Cost effectiveness evaluation of hepatitis C therapy in Lahore

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Abstract: Approximately 10 million Pakistan's of population is a victim of Hepatitis C virus. A comparative study of two treatments for Hepatitis C being provided in private clinics and government hospitals was conducted to evaluate the cost effectiveness of these treatments. The quality adjusted life years (QALYs) for each treatment plan was determined with the help of health utilities, using EQ-5D scores. A comprehensive data collection form aided in scrutinizing the cause and effect of each treatment on the patient's quality of life. The total sample size for this study is 200 total from the public and private sectors. For both the treatment strategies, values for quality adjusted life years (QALYs), incremental cost effective ratio (ICER) and cost effective analysis (CEA) were calculated. The Hepatitis C virus 3a and 3b genotypic patients who were treated with pegylated interferon α-2a and ribavirin combination (strategy 2) showed an increased quality adjusted life years (QALYs) of two years, as compared to those who received interferon α-2a and ribavirin regimen (strategy 1). An incremental cost effectiveness ratio (ICER) of Rs 144673.5 per quality adjusted life year (QALYs) was gained by patients treated with strategy 2. The therapy followed by the government sector (strategy 1) is relatively inexpensive accounting for Rs 654.5/quality adjusted life years (QALY) and therapy provided at the clinic sector (strategy 2) is relatively expensive Rs 5620.6/ quality adjusted life years (QALY). However, the cost effectiveness analysis for the pegylated interferon therapy is quite comparable with the other standard treatments; hence it can be called cost effective according to the quality adjusted life years (QALYs) gained and efficacy of the said therapy.

Keywords: Hepatitis C, Lahore (Pakistan), Quality adjusted life years (QALYs), Cost effectiveness analysis (CEA), Incremental cost effectiveness ratio (ICER), Interferon, Ribavirin.

INTRODUCTION

Hepatitis C is severely affecting 150 million people, and approximately 350,000 people are dying every year (Wong *et al*, 2009). The pharmaco-economic study involves two important components namely the cost and effects of a drug. The results are mainly expressed in cost-effectiveness ratio that is cost per health outcome. Hepatitis C is disease of liver and the causative agent is hepatitis C virus. Major cause for Hepatitis C transmission is through contaminated blood transfusions and injections given with contaminated syringes and invasive use of drugs. The seroprevalence of hepatitis C virus (HCV) was found to be 1.8% among the male blood donors of Karachi, Pakistan in addition with increasing proportion of positive donors (ref). Treatment with combination of interferon and ribavirin is effective treatment of hepatitis C. The standard interferon is administered 3 times a week whereas pegylated interferon only has to be given once a week. As per Investment Management Association surveys in 2008, Pakistan imports of interferon was worth Rs2.3 billion so if the current trend continues Pakistan will have to spend 2 billion rupees by 2020 (4). Gastrointestinal Endoscopy and Pakistan Society of Gastroenterology suggested that patients with genotypes 2 and 3 should be treated with conventional interferon in combination with ribavirin and only non-responders and relapsers should be treated with pegylated interferon and ribavirin (Wong *et al*., 2000). Ribavirin is antiviral and combining ribavirin with pegylated interferon enhances cure rates and risk of relapse is reduced. Many studies conducted showed that the interferon alone strategy compared with the 24 or 48 week of combination therapy could prolong life expectancy by 1.4 to 2.0 year (Younossi *et al* 2009) and a typical patient who has taken the combination therapy for 12 months showed increase of 1.55 quality-adjusted life years and 0.80 years (7). Therefore, the aim of the study was to shed light on different strategies adopted for the HCV treatment in Pakistan and their cost-effective evaluation. This is clearly highlighting individual benefits offered by the strategies.

