Treating hepatitis C in HIV/HCV co-infected patients in Malaysia- the outcomes and challenges

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ABSTRACT

Background: Co-infection by human immunodeficiency and hepatitis C viruses (HIV/HCV) is common and results in significant morbidity and mortality despite effective anti-retroviral therapies (ART).

Method: A retrospective and prospective evaluation of the efficacy and safety of pegylated interferon alfa 2a/2b plus ribavirin (PEG-IFN/RBV) in consecutive HIV/HCV co-infected patients treated in real life clinical practice in Malaysia.

Results: Forty-five HIV/HCV co-infected patients with a median age (interquartile range, IQR) of 41 years (37; 47) were assessed for treatment with PEG-IFN/RBV. All except one are of male gender and the most common risk behaviour was injecting drug use. At baseline 75.5% was on ART and the median (IQR) CD4 count was 492 cells/µl (376; 621). The HCV genotypes (GT) were 73 % GT3 and 27% GT1. Liver biopsies in forty patients showed 10% had liver cirrhosis and another 50% had significant liver fibrosis. The treatment completion rate was 79.5% with 15.9% dropped out of treatment due to adverse effects (AE) or default and 4.6% due to lack of early virological response. The AE causing premature discontinuations were neuropsychiatric and haematological. The overall sustained virological response (SVR) was 63.6% with a trend towards higher SVR in GT3 compared with GT1 (71.9% vs. 41.7%; p=0.064). In patients with bridging fibrosis plus occasional nodules or cirrhosis on liver biopsy, the SVR was significantly lower at 20% (p=0.030) compared to those with milder fibrosis.

Conclusion: HIV/HCV co-infected patients can be successfully and safely treated with PEG-IFN/RBV achieving high rates of SVR except in cirrhotic patients.

KEY WORDS:
Sustained virological response, HIV/HCV co-infection, Pegylated interferon and Ribavirin, Injecting drug use

INTRODUCTION

Malaysia, an upper middle income country has 79,855 people reported living with the human immunodeficiency virus (HIV) at the end of 2011, which was roughly a quarter of a century after the country's first reported case.[1,2]

Injecting drug use (IDU) was one of the key drivers of the earlier phase of the HIV epidemic.[2] As a result of the shared modes of transmission in IDU, co-infection by HIV and hepatitis C (HCV) is relatively common. Studies of drug users in our country showed that the prevalence rate of anti-hepatitis C antibody (anti-HCV) ranged from 65.4 to 89.9%, which was almost five times higher than the rate of HIV antibody.[3,4] It was also shown that 43.2% of those with anti-HCV antibody were also co-infected with HIV.[4]

In our country, anti-retroviral therapy (ART) has been available for all patients with HIV who meet appropriate treatment criteria since the beginning of 2001. Harm reduction initiatives, which comprise of needle syringe exchange program and opiate substitution therapy have also been introduced as part of the national strategic plan on HIV/AIDS. Currently the first line ARTs are provided free and the second line regime is subsidised by the government.

In countries which had implemented access to effective ART earlier, HIV/HCV co-infected individuals now suffer a higher risk of death from HIV and/or AIDS, and from hepatitis or liver disease mortality compared to the HIV mono-infected individuals.[5,6] Although there is no local published data, it is likely that liver disease in particular related to HCV infection will also emerge as a clinically important disease in HIV infected patients due to the high prevalence of this co-infection. If left unchecked progressive liver disease culminating to end stage liver disease as well as hepatocellular carcinoma will become a burden to the health system.

Response to HCV treatment is measured as sustained virological response (SVR), which is defined as undetectable HCV RNA by polymerase chain reaction (PCR) at 24 weeks post treatment. The achievement of SVR in HIV/HCV co-infected is associated with a reduction in HIV progression and a decreased risk for liver-specific as well as non-liver disease related mortality in the HIV/HCV co-infected.[7-9]

In registration trials, the SVR rate in HIV/HCV co-infected patients treated with pegylated interferon and ribavirin (PEG-IFN/RBV) is lower than the HCV mono-infected at 37% overall, with higher SVR in HCV genotypes 2 and 3 at 56% compared to genotype 1 and 4 patients at 26%.[10] Fortunately similar to the HCV mono-infected population, the SVR in HIV/HCV co-infected has been shown to be 99% durable up to four years of follow-up.[11]

Since the early 2000s, PEG-IFN/RBV was already approved for treatment of hepatitis C in our country, but unlike the ART program, anti-HCV therapies were not as widely available. In

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the public health facilities, PEG-IFN/RBV is funded by the government in certain allocated numbers yearly.

