosis stage, they may remain at the same stage or can move towards to DCLD or death state. The same is with the DCLD stage. People from these stages cannot move back to previous stages in the model of present study. The last stage which is death is considered an absorbing stage in this model. Absorbing stage is the stage that once entered cannot be left.

3.3.1.3 Transition Probabilities:

The transition probabilities for each state are calculated through the following formula:

$$\boldsymbol{Trasnsition\ Probability} = \frac{\boldsymbol{Event}}{\boldsymbol{Complement}}$$

Event contains the number of people in the specific state whose transition probability is to be calculated while the complement contains the number of people other than this state i.e., the number of people in all other states. The obtained transition probabilities will be entered in the transition matrix for analysis. The transition probabilities in this model are stated below:

tpA2A = Transition probability of being in state A – Hepatitis C.

tpA2B = Transition probability from state A – Hepatitis C to state B - Cirrhosis.

tpA2C = Transition probability from state A – Hepatitis to state C - DCLD.

tpA2D = Transition probability from state A – Hepatitis to state D - Death.

tpB2B = Transition probability of being in state B - Cirrhosis.

tpB2C = Transition probability from state B Cirrhosis to state C - DCLD.

tpB2D = Transition probability from state B Cirrhosis to state D - Death.

tpC2C = Transition probability of being in state C - DCLD.

tpC2D = Transition probability from state C DCLD to Death.

tpD2D = Transition probability of being in state D - Death.

3.3.1.4 Transition Matrix:

The transition probabilities are entered in a matrix which is called state transition matrix or transition probability matrix and is shown by P. The state transition matrix for the four states of this model is given below:

$$P = \begin{Bmatrix} tp_{11} & tp_{12} & tp_{13} & tp_{14} \\ tp_{21} & tp_{22} & tp_{23} & tp_{24} \\ tp_{31} & tp_{32} & tp_{33} & tp_{34} \end{Bmatrix}$$

In the above matrix, each state represents the calculated transition probability for that state. The sum of all the rows of this transition probability matrix should be equal to one.

3.3.1.5. Cycle Length:

Markov models are based on specified number of cycles. These cycles end in an absorbing stage which is termed as termination stage from where the process cannot move forward. In this model, cycle length is taken as termination stage. This cycle length is an important component of Markov model. Generally, cycle length is selected by determining approximate length to clinical follow-up or available data (Glick, 2007). Due to the error reducing capacity of shorter cycles, this study has taken shorter cycle length to capture the frequency of events (Chhatwal, 2016). In this model, cycle length is taken up to 6 months because the treatment duration for hepatitis C is taken as 6 months.

3.4. Costs:

The final stage in the Markov model is assigning the values to each health state like costs and effects value. Economic costs are defined in terms of opportunity costs; the value of resources in their best forgone alternative use. In case of health care, costs can be termed as the loss of non-health consumption welfare foregone as the resources are used to provide health intervention (Drummond et al., 1997). The types and scope of costs vary with the perspective of evaluation. The present study is employing provider perspective for estimating cost-effectiveness of hepatitis C treatments. So only direct medical costs will be considered because they cover each and every aspect if cost which is incurred by provider while providing the treatment.

3.4.1. Direct Medical Costs:

The direct cost includes all the costs which are incurred due to the use of healthcare intervention or treatment of illness. In this study, only direct medical costs are considered which are divided further into the two types of costs which are incurred while purchasing the medical services. The costs which are to be estimated in this study are mentioned below:

i) Fixed Costs.
ii) Variable Costs.

3.4.1.1. Fixed Costs:

The costs which do not change with the number of units of goods and services produced in short and medium term are termed as fixed costs. Fixed costs include costs of administration, maintenance, wages, rent and salaries. In this study, capital expenditure, employee salaries and

utilities are considered as fixed costs and they are merged as a single component named as hospitalization cost.

3.4.1.2. Variable Cost:

Variable costs are those which change as the number of intervention recipients changes. Costs included in this category are those of drugs, vaccines and supplies among other things. In this study, supplies costs, diagnostic costs and medication costs are considered as variable costs.

