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Combined Sofosbuvir/Daclatasvir and Chemotherapy Markedly Improve The Outcome of B-Lymphoid Malignancies in Patients with Both HCV Infection and B-Lymphoid Malignancy

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ABSTRACT

Background: A high prevalence of hepatitis C virus (HCV) seropositivity is found in patients with B-cell lymphoproliferative disorders. Many studies show improvement of lymphoid malignancies outcome with the use of anti HCV treatment in patients with HCV infection and lymphoid malignancies especially indolent B cell lymphoma.

Objective: This study aimed to examine the hypothesis if sofosbuvir based direct-acting antivirals (DAAs) combination could improve the outcome of patients with B cell lymphoid malignancies and HCV infection.

Patient and Methods: During the period from January 2017 to December 2019 all eligible patients diagnosed with B-lymphoid malignancies presented at Sohag University Hospital and Sohag Cancer Institute were included in the study. HCV positive patients were randomized to receive sofosbuvir based DAAs combination either concomitant with or after the end of chemotherapy.

Results: Patients with HCV infection are more likely to have advanced stage disease (stage 3/4), extra-nodal presentation, liver and BM infiltration. Disease free survival (DFS) and overall survival (OS) were better in the group that received sofosbuvir DAAs combination after the end of chemotherapy treatment compared to the other groups (P = 0.000, 0.000 respectively) and was not different between patients who received sofosbuvir based combination concomitant with chemotherapy and HCV negative B-lymphoid malignancies.

Conclusion: Sofosbuvir based DAAs combination improve the outcome of different types of lymphoid malignancies (DFS, OS) in patients with HCV infection associated lymphoid malignancies especially when given after the end of chemotherapy.

Keywords: HCV, B-lymphoid malignancies, Sofosbuvir, Daclatasvir, DAAs.

INTRODUCTION

HCV is RNA virus widely known for the development of hepatitis and its hepatotropism. This virus is also a lymphotropic one because it has recently been linked to some types of non-lymphoma Hodgkin's (NHL), particularly B cell NHL [(1)].

Numerous studies have found that patients with B-cell lymphoproliferative disorders, notably B-cell NHL, have a high prevalence of HCV seropositivity. However, the evidence for a connection with T-cell lymphoma, Hodgkin lymphoma, and plasma cell disorders is less compelling [(2, 3)]. The association with B-cell NHL is particularly evident in countries with a high prevalence of HCV infection. Egypt is one of the countries with a very high incidence of both HCV infection and lymphoid malignancies. Egypt is one of the few developing nations where hematopoietic malignancies are more common than average. More so than even the United States, Egypt has one of the highest incidence rates of lymphoma in the world, specifically NHL [(4)].

According to the National Cancer Institute (NCI), NHL accounts for 10.9% of all cancers in Egypt diagnosed every year representing the third most common malignancy in adult men and second most common one in women [(5)]. The most prevalent subtype of NHL in Egypt is diffuse large B-cell lymphoma (DLBCL), which represents about 49% of all NHL cases reported to the NCI. lymphoid neoplasms collectively represent the 2nd most common malignancy (11.7%) 2nd only to breast cancer (21.8%) and followed by bladder (7.6%) and lung (6.8%) cancer with NHL representing the most common type [(6)].

The frequency of HCV chronic infection varies significantly by region, with Egypt, Central Africa, Mongolia, and Bolivia having the highest rates (approximately 10%) [(7)]. The mechanism of HCV-induced lymphogenesis is not fully understood but indirect and direct mechanisms are suggested [(8)]. Many studies shows that patients with HCV infection and lymphoid malignancies usually presented with a higher stage, has a higher frequency of extra-nodal presentation and a lower response rate (RR), DFS and OS compared to other patients with lymphoid malignancies without HCV infection [(9, 10)]. According to this it is reasonable to say that eradication of HCV infection in patients with lymphoid malignancies and infected with HCV will lead to improvement of the lymphoid malignancy outcome.