This study aims to explore if providing PEG-IFN/RBV in HIV/HCV co-infected patients using our existing public health facilities and resources can produce safe and reasonable response. This is timely because with the success of the government-initiated programs for HIV control, people living with HIV are now well and living longer with the improved medical care. The HIV/HCV co-infected individuals with untreated HCV require treatment to prevent the risk of severe liver disease and its complications. We hope such data will assist the policy makers and clinicians in planning and implementing effective anti-HCV therapies with PEG-IFN/RBV for the HIV/HCV co-infected patients.

MATERIALS AND METHODS

Treatment setting

HIV patients co-infected with viral hepatitis were seen in the co-infection clinics at Sungai Buloh Hospital, which is the national infectious disease referral centre. In the clinics, HIV/HCV co-infected patients were jointly assessed by the infectious disease specialists and the visiting hepatologists. Patients without obvious contraindications to PEG-IFN/RBV were informed about the treatment, the potential side effects, response rates and the follow-up plan. Only patients who agreed and willing to receive treatment were assessed further and eventually proceed to liver biopsy. The PEG-IFN/RBV treatment was initiated and followed up by the hepatologists at Selayang Hospital, which is the national liver referral centre. During the PEG-IFN/RBV treatment period, the patients also continued their usual follow-up in the infectious disease clinics in Sungai Buloh Hospital. From the year 2010 onwards, the patients were also co-managed with our pharmacists in the medications therapy adherence clinics (MTAC).

Both the first-line ART and PEG-IFN/RBV were provided free-of-charge however HCV genotyping and HCV RNA tests were paid by the patients unless donated free tests were available at that time. If there were no free tests and the patients have limited funds, only the HCV genotype was performed.

Study population

Patients included in this study were cases who were fully assessed and ready for PEG-IFN/RBV treatment from 2006 and subsequently completed treatments as well as follow-up assessments by the end of 2011. Our criteria for PEG-IFN/RBV were: HIV/HCV co-infected patients with compensated liver disease who are willing to be treated and able to adhere to treatment. Patients were required to have baseline CD4 ≥200 cells/μL, adequate haematological parameters (i.e., haemoglobin [Hb] level ≥10 g/dL, white cell count ≥3.0 × 10^9/L, neutrophil count ≥1.5 × 10^9/L, and platelet count ≥80 × 10^9/L), normal thyroid-stimulating hormone level, antinuclear antibody ratio ≤1:320 and no contraindications to interferon and ribavirin. Patients on didanosine were contraindicated and zidovudine was replaced with another ART whenever feasible.

Evaluation and Treatment

The baseline assessments consist of full clinical assessments and psychiatric evaluation if indicated. The investigations were blood counts, liver function tests, renal profile, thyroid function tests, antinuclear antibody, anti-HCV antibody, HCVRNA [Quantitative analysis: Cobas Amplicor Monitor Test V2.0 (Roche, Branchburg, NJ, USA); range: 600–700 000 IU/ mL. After March 2006: Cobas AmpliPrep/Taqman (Roche, Branchburg, NJ, USA); range: 43-69,000,000 iu/ml], HCV genotype [INNO-LIPA HCV 2.0 (Innogenetics NV, Ghent, Belgium). After 2008: Siemens Versant HCV Genotype assay (LiPA) 2.0], HBsAg and liver biopsy. Patient who refused liver biopsy was still eligible for treatment if they fulfilled the treatment criteria and were otherwise motivated to receive treatments. Data were collected both retrospective and prospectively.

The treatments consist of either Pegylated interferon alfa 2a at 180 μg or 2b at 1.5 μg/kg subcutaneous injection once weekly plus oral ribavirin at 800 mg daily for genotype 3 or 1000 mg for body weight of 75 kg and below or 1200 mg for body weight above 75 kg for genotype 1.

The duration of treatment was 48 weeks regardless of genotype. In later part of the study period from 2008 onwards, genotype 3 patients were given a shortened duration of treatment of 24 weeks if they have troublesome adverse effects (AE) but possessed criteria for good response like low baseline HCV RNA, minimal liver fibrosis and rapid virological response (undetectable HCVRNA at week 4 of treatment). Genotype 1 patients who achieved a less than 2 log10 reduction in HCVRNA titre at week 12 compared to baseline viral load were considered non-responders and withdrawn from treatment for having failed to achieve early virological response (EVR) which is predictive of lack of SVR.