3.4.2. Ingredients Approach to Costing:

The "World Health Organization (WHO) guide for standardization of economic evaluations of immunization programs" recommends the use of 'ingredients approach' for the assessment of costs. In this approach, costs are calculated following three basic steps that are mentioned below:

i) In the first step, all relevant resources consumed are identified.
ii) In the second step, the identification is followed by the quantification of resource use.
iii) The final step is to assign unit costs or prices to each resource use. The unit costs are assigned using market prices. All costs are aggregated to get total costs.

This is calculated through the following formula:

$$\boldsymbol{Cost\ of\ X\ =\ Number\ of\ units\ of\ X\ *\ Unit\ cost\ of\ X}$$

In this study, both the fixed and variable costs per patient for each state are determined according to their respective components. The total costs are obtained through the following formula:

$$\boldsymbol{Total\ cost\ =\ Proportion\ of\ patients\ *\ \sum (Fixed\ and\ Variable\ Costs)}$$

For models with the time horizon of over 1 years, present value of future costs should also be generated through discounting (Petrou, 2011). The values for discounted costs are calculated through the following formula:

$$\boldsymbol{Discounted\ Costs} = \left(\frac{\boldsymbol{Cost\ without\ discounting}}{\boldsymbol{1 + Annual\ dicouting\ rate\ for\ costs}}\right) \text{^ } \mathbf{Year}$$

3.5. Effects:

Economic evaluation deals with inputs as well as outputs often termed as costs and effects (Drummond et al. 1997). The effects assess the effectiveness of interventions through various outcome measures. It is imperative that the outcome measures used for economic evaluation be related to the program objectives (Stephanie, 2010). As we are evaluating an intervention for hepatitis C treatments, therefore, following outcome measures will be measured to capture the effects of the intervention:

i) Treatment effect.
ii) Life years gained.

3.5.1 Treatment Effect:

The treatment effect which is also called effect size of a treatment is a dimensionless measure which is calculated for the comparison of the efficacy of different treatments by quantifying the difference in outcomes. Generally, there are five methods to measure effect size which are listed below:

i) Cohen's d approach.
ii) Relative risk ratio (RR).
iii) Odds ratio (OR).
iv) Number needed to treat (NNT).
v) Area under curve (AUC).

This present study is using relative risk ratio to determine the treatment effect as it is a prospective study. Relative risk ratio is the ratio of response of patients towards the treatments. It is calculated through the following formula:

$$\boldsymbol{Relative\ Risk\ Ratio} = \frac{\boldsymbol{Probability\ of\ patients\ in\ interention\ group}}{\boldsymbol{Probability\ of\ patients\ in\ comparative\ group}}$$

3.5.2 Years of Life Gained:

Years of Life years gained are measured to know the additional number of years of life that a person gains after the treatment. It is one of the main outcome of the present study. Life years will be calculated by adding number of alive people who spent a year

in the cycle in each state except the death state i.e. the proportion of people in each state. It will be calculated through following formula:

$$\boldsymbol{Life\ years\ =\ \sum (Proportion\ of\ patients\ in\ each\ state)}$$

For models with the time horizon of over 1 years, present value of expected life years gained in future (Petrou, 2011). Due to the time horizon of over one year, discounting is applied to generate the present value of expected life years gained (Petrou, 2011). It is usually done to assess whether the outcome is more beneficial at present or in the future. The discounted value of life years gained are calculated through the following formula:

$$\boldsymbol{Discounted\ Life\ Years\ Gained}$$

$$= \left(\frac{\boldsymbol{Life\ years\ without\ discounting}}{\mathbf{1} + \boldsymbol{Annual\ dicouting\ rate\ for\ benefits}}\right) \text{^ } \mathbf{Year}$$

3.6 Incremental Cost-Effectiveness Ratio:

In economic evaluation, the estimation of costs and effects of the intervention and its alternatives is followed by the calculation of differences in costs and effects. The differences are then put together in the form of a ratio i.e., cost per unit of effect and is known as incremental cost effectiveness ratio (ICER) (Gray et al, 2011). The ICER is the final outcome of this study. It is a statistics which summarizes the results of cost-effectiveness of a health care intervention. It can be interpreted as the cost of obtaining an extra unit of effectiveness and it quantifies the trade-offs between patient outcomes gained and resources spent. The ICER threshold, may be understood as the upper limit of what society is willing to pay for an additional unit of health benefit (Blumenschein et al., 2001). The ICER which provides average incremental cost incurred for each unit of effect is calculated through the following formula:

$$\boldsymbol{ICER = \frac{Cost_A\ -\ Cost_B}{Effect_A\ -\ Effect_B}}$$

It will be calculated by dividing the difference in the costs of treatments by difference in the life years gained in this study. The resulting ratio will yield the required information that which treatment therapy is more effective in terms of costs and quality.