MATERIALS AND METHODS

We adopted EQ-5D model formulated by Ceri Phillips and Guy Thompson, (Muhammad Umar *et al* 2012) for the simulation of disease advancement in the Hepatitis C treated and untreated patients to evaluate the QALYs and the cost related to different treatment plan opted in government and private hospitals. The previous history of the disease parameters was estimated through an extensive questionnaire based analysis and patients were directly interviewed and data was recorded. The inclusion criteria of our study was random patients (both male and female) having age limit 15-70 with diagnosis of Hepatitis C being treated with combination therapy of interferon and ribavirin which further include relapse patients and non-responders. The exclusion criteria of our study was patients with chronic ailments and drug addicts. The study

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duration was of three months starting from June 2014 - August 2014.The EQ-5D score are engendered from the individual's ability to perform in five dimensions that are mobility, pain/discomfort, self-care, anxiety, and other activities. The target population constituted of the people of both genders from age of fifteen and plus. They had elevated alanine amino transferase levels with positive Polymerase chain reaction (both qualitative and quantitative test). The different strategies used were firstly combination therapy of ribavirin and standard interferon (government treatment) and secondly Combination therapy with peg-interferon (private treatment). The treatment carried on for 6-12 months according to the clinical response patients showed during the course of the prescribed therapy. The comparative efficiency of both the treatments was measured by the help of the incremental cost effectiveness ratio which is expressed as the additional cost on the alternative therapy for the achievement of the required outcomes.

RESULTS

Acute Hepatitis C virus infection is often asymptomatic which usually makes it difficult to detect it at early ages, different diagnosis methods were adopted to ensure and evaluate the stage of the infection. The most key method adopted was the Polymerase chain reaction test including both the qualitative and quantitative analysis and there were other methods as specified in table 1.

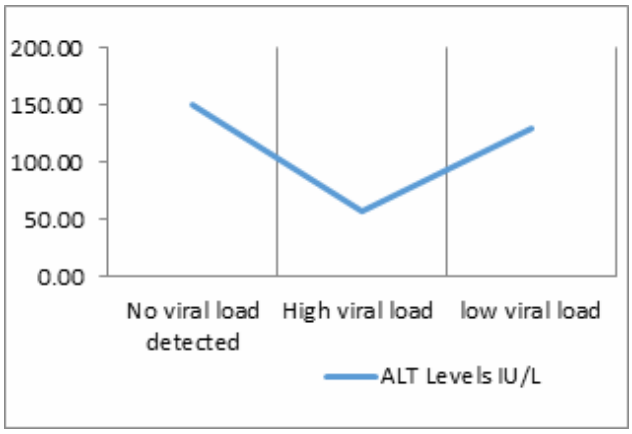

Fig. 1: Shows the relationship between the Polymerase chain reaction (PCR) and Liver function test (LFT). Above variations indicated that no direct correlation exists between these two components.

Retrospective data for the different polymerase chain reaction (PCR) values was collected from both the government and private settings. The compliance of the patients was evaluated through a comprehensive interview and different dimensions of the EQ-5D were covered during the course. Relationship between the polymerase chain reaction (PCR) values and the liver function tests (LFTs) was analyzed illustrated in figure 1 which provided with the evidence that no prominent correlation exist between them. Different laboratories have different settings and their set range for the normal values also varies. The sampling of patients with elevated Alanine aminotransferase (ALT) / aspartate aminotransferase (AST) levels had undetected virus but were also suffering from the fatty liver which caused the raised levels. With the help of the concurrent data and the retrospective data the complete side effects profile and their respective management were appraised which further aided in the estimation of the patients compliance and effectiveness of the therapy.