During treatment the patients were followed up in the liver clinics at 2 weeks and thereafter at 4 weekly intervals with blood counts and liver function tests. More frequent follow-up was performed in problematic cases at the attending clinician's discretions. Thyroid function tests were carried out 3 monthly. Anaemia was managed by ribavirin dose reduction and blood transfusion if symptomatic.

In the MTAC, the pharmacists assisted in ensuring treatment adherence and checking for proper injection techniques as well as the storing of medications.

Assessment of response and safety

The response to treatment was assessed at the end of treatment for end of treatment response (ETR) and at 24 weeks after the completion of treatment for SVR. Both are defined as undetectable levels of hepatitis C virus ribonucleic acid in the serum at their respective time points [HCVRNA < 50 IU/ml, Qualitative analysis: Cobas Amplicor Hepatitis C Virus test v. 2.0 (Roche, Branchburg, NJ, USA); detection limit: 50 IU/mL]. SVR is the end point and goal of HCV therapy.
Patients who defaulted ETR or SVR assessments were recalled and undetectable HCV RNA beyond the 24 weeks post treatment were used to define SVR. Those who cannot be traced or recalled were counted as non-ETR and non-SVR.

Safety was assessed by clinical evaluation for AE during therapy and laboratory tests.

Analysis

Results were analysed using SPSS version 20 (SPSS IBM, New York, USA). Patients who received at least one dose of PEG-IFN/RBV are included into analysis for efficacy and safety. It was assumed that missing efficacy data (ETR or SVR) did not meet the criteria for response. Categorical variables were summarized with the use of proportions and continuous data were summarized as median and interquartile range. Differences between categorical data were compared for statistical significance using the Chi-Square or Fisher's exact tests. Differences between continuous data were tested using the Mann-Whitney *U* test.

RESULTS

Baseline characteristics

Overall, 45 patients with HIV/HCV co-infection were fully assessed and ready for PEG-IFN/RBV therapy. The baseline characteristics of these patients are presented in Table I. There were 98 % male patients with a median age [and interquartile range (IQR)] of 41 years (37; 47) and the most common risk behaviour was IDU at 77.8%. Three (6.7%) of the patients were on opioid substitution therapy, 75.5 % were ART treated, the median (IQR) CD4 cell count was 492 (376; 621) cells/μL and all thirty patients (85.7%) who had baseline HIV RNA levels performed, had levels of <50 copies/ml. The ART treatment regimens were: tenofovir + lamivudine + efavirenz (n=22, 64.7%), stavudine + lamivudine + efavirenz (n=8, 23.5%), tenofovir + lamivudine + nevirapine (n=2, 5.9%), lamivudine + efavirenz + zidovudine (n=2, 5.9%) and there were another 11 patients who did not require ART.

The most frequent HCV genotype was genotype 3 at 73.3 % (n=33) and the remaining was of genotype 1. Majority of the patients (72.1%) had high HCV RNA at > 400,000 IU/ml. Triple infection with HIV, HCV and hepatitis B defined as HBsAg positive was found in 13.3%.

The alanine transaminase (ALT) levels were mildly elevated and 86.7% of the patients had ALT values above the upper limit of normal for our laboratory. Liver biopsies were available for 40 patients with 50% having significant fibrosis with fibrosis score >3 and 61.6% had inflammatory grades >4 on the modified HAI scoring system. Biopsy proven liver cirrhosis (fibrosis score=6) was found in 10% of cases.

Table I: Baseline characteristics of patients assessed for treatment (n=45)