3.7 Data Sources:

The methodology which is explained above in detail is applied on the data obtained through the meta-analysis of different cost effectiveness studies and hospital records. The data consists of patient record for transition matrix, expenditure statements and administrative records. The data for patient record is obtained through meta-analysis and the data for the costs is obtained from the hospital records for the period of 2016-17. Consultant physicians and medial officers were consulted to get their opinion regarding the technical aspects of certain parameters used in this study.

3.7.1 Target Population:

The data for target population is obtained through the literature review due to the non-availability of real data. No specific age group is assumed because this blood bone virus is independent of the age. The values are extracted from related base studies due to the lack of real data. The data for patients is divided into four groups based on the health states among which the transition from one state to another is observed. The total population affected with Hepatitis C for this study was taken as 697. Out of which the sample size for different health states are selected based on the probability of patients in these states. For the state A, Hepatitis C, the sample size was 500, for state B, Cirrhosis, the sample size was 160, for state C, DLD, the sample size is 192 and for state D, Death, sample size is taken as 1. From these sample sizes, the transition between the other states were compared. The studies considered for this purpose are Chancellor et al., (1997) and Sato, (2010).

3.7.2 Transition Matrix:

The data for all the health states and the transition between the states for hepatitis C infection i.e., Cirrhosis, DCLD and Death is obtained through the meta-analysis. The transition probabilities for all these states are calculated through the respective formula which is stated above in the methodological section. These probabilities represent the rate of movement between these health states which is represented in the below matrix:

Table 3.1. Transition Probabilities for Hepatitis C Disease Progression States.

	A	B	C	D
A	0.433	0.283	0.19	0.093
B		0.64	0.292	0.068
C			0.626	0.374
D				1

The above transition probabilities indicate that out of 100, the total population affected with Hepatitis C was 72%. Out of 72%, 20% population moved from Hepatitis C to Cirrhosis, 6.7% population moved from Hepatitis C to DCLD and 1% of the population suffered death. 58% of the population was affected with cirrhosis, out of which, 40% moved to DCLD and 1.2% suffered death. 75% population was affected with DCLD, out of which 25% suffered death. And 1% population suffered death directly due to hepatitis C.

3.7.3 Cycle Length:

Cycle length is basically the duration of illness from onset to retardation or death. This is obtained through literature review and experts consultation. In this study, the cycle length is taken as 6 months depending on the duration of treatment for hepatitis C.

3.7.4 Data Limitations:

The real data for the health states for hepatitis C is not available because the health care facilities do not keep a track of this data. Due to increasing disease prevalence, government has established hepatitis centers in different health care facilities but they only have the record of patients who are receiving hepatitis C treatments. They don't have the data for the transition of hepatitis C towards advanced stages which the requirement is if the present study. Along with this, no cost-effectiveness study has been done to evaluate that which treatment is more effective and less costly in order to lower the disease and financial burden of the society. Planning Commission is now working on establishing new and enhancing the previously established hepatitis C clinics in tertiary care hospitals in most of the cities of Pakistan which will also enable the health care system to work on keeping a track of patient's data in order to compare the past and present situations and to formulate a strategy for the future to improve the health care system by lowering the disease and financial burden.

3.7.5. Costs:

As the cost component which is taken as direct medical cost in this study is divided into two categories i.e., fixed and variable cost as described earlier in the study so the data is gathered according to these categories. These are obtained through hospital expenditure statements and administrative records. Other than the fixed and variable costs, the drugs costs is also obtained which is a component of cost for the present study. The drug cost which is the cost of drugs used in both types of treatment strategies is obtained through the pharmaceutical

records. The cost categories for both intervention and comparative strategy along with their detailed description are illustrated in the table 3.3 below:

Table 3.2. Cost categories including their description both for intervention and comparative strategy of treatment.