Cost analysis

The cost of both the interventions was calculated covering multiple aspects during the treatment course and total cost per strategy was measured which included detailed resource utilization estimates, outpatients visitation costs, transportation cost, laboratory test costs, medication cost and physician fee. The cost effectiveness analysis (CEA) and incremental cost effectiveness ratio (ICER) were further evaluated. For the private sector the estimate cost was approximately ranging from the 2.5-4 lakhs according to the duration of the therapy. (table 2)

There were patients who were non responders who did not achieve viral clearance at established milestone of 12 or 24 weeks of therapy. Relapsers achieve an undetectable level of hepatitis c virus (HCV) RNA by the end of selected strategy but hepatitis C virus (HCV) levels became detectable sometime later after the initial therapy. (table 3)

The cost effectiveness analysis (CEA), incremental cost effectiveness ratio (ICER) and the costs per quality adjusted life years (QALY)for both strategies were evaluated to be Rs.654.5 per quality adjusted life years (QALY) and Rs5620.6 per quality adjusted life years (QALY)respectively specified in table 4. In patients infected with HCV 3a and 3b genotypes, pegylated interferon α-2a plus ribavirin increased quality adjusted life years (QALY) by 2years, in comparison with interferon α-2a plus ribavirin.

DISCUSSION

The study on evaluation of Cost-effectiveness for hepatitis C therapy was conducted at two levels, sampling of the patients was done firstly in the government sector and then in the clinic/private sector. With the help of EQ-5D, health state is calculated and the quality adjusted life years (QALY) is deduced from it as specified in table 5. A study suggested that peginterferon α-2a plus ribavirin is cost effective compared with conventional interferon α-2b plus ribavirin for treatment-naive adults with hepatitis C. (Idrees *et al*., 2009). The incremental cost was due to many factors like the most important was the price of the pegylated interferon which was very high than the

Table 1: Different methods of diagnosis

	HCV RNA Testing	HCV Viral Loading Testing	HCV Genotypic Testing	Liver ultrasound	CBC	Liver function Test	Anti- HCV Testing
Government hospital	100%	100%	100%	70%	80%	100%	100%
Clinic	100%	100%	100%	80%	90%	100%	25%

Table 2: Estimate cost of therapy

Source	Cost per Month	Cost per treatment
Interferon	Free	Free
Ribavirin	Free	Free
Other medicines	Free	Free
Tests	2,500 Rs	15,000
Doctor fee	5 Rs	30 Rs
Transportation	100- 400 Rs	2400
Special diet	3,000 Rs	18,000
Total cost:	6,000 Rs	35,430 Rs

interferon α-2a, in the government sector the medicines and few tests were free of cost unlike the treatment carried in the clinic in which the patients has to do all the expenditures from his own pocket. Pegylated interferon therapy can be said cost effective even there is large difference in the cost per treatment but the reliability and the satisfaction of the patient. If the patient belongs to the lower society he could opt for the government treatment but if the patient is willing to spend Rs.144673/quality adjusted life years (QALY) then it's his choice because it's the patient psyche that government hospital doesn't provide authentic treatment (Brian and Maria 2010). According to the previous studies it is suggested that the most suitable therapy for severe hepatitis C is pegylated interferon alfa-2b and ribavirin (Sean *et al*., 2009). Some patients only partially respond to their treatment, experiencing a modest 1–2 log10 drop in hepatitis c virus (HCV) RNA levels. So during the visit in the hospital there were about (n=15) relapsers who got their first treatment in 2013 as specified in table 3. These patients were treated with standard interferon plus ribavirin. If we look at the relapsers for the peg interferon plus the ribavirin therapy the number is quite less. Even some patients for the pegylated therapy relapsed after 5 years or so. Therefore, the treatment 2 given in government hospitals is given more weight age, before opting for the combination therapy. As the chances are less for relapse and making it cost effective in long run. The combination therapy with pegylated interferon in 24 weeks therapy reduces the risk of liver problems, extend life, progress quality of life and be cost-effective for the initial treatment of hepatitis C virus (HCV) infection as per mentioned in a study. It is more difficult to treat relapse patients. If the patient had been treated with only six months of combination treatment and had a favorable response initially and then relapsed, then it would be reasonable to consider re-treating this patient for up to a year. But if the patient has already received a year's worth of combination treatment then there is unlikely that re-treatment with the same combination for an additional year is going to do anything better for this patient. Sustained viral eradication is the most important endpoint. The patients were very compliant towards their therapy and health conscious and very particular about the diet.