Variable	Overall, (n=45)
Age (years), Median (IQR)	41 (37; 47)
Body mass index (kg/m2), Median (IQR)	22 (20.5; 25.5)
Gender, n (%)	
Male	44 (98%)
Female	1 (2%)
Risk behaviour, n (%)	
IDU	31 (68.9%)
IDU and sexual	4 (8.9%)
Sexual	
Heterosexual	5 (11.1%)
Homosexual	2 (4.4%)
Unknown and others	3 (6.7%)
Co-morbid illness, n (%)	
No	38 (84.4%)
Psychiatric	2 (4.4%)
Diabetes	3 (6.7%)
Others	2 (4.4%)
CD4 (cells/μL), Median (IQR)	492 (376; 621)
HIV viral load (copies/ml)*	
Not available, n (%)	10 (22.2%)
< 50 copies/ml, n (%)	30 (85.7%)
Receiving anti-viral therapy, n (%)	
No	11 (24.4%)
Yes	34 (75.5%)
HCV viral load (IU/ml) ^	
<400,000, n (%)	12 (27.9%)
>400,000, n (%)	31 (72.1%)
HCV genotype, n (%)	
Genotype 1	12 (26.7%)
Genotype 3	33 (73.3%)
HBsAg positivity, n (%)	6 (13.3%)
Liver histology, n (%) #	
Fibrosis score	
0-2	20 (50%)
3-4	15 (37.5%)
5-6	5 (12.5%)
Inflammatory grade	
1-3	15 (38.5%)
4-6	20 (51.3%)
7-10	4 (10.3%)
Alanine transaminase (IU/l), Median (IQR)	72 (57; 109)
Hemoglobin (g/dl), Median (IQR)	15.2 (14.3; 15.8)
Neutrophil (x103/μl), Median (IQR)	3.4 (2.7; 4)
Platelet count (x103/μl), Median(IQR)	165 (136; 198)

*Available in 30 patients, ^Available in 43 patients, #Available in 40 patients.
IQR=interquartile range, HCV=hepatitis C virus, IDU= Intravenous drug use, ULN=upper limit of normal (laboratory upper limit of normal for ALT male=43 u/l, female=33 u/l), Liver histology was scored used modified HAI scoring system.

Treatment details

Out of the 45 patients, 44 patients were initiated on PEG-IFN/RBV and one patient changed his mind and declined treatment before receiving the first dose.

The types of PEG-IFN used were PEG-IFN alfa 2a at 180 μg once weekly (n=34) and PEG-IFN alfa 2b at 1.5 μg/kg once weekly (n=10).

During treatment, eleven (25%) patients required reduction in PEG-IFN dose while 12 (27.3%) required RBV dose reductions. The dose reductions did not affect the efficacy (p=0.469 and 0.654 for PEG-IFN and RBV dose reductions respectively).

Follow-up, safety and adverse effects

By the end of 2011, 35 (79.5%) patients had completed treatment, which consist of 48 weeks PEG-IFN/RBV (n=31) and 24 weeks PEG-IFN/RBV (n=4). The nine (20.5%) patients who did not complete the planned duration of treatment had early discontinuation due to various reasons, see Figure 1

The three patients, who were lost to follow-up and cannot be recalled, had defaulted at the 3rd week, 4th month and 6th month of therapy. The patient who defaulted at 3rd week of therapy was witnessed to have returned to drug use.

The AE not amenable to treatment dose reduction and caused early treatment terminations in 4 patients were severe

Table II : Virological response at the end of treatment and follow-up

	Overall (n=44)	Genotype 1 (n=12)	Genotype 3 (n=32)	P value
ETR	32/44 (72.7%)	6/12 (50%)	26/32 (81.3%)	0.038
SVR	28/44 (63.6%)	5/12 (41.7%)	23/32 (71.9%)	0.064

ETR=end-of-treatment response, SVR=sustained virological response.

Table III: Baseline characteristics of patients who received treatment (n=44) according to outcome