Cost Categories/ Items	Description
Drug Cost	This includes the costs of medicines which are used for hepatitis C treatments.
Laboratory Cost	This includes the costs of tests which are performed for the diagnosis of hepatitis C i.e., blood CP, LFT, RFT, PCR qualitative and genotype.
Other Diagnostic Cost	This includes the costs of imaging test i.e., ultrasound to know about the liver state.
Supplies Costs	This includes the costs of syringes, test tubes and needle box cutters.
Hospitalization Cost	This includes the overhead cost i.e. consultant fee, cost of nursing care

CHAPTER 4

DATA ANALYSIS AND RESULTS

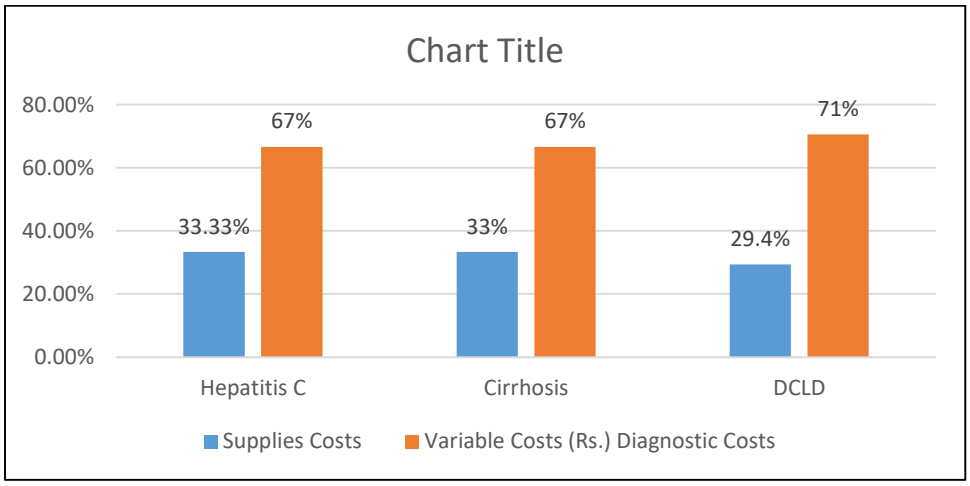
4.1. Introduction:

The results for the analysis of cost-effectiveness for hepatitis C treatments in genotype 3 patients are presented in this chapter. This chapter is comprised of three sections. First section presents the results for the cost analysis. In the second section, the results of outcome measures i.e., treatment effect and life years gained are discussed. In the third and the last section, the results for the main outcome of this study i.e., incremental cost effectiveness ratios (ICERs) have been shown and discussed.

4.2. Costs:

As cost is one of the main outcomes of this study, so it is important to know the total costs incurred while providing the treatment through both the treatment strategies i.e., Intervention and comparative in order to evaluate the cost effectiveness. All the three types of costs which are related to the both treatment strategies for hepatitis C have been estimated through provider perspective after reviewing the pharmaceuticals records and hospital's expenditure statement.

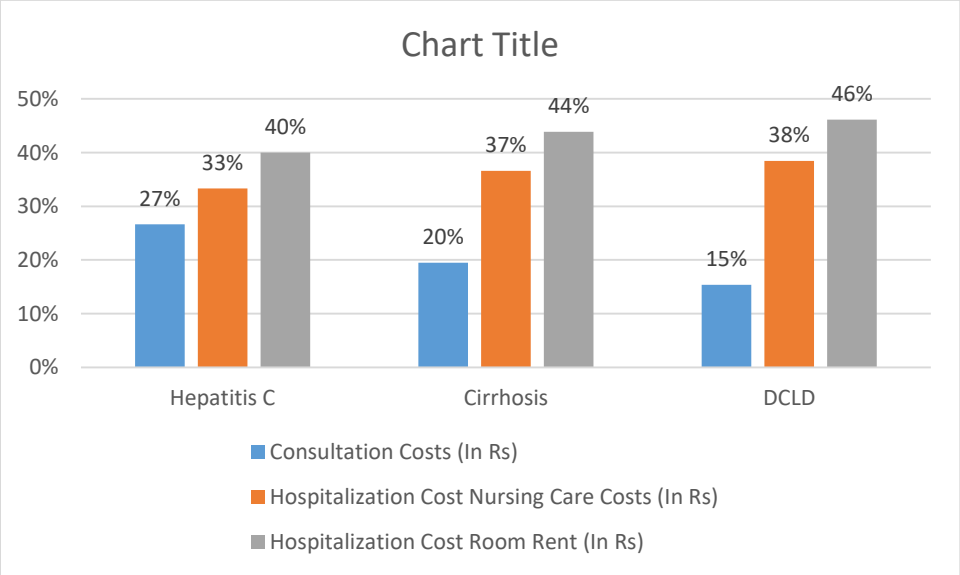
Fig.4.1. Health Care spending for Hepatitis C Treatment's in terms of Variable Costs.