In the past interferon alpha (IFNa) and pegylated interferon (peg INF) plus minus ribavirin (RBV) were the standard treatment for HCV infection and many studies show improvement of lymphoid malignancies outcome with the use of these drugs in patient with HCV infection and lymphoid malignancies especially indolent B cell lymphoma and the lymphoid malignancy response was

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directly related to the viral response [11-18]. Unfortunately, these medications have a significant toxicity profile and a weak virological response. In addition, rather than the virological reaction, the haematological response may be attributable to the direct antiproliferative effect of INF [19].

Recently, the approval of the new IFN-free antiviral therapy with DAAs revolutionized the treatment of chronic HCV infection by enabling achievement of SVR rates that reached peaks of 100% in all viral genotypes and, notably, with almost negligible toxicity [20]. DAAs lacks the direct anti proliferative effect of interferon and improvement of the lymphoid malignancies outcome with these drugs would give a better prove for the association between HCV infection and lymphoid malignancies [19]. The goal of this study was to test the hypothesis if sofosbuvir based DAAs combination can improve the outcome (RR, DFS and OS) of the lymphoid malignancies in patients with HCV positive lymphoid malignancies.

PATIENTS AND METHODS

From January 2017 to December 2019, at Sohag University Hospital and Sohag Cancer Institute, 174 patients diagnosed with different types of lymphoid malignancies are included to the study according to inclusion and exclusion criteria.

Inclusion criteria: Age between 18 and 70 years, all types of NHL according to WHO classification, plasma cell neoplasms, Hodgkin lymphoma (HL) and performance status (PS 0-2).

Exclusion Criteria:

Children up to 17 years, age above 70 years, decompensated liver cell failure and PS >2.

The most prevalent diagnosis was DLBCL (32.8 %) followed by HL (31 %), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) (17.3 %), follicular lymphoma (FL) (8 %), mucosa associated lymphoid tissue lymphoma (MALT) (4 %), multiple myeloma (MM) (2.3%), splenic marginal zone lymphoma (SMZL) (1.7%) and others (2.9%).

HCV serology and PCR were done for all patients, 28 patients were HCV positive and 146 were HCV negative. Patients with HCV positive lymphoid malignancies were randomized into 2 groups:

- **Group A:** It contained 15 patients who received sofosbuvir-based combination concomitantly with chemotherapy.
- **Group B:** It contained 13 patients who received sofosbuvir-based combination after chemotherapy.
- **Group C (control group):** It contained 146 patients with HCV negative at the time of lymphoid malignancy diagnosis.

First-line chemotherapy protocols administered according to the specific type of hematological malignancy and all HCV PCR positive patients received sofosbuvir/daclatasvir combination for 12 weeks either concomitantly with chemotherapy (group A) or after the end of chemotherapy (group B) with sofosbuvir given at a dose of 400 mg daily and daclatasvir at a dose of 60 mg daily.

The lymphoid malignancy response determined according to standardized response criteria [21]. HCV PCR determined sustained virological response (SVR) for patients who received sofosbuvir/daclatasvir after 12 weeks antiviral therapy. Relapsed and primary refractory cases received second set of chemotherapy according to the specific type of hematological malignancy.

Routine labs assessed before each cycle and the toxicity of treatment was assessed according to CTCAE version 5 [22].

All patients had followed up by clinical history, examination, suitable lab investigations once every 4 months for the first 2 years post-treatment end, and every 6 months in the next 3 years, follow up images done every 6 months.

Ethical consent:

The Academic and Ethical Committee, Sohag University approved the study. Every patient signed an informed written consent for acceptance of the treatment. This work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Statistical analysis was done using the statistical package for social science (SPSS) software program. We used SPSS for windows, version 20. Statistical methods included descriptive methods as mean (M), standard deviation (SD), frequency distribution, cross tabulation and significance tests as Chi-square test (χ^2), which was used to study the association between two qualitative variables. Kaplan Meyer test was used for survival comparison between deferent groups. Pearson correlation test (r) was used for estimation of the correlation between quantitative variables. The significance level was accepted if the P value less than or equal 0.05.