Variable	Achieved SVR (n=28)	No SVR (n=16)	P value
Age (years), Median (IQR)	41 (37; 47)	42.5 (38.5; 48.2)	0.651
Body mass index (kg/m2), Median (IQR)	22 (21; 24)	22.5 (20.2; 26)	0355
Gender, n(%)			
Male	28 (100%)	15 (93.8%)	0.364
Female	0	1 (6.2%)	
Risk behaviour, n (%)			
IDU	20 (71.4%)	10 (62.5%)	0.556
IDU and sexual	2 (7.1%)	2 (12.5%)	
Sexual			
Heterosexual	2 (7.1%)	3 (18.8%)	
Homosexual	1 (3.6%)	1 (6.2%)	
Unknown and others	3 (10.7%)	0	
Co-morbid illness, n (%)			
No	25 (89.3%)	12 (75%)	0.371
Psychiatric	1 (3.6%)	1 (6.2%)	
Diabetes	1 (3.6%)	2 (12.5%)	
Others	1 (3.6%)	1 (6.2%)	
0.371			
CD4 (cells/uL), Median (IQR)	474.5 (365; 629)	560 (415.5; 635.8)	0.534
HIV viral load (copies/ml)			
Not available, n (%)	6 (21.4%)	3 (18.8%)	0.337
< 50 copies/ml, n (%)	20 (71.4%)	10 (62.5%)	
Receiving anti-viral therapy, n (%)			
No	7 (25%)	4 (25%)	1.000
Yes	21 (75%)	12 (75%)	
HCV viral load (iu/ml)			
<400,000, n (%)	9 (34.6%)	3 (18.8%)	0.269
>400,000, n (%)	17 (65.4%)	13 (81.2%)	
HCV genotype, n (%)			
Genotype 1	5 (17.9%)	7 (43.8%)	0.064
Genotype 3	23 (82.1%)	9 (56.2%)	
HBsAg positivity, n (%)	5 (17.9%)	1 (6.2%)	0.392
Liver histology, n (%)			
Fibrosis score	(n=23)	(n=16)	
0-2	15 (65.2%)	4 (25%)	0.030
3-4	7 (30.4%)	8 (50%)	
5-6	1 (4.3%)	4 (25%)	
Inflammatory grade			
1-3	10 (43.5%)	5 (33.3%)	0.804
4-6	11 (47.8%)	8 (53.3%)	
7-10	2 (8.7%)	2 (13.3%)	
Alanine transaminase (u/l), Median (IQR)	68 (55.5; 96.2)	72.5 (57.8; 120.8)	0.464
Hemoglobin (g/dl), Median (IQR)	15.2 (14.5; 15.8)	15.4 (13.8; 15.8)	0.723
Neutrophil (x10^3/ul), Median (IQR)	3.4 (2.6; 4.2)	3.4 (2.9; 4)	0.855
Platelet count (x10^3/ul), Median(IQR)	162.5 (133.5; 180.8)	173 (134.5; 234.2)	0.407

SVR=Sustained virological response, IQR=interquartile range, HCV=hepatitis C virus, IDU= Intravenous drug use, ULN=upper limit of normal (laboratory upper limit of normal for ALT male=43 u/l, female=33 u/l), Liver histology was scored used modified HAI scoring system.

prolonged insomnia despite medications, moderate depression despite anti-depressants, thrombocytopenia (nadir : 25x10^3/µl) and neutropenia (nadir: 0.3 x10^3/µl).

However, at least one AE was reported by 41 of the 44 patients (93.2 %) who received PEG-IFN/RBV treatment. By order of frequency, the common AE were fatigue (n = 23), aches and pain (n=16), sleep disturbances (n=16), depressive symptoms/irritability (n=14), fever (n=13), gastrointestinal symptoms namely nausea, poor appetite, diarrhea, weight loss (n=11), anaemia with Hb < 10 g/dl (n=7), rash (n=6), headaches (n=5), hair loss (n=5), cough (n=4), and pruritus (n=2).

Of those who complained of depression or irritability, only two (14.3%) required anti-depressive medications. While the three patients who were on opioid substitution therapy tolerated and completed 48 weeks of PEG-IFN/RBV without significant AE.

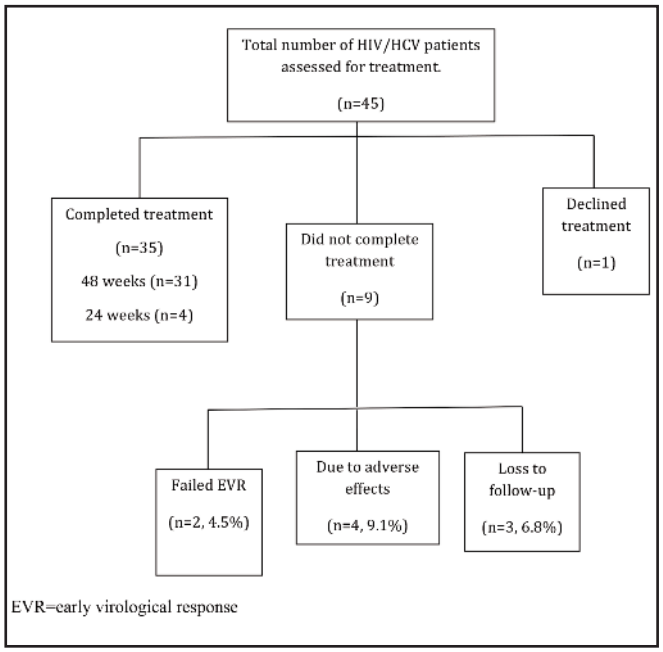

Fig. 1: The distribution of study population according to treatment completions and reasons for premature discontinuation.