The above figure represents the health care spending in terms of variable costs for each state. These costs are calculated by multiplying the per head cost in each state with the total number of patients in that state. The total variable cost is higher for state C; DCLD which is estimated to be as 16.4 million. Due to the complexity of the disease, more procedures and

diagnostics are required which prone to a higher cost. The supplies costs tend to be 29.4% of the total costs which constitutes Rs. 4.8 million and the diagnostic cost for this state is 71% of the total costs which constitute Rs. 11.6 million. The total variable cost for the other two states vary with a slight difference as compared to the DCLD state. The supplies cost for state A; Hepatitis C and state B: Cirrhosis is 33% and 67% constituting Rs. 1.8 and Rs. 2.1 million respectively.

Fig. 4.2. Health Care spending for Hepatitis C treatments in terms of Fixed Costs.



In the above figure, the fixed costs are shown which are incurred during the treatment by the health care provider's i.e. hospitals. Fixed cost is basically the cost for hospitalization expense or overhead expense. These are divided into three components i.e. consultation costs, nursing care and equipment costs. The total fixed cost for the state C; DCLD is higher as compared to the other states which tends to be Rs. 25 million. Of the total cost, due to the complexity of the disease, the cost for hospital stay is more, estimated to be 46% constituting Rs. 11.6 million. The consultant cost is same for all the states which is 15% of the total cost. The other two costs differ for the different states. The duration of hospital stay is fixed at 10 days for hepatitis C, 15 days for cirrhosis and 20 days for DCLD. The fixed cost is more for DCLD state because of the long stay in hospital depending on the complexity of the disease.

Table 4.1. Total Health Care Spending for the Treatment of Hepatitis C.

	Total Costs for Intervention (In Rs)	Total Costs for Comparator (In Rs)	Difference
Discounted Values	**264,657/-**	**152,230/-**	**112,427/-**
Non-Discounted Values	**425,124/-**	**211,833/-**	**213,291/-**

The above table shows the total discounted and non-discounted values for both comparative and intervention strategy of treatment. Both the discounted and non-discounted costs for intervention strategy are two times as compared to the comparative strategy as indicated by the difference between the two costs. The discounting value for cost is estimated in order to know the time value of costs; the present value of future costs.

4.3. Effects:

The results of estimated effects in terms of treatment effect and life years gained is discussed in this section. The treatment effect or relative risk ratio is estimated to be 0.509 which is less than 1.It describes that the patients who are given intervention strategy of treatment i.e., sofosbuvir and daclatasvir are less likely to get the disease than those who are given comparative strategy of treatment i.e., pegylated interferon and ribavirin. This means that the patients who are being provided treatment with intervention strategy have 50.9% more chances of survival than those patients who are being provided with comparative strategy.

The benefit or life years gained through intervention strategy are also more as compared to the comparative strategy. The discounted life years gained through comparative strategy are 6.77 years and non-discounted life years gained are 7.99 years. The discounted life years gained through intervention strategy are 10.86 years and non-discounted life years gained are 13.85 years. The difference between the discounted life years gained through these both strategies is of 5.86 years and the difference between the non-discounting values for life years gained through these strategies is of 4.09 years. The table below shows the life years gained through two different types of treatment strategies.

Table 4.2. Life Years Gained through Both Treatments Strategies.