RESULTS

Table (1) showed that patients with HCV infection (group A & B) were more likely to have advanced stage disease (stage 3/4) (group A 86.7%, group B 69.2%) compared to patients with HCV negative lymphoid malignancies (group C 50.7%). In addition, HCV positive patients were more likely to have extranodal disease, liver and BM infiltration.

Table (1): Patients characters:

Parameter	Group A	Group B	Group C	*P* value
Sex [n (%)]				0.980
Male	8 (53.3)	7 (53.8)	73 (50)	
Female	7 (46.7)	6 (46.2)	73 (50)	
Age (years)				0.813
Mean	56.2	55	45.25	
Range	21-68	32-70	18-70	
B-symptoms [n (%)]				0.531
Present	6 (40)	2 (15.4)	45 (30.8)	
Absent	9 (60)	11 (84.6)	101 (69.2)	
Diagnosis [n (%)]				0.008
DLBCL	6 (9.5)	4(6.4)	47 (74.6)	
FL	2 (11.1)	3 (16.7)	9 (50)	
HL	1 (1.8)	0 (0.0)	53 (96.4)	
MALT	0 (0.0)	1 (11.1)	6 (66.7)	
MM	1 (20)	0 (0.0)	3 (60)	
CLL/SLL	3 (7.7)	3 (7.7)	24 (61.5)	
SMZL	1 (33.3)	1 (33.3)	1(33.3)	
OTHERS	1 (20)	1 (20)	3 (60)	
Stage [n (%)]				0.012
1/2	2 (13.3)	4 (30.8)	72 (49.3)	
3/4	13 (86.7)	9 (69.2)	74 (50.7)	
Extranodal disease [n (%)]				0.090
NO	8 (53.3)	5 (38.4)	97 (66.4)	
1 site	4 (26.7)	5 (38.4)	36 (24.7)	
>1 site	3 (20)	3 (23.2)	13 (8.9)	
Splenic infiltration [n (%)]				0.105
Present	3 (20)	2 (15.4)	11 (7.5)	
absent	12 (80)	11 (84.6)	135 (92.5)	
Liver infiltration [n (%)]				0.031
Present	3 (20)	0 (0)	6 (4.1)	
absent	12 (80)	13 (100)	140 (95.2)	
BM infiltration [n (%)]				0.023
Present	1 (6.7)	2 (15.4)	2 (1.4)	
absent	14 (93.3)	11 (84.6)	144 (98.6)	
Bulky disease [n (%)]				0.464
Present	5 (33.3)	4 (30.8)	35 (24)	
absent	10 (66.7)	9 (69.2)	111 (76)	

The response to 1st line chemotherapy was not significantly different between the 3 groups [(P = 0.245) (10/15 achieved CR &PR in group A (73.3 %), 12 /13 in group B (92.3 %) and 124 /146 in group C (84.9 %)]. Two patients died during treatment in group A (13.3 %), 5 patients in group C (3.4 %), and no death occurred during treatment in group B (table 2).

Table (2): response rate to first line chemotherapy

response	Group A [n (%)]	Group B [n (%)]	Group C [n (%)]	*P* value
CR	9 (60)	11 (84.6)	97 (66.4)	0.245
PR	2 (13.3)	1 (7.7)	27 (18.5)	0.245
SD	1 (6.7)	0 (0.0)	8 (5.5)	0.245
PD	1 (6.7)	1 (7.7)	9 (6.2)	0.245
Died during treatment	2 (13.3)	0 (0.0)	5 (3.4)	0.245
Total	15 (100)	13 (100)	146 (100)	0.245

As regards HCV response, all patients (100 %) in group A and B reach a SVR defined as undetectable level of HCV PCR by week 12 after sofosbuvir /daclatasvir treatment. Analysis of the DFS for all groups showed a highly significant increase (P= 0.000) in DFS (mean 42.583 months) in group B compared to group A, and C (mean 23.800 months and 19.970 months respectively) (Table 5 and figure 1).