Table 3: Relapsers and non responders

	No. of relapse patients (2014)
Government hospital	15
Clinic	4

Though mostly were not involved in any kind of healthy exercise and liver friendly foods. The psychotherapy was also nearly non-existent among both sectors. (Joshua *et al*., 2010).A study conducted a comparative study for the treatment of Hepatitis C. In one analysis the cost-effectiveness of pegylated interferon alpha-2a is 4,569/quality adjusted life year (QALY) gained. In the second analysis, the result was 14,763 euros/QALY and in third analysis the result was 903 per QALY gained which concluded up that pegylated interferon alpha-2a is cost-effective in the management of Hepatitis C patients. (Annemans *et al*., 2010). The strengths of our study are face to face interactions with the patients and counseling the patients about their respective treatments and the side effects. Providence of moral support to the disheartened patients. Doctors provided the judgment for better treatment which caused the patient compliance rate and work productivity high. The cost and affectivity was determined and quality of life was highlighted. The long term clinical consequences were estimated of the combination therapy and the prevalence of Hepatitis C was observed in Lahore. The limitations of our study are incomplete data availability at the hospitals which caused

Table 4: Cost analysis and quality adjusted life years (QALY) gained (all values are in Pakistani rupees)

Treatment/strategy	QALY Gained	Net Cost (Rs)	CEA= Net cost/ QALY	ICER= Rs 144673.5 Per QALY
1	56	36,653	654.5	
2	58	326,000	5620.6	

Table 5: EQ-5D Health State Valuation (developed by Ceri Phillips supported by Sanofi-Aventis)

Health state	Description	Valuation
11111	No problems	1.000
11221	No problems walking about; no problems with self-care; some problems with performing usual activities; some pain or discomfort; not anxious or depressed	0.760
22222	Some problems walking about; some problems washing or dressing self; some problems with performing usual activities; moderate pain or discomfort; moderately anxious or depressed	0.516
12321	No problems walking about; some problems washing or dressing self; unable to perform usual activities; some pain or discomfort; not anxious or depressed	0.329
21123	Some problems walking about; no problems with self-care; no problems with performing usual activities; moderate pain or discomfort; extremely anxious or depressed	0.222
23322	Some problems walking about, unable to wash or dress self, unable to perform usual activities, moderate pain or discomfort, moderately anxious or depressed	0.079
33332	Confined to bed; unable to wash or dress self; unable to perform usual activities; extreme pain or discomfort; moderately anxious or depressed	–0.429

extensive questioning and a lot of time consumption. The patients were unaware about the disease.

CONCLUSION

Our study suggests that for the treatment of hepatitis C virus 3 genotype peginterferon α-2a and ribavirin is cost effective compared with conventional interferon α-2b and ribavirin. Due to the repercussion of the cost of anti-viral therapy the use of standard interferon and ribavirin remains the drug of choice within the governmental hospitals. But the new trend of prescribing peg interferon is being followed by the health practitioners doing the private practice. The cost effective analysis ratio per quality adjusted life years (QALY) was evaluated to be Rs 654.5 per quality adjusted life years (QALY) for treatment 1 and Rs 5610.6 per quality adjusted life years (QALY) for treatment 2. In patients infected with hepatitis c virus (HCV) 3a and 3b genotypes, pegylated interferon α-2a plus ribavirin increased quality adjusted life years (QALY) by 2years, compared with interferon α-2a plus ribavirin. The incremental cost per quality adjusted life years (QALY) gained was Rs.28,9347and incremental cost effectiveness ratio (ICER) for genotype 3 per quality adjusted life years (QALY) gained was Rs 144673.5. The success rate for both the treatments was comparable and it's up to the patient's affordability and health consciousness whether he is willing to spend approx.145000/quality adjusted life years (QALY) to attain the best possible treatment which could improve his quality of life more effectively.

Abbreviations

HCV: Hepatitis C virus; CEA: Cost effectiveness analysis; ICER: Incremental cost effectiveness ratio; QALY: Quality adjusted life years.

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