	Life Years Gained through Comparator	Life Years Gained through Intervention	Difference
Discounted	**6.77**	**10.86**	**5.86**
Non-Discounted	**7.99**	**13.85**	**4.09**

4.4. Incremental Cost-Effectiveness Ratio:

As the focus of this study is to measure the cost-effectiveness for hepatitis C treatments so for that purpose, incremental cost-effectiveness ratio is the main outcome. It is obtained by dividing the difference of cost with the difference of benefits of both treatments. Table 4.6 below shows the values for ICER.

Table 4.3. Value for Incremental Cost-Effectiveness Ratio

	ICER
Discounted Value	**36,398/-**
Non-Discounted Value	**27,488/-**

The difference in life years gained is of 5.86 years and difference in costs is Rs. 112,427 which is incremental cost. Through this, the value of ICER is estimated to be Rs. 36,398 which is non-discounting value. This means that for gaining one additional benefit from the intervention strategy, we have to incur Rs. 36,398 less than the comparative strategy.

4.5. Discussion:

According to the present study which has analyzed the cost-effectiveness for hepatitis C treatments, the intervention is effective as it is generating an increase of life years gained and a drop in the direct medical costs. The results of CEA in this study are consistent with the studies of "Linas et al., (2012), Chhatwal et al., (2015), Moshyk, (2015), Zhang et al., (2015) & Jona et al., (2017)". Conferring the literature on cost effectiveness analysis, if an intervention strategy is less costly as well as effective than the comparator strategy, a decision has to be made regarding its adoption based on some standard threshold benchmarks. The current

intervention is cost effective because it is incurring less cost and increasing more life years gained. Although the intervention is more beneficial than the comparator, but it is dependent on the Willingness to Pay (WTP) of health care providers for incurring the cost i.e. how much they are willing to pay for gaining an additional year of life. Therefore, here willingness to spend on a more expensive but more effective drug will be the

CHAPTER 5

CONCLUSION AND RECOMMENDATION

5.1. Introduction:

This chapter is aimed at summarizing the analysis of the cost-effectiveness for the treatments of hepatitis C. Using the results of the analysis, represented in the previous chapter, conclusions shall be drawn about the use of intervention strategy due to yielding more health benefits. Further; a few recommendations have been presented to assist policy makers while drawing and implementing the elimination strategy for hepatitis C.

5.2. Summary and Conclusions:

The present study has conducted the cost-effectiveness analysis of hepatitis C treatments which is delivered through the two treatment strategies i.e., comparative and intervention strategy. The analysis was done within the framework of decision analytic modelling i.e., Markov model by comparing the costs and effects of comparative strategy to the cost and effects of intervention strategy for the year 20106-17 with a total sample of 300 obtained through meta-analysis. The results of the analysis indicate that intervention is effective in terms of the health care benefits because it is yielding an increase in life years gained as compared to the comparative strategy. The life years gained through intervention strategy are 13.85 years and through comparative strategy are 7.99 years which indicates that if the HCV patient is treated through intervention strategy, he will gain 5.86 more years to live as compared to the comparative strategy. Though the costs for intervention strategy is higher as compared to comparative strategy but benefits are more. Hence, the above results lead to the conclusion that intervention strategy is a cost effective intervention for the treatment of hepatitis C. From this it can be concluded that the present intervention strategy i.e., combination of sofosbuvir and daclatasvir fulfils the Kaldor Hicks criterion in the sense that net gain measured through incremental cost effectiveness ratio is positive

5.3. Policy Recommendations:

The present study recommends the following points based on the estimation of cost-effectiveness analysis for hepatitis C treatments:

1. As the intervention strategy is cost-effective, public health care authorities should ensure the availability and coverage of these drugs to the general public.

2. Focus on the research in this area to evaluate the costs-effective treatment strategies in order to monitor & provide the effective strategy which could help in elimination of the virus from the country.

5.4. Limitations:

The present cost-effectiveness analysis has been done with the following limitations:

1. Due to a shorter analytical period (one year), all the costs and effects have not been fully captured. A more complete analysis may require a longer analytical period.
2. Due to the non-availability of real data, literature review is used to extract data which could lead to the under estimation of the cost effectiveness analysis of hepatitis C treatments.

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