Symptomatic anaemia requiring blood transfusion occurred in 4 patients and a total of 19 pints of packed cells were transfused (range 1-9 pints per patient). These 4 patients were male, age between 31-50 years old, the average baseline Hb was 14.8 g/dl and two patients had severe liver fibrosis/cirrhosis. All of them received appropriate starting dose of ribavirin at 800 or 1000 mg per day according to the genotype and the ART were tenofovir, lamivudine and nevirapine or efavirenz. The patient who required 9 pints of packed cells transfusion were later found to have heterozygous for HbJ hemoglobinopathy and eliptocytosis. Peripheral blood pictures before blood transfusion showed macrocytosis with pencil cells and teardrop cells suggestive of iron and B12/folate deficiencies in 2 patients.

Interestingly in the two patients who received zidovudine containing ART during PEG-IFN/RBV, their lowest Hb during treatment were 10.3 and 11.4 g/dl respectively.

At the 3rd month of PEG-IFN/RBV treatment, the median CD4 counts available in 35 patients dropped from 472 cells/μL (371.5;617.5) at baseline to 359.5 cells/μL (276.5; 425.8) and subsequently returned to a higher value at 534 cells/μL (398; 633) after completion of treatment.

One patient died at about 11 weeks after completion of 24 weeks PEG-IFN/RBV. At baseline, he was on ART with CD4 count of 422 cells/μL and the HIV viral load suppressed to < 20 copies/ml. He achieved ETR but 2 weeks after treatment completion, he returned complaining of productive cough and weight loss while his CD4 count was 328 cells/μL. Investigations showed sputum positive tuberculosis (Ziel Nielson stain > 50/1L) and chest x-ray revealed bilateral upper lobes haziness with reticulo-nodular changes and multiple small cavities in both the middle and lower zones. Anti-tuberculous treatment (ATT) was initiated and followed up with directly observed therapy. However he did not respond to ATT and presented about two months later with pancytopenia and acute kidney injury. At that time the sputum was still positive for acid-fast bacilli and he succumbed a few days later. The sputum cultures before ATT and at the second presentation grew Mycobacterium tuberculosis complex with strains sensitive to the ATT prescribed. The clinical impression was disseminated TB with high acid-fast bacilli density not responding to appropriate ATT.

Response to treatment

At the end of treatment, the overall ETR was 72.7% with significantly higher rates in genotype 3 patients compared to genotype 1 patients (81.3% versus 50%, p= 0.038). The SVR rate was 63.6% for all patients and there was a trend towards higher SVR in genotype 3 patients compared to genotype 1 (71.9% versus 41.7%, p= 0.064). See Table II.

The SVR rate in patients with marked bridging plus occasional nodules or cirrhosis (modified HAI fibrosis score F5 and F6, n=5) at 20% was significantly lower (p=0.030). See table III for other parameters comparing SVR to non-SVR.

All the 4 patients with anaemia requiring transfusions and the 3 patients on opioid substitution therapy achieved SVR.

DISCUSSION

We present the results of HCV treatment with PEG-IFN/RBV in 44 HIV/HCV co-infected patients who were mainly previous IDU. In the set-up of our routine clinic practice, the treatment completion rates were 79.5%, while 15.9% of our patients stopped or dropped out of treatment due to adverse effects or default and the remaining 4.6% were treatment discontinuation due to lack of EVR. Our patients achieved an overall SVR rate of 63.6% with a trend towards higher SVR in genotype 3 (71.9% for genotype 3 and 41.7% for genotype 1, p=0.064). While patients with marked bridging plus occasional nodules or cirrhosis have a significantly lower SVR at 20% compared to those with less liver fibrosis (p=0.030).

Our SVR rates are encouraging compared to a recent Cochrane Systematic Review of clinical trials which reported that around 37% of HIV/HCV co-infected patients achieved SVR with PEG-IFN/RBV and the SVR in genotype 1/4 patients was 26% while in genotypes 2/3, it was 56%.[10] Similarly when we compared to a meta-analysis of observational cohorts, the reported overall SVR was 38%, the genotype breakdown revealed SVR of 24.5 % for genotype 1 /4 and 59.8% in genotype 2/3 patients.[12]

We do not have the interleukin-28B gene polymorphism in our cohort. The host interleukin-28B rs12979860 single nucleotide polymorphism had been shown to be independently predictive of SVR in HIV/HCV co-infected patients.[13] The presence of these favourable alleles may have increased the SVR in some of our HIV/HCV co-infected patients.

Our treatment completion rate is slightly lower compared to a meta-analysis on treatment completion in drug users,

which reported a rate of 83.4%. In that study, factors that cause a lower rate of completion were infection with genotype 1/ 4, HIV-infected individuals, male gender, non treatment of addiction and lack of support services during HCV therapy.[14] Unfortunately, most of those factors were present in our cohort namely all of our patients were HIV-co-infected with all but one were male, about 80% were ex-drug users and only 3 were receiving treatment for addiction. Furthermore compounded by poor social circumstances like unemployment and living in shelter homes. Interestingly, all of the patients who were on opioid substitution therapy successfully completed 48 weeks of PEG-IFN/RBV and achieved SVR.

The rates of drop-out due to AE (9.1% versus 4.3%) and loss to follow-up while on treatment (6.8% versus 5.1%) are also higher than a recent systematic review of reports on observational cohorts of HIV/HCV co-infected patients.[12] These suggest the need in our clinic set-up of a multidisciplinary team for better management of AE in particular the neuropsychiatric components, access to opioid substitution program and social support services like peer support.

Tuberculosis had been reported to complicate HCV treatment in HIV-infected patients. The incidence reported in a series of more than 500 cases of HIV/HCV co-infection receiving HCV treatment was not higher than the background incidence in HIV patients on ART. [15] However there is a tendency in delayed diagnosis as the tuberculosis symptoms were mistakenly attributed to AE from interferon and the clinical course tends to be severe with disseminated infection as in our case. [15] However unlike our case, a decrease in CD4 counts was frequently present. [15,16]

This study has several limitations for being small in number and also being a retrospective observational cohort study. Consequently, it was not possible to analyse on-treatment viral kinetics like rapid virological response, adherence to PEG-IFN/RBV and the full impact of adverse effects and quality of life during treatment. However it reflects the real life clinical practice in our country.

Worldwide, only a minority of HCV mono-infected and HIV/HCV co-infected individuals actually received treatment for hepatitis C.[17] There are many barriers reported, at patient level factors like comorbid medical and psychiatric conditions make current HCV treatment with PEG-IFN/RBV unsafe while social circumstances and active substance abuse limit the ability to take and adhere to the complex HCV treatment regimens. In countries with resource constraints additional factors include lack of availability of diagnostics tests and antiviral drugs, the high cost, concerns that treatment success rates will be poor especially in HIV co-infected patients and shortage of HCV specialists.[18]

However, studies with paired liver biopsies have shown that HIV leads to faster liver disease progression in patients with chronic viral hepatitis.[19,20] Liver cirrhosis and hepatocellular carcinoma are major cause of morbidity and mortality in people living with HIV who are hepatitis B or C co-infected.[21,22] Hence the potentially modifiable risk to avert this increase in end stage liver disease burden is the prevention and treatment of viral hepatitis in people living with HIV. Treatment of viral hepatitis B and C will also enhance the potential benefits from the HIV control strategies.

The results of our study carried out in routine clinic practice, suggest that the treatment of HCV with PEG-IFN/RBV in HIV/HCV co-infected patients can be safely provided and achieved good comparable response rates. On this basis, we would recommend that stable HIV/HCV co-infected individuals should be considered for HCV therapy using with PEG-IFN/RBV under the same priority as HCV mono-infected patients with minor adjustments to their care and incorporating other relevant services that may improve treatment adherence. The poor SVR in our cirrhotic patients beckons the urgent need for earlier detection and management of the HCV disease as well as more effective HCV therapy with less adverse effects. Since 2011, there are now newer therapies for hepatitis C using the direct acting antiviral (DAA) which are more effective and also better side effect profiles.[23] Data on the HIV/HCV co-infected HCV genotype 1 patients revealed much improved SVR with combinations of the oral DAAs. [24] Unfortunately apart from the first generation (DAA) namely Boceprevir which still need the back bone of PEG-IFN/RBV to treat HCV, it will be a while before these promising therapies land on our shore. Moreover the cost of these medications may impose an additional challenge to treat everyone living with HCV.

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