Table (5): Disease free survival

Groups	Estimated Mean	SD	95% confidence interval		*P* Value.
			Lower bound	Upper bound	
Group A	23.800	5.352	13.311	34.289	0.000
Group B	42.583	3.241	36.230	48.937	0.000
Group C	19.970	1.041	17.930	22.011	0.000
Over all	22.130	1.094	19.986	24.273	0.000

Figure (1): Disease free survival.

Patients in group B had the highest mean OS between the 3 groups (55.250 months) compared to 34.235 months for group A and 31.241 months for group C (P = 0.000) (Table 6 & figure 2).

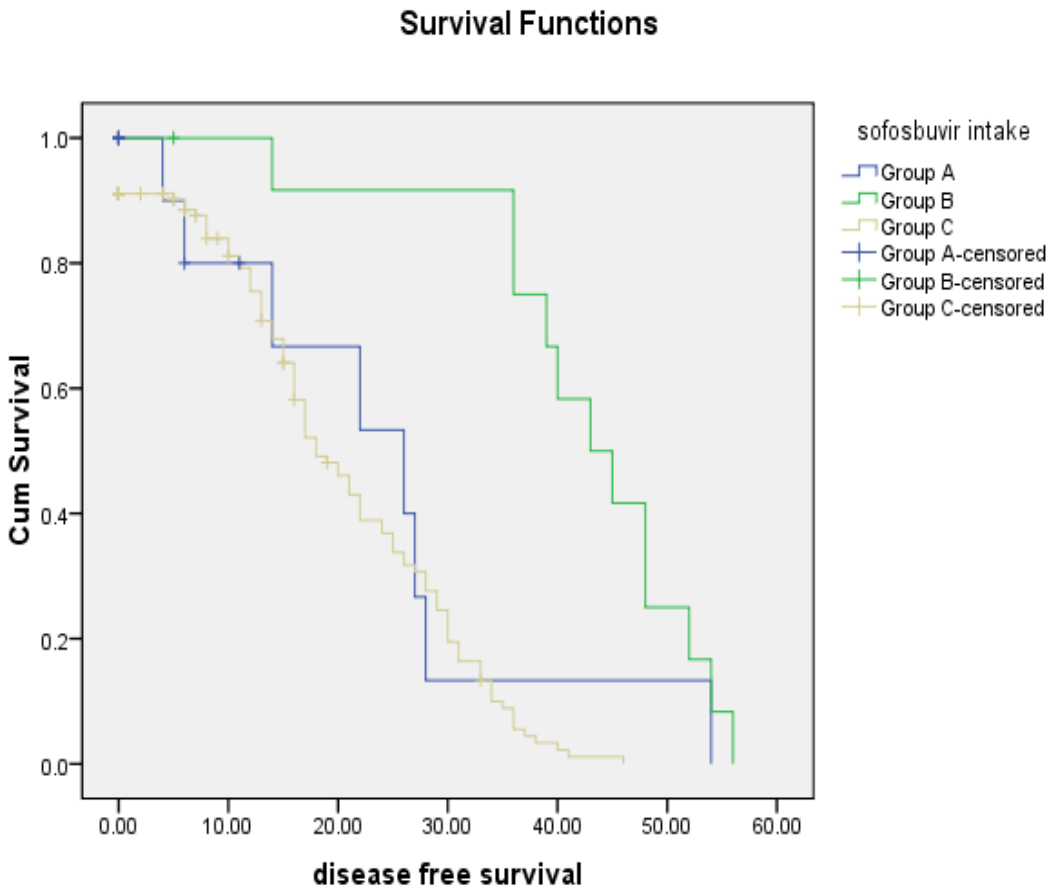

Table (6): Overall survival:

	Estimated Mean	SD	95% confidence interval		*P* Value.
			Lower bound	Upper bound	
Group A	34.235	5.101	24.237	44.233	.000
Group B	55.250	1.939	51.450	59.050	.000
Group C	31.241	0.916	29.446	33.037	.000
Over all	33.472	1.042	31.430	35.514	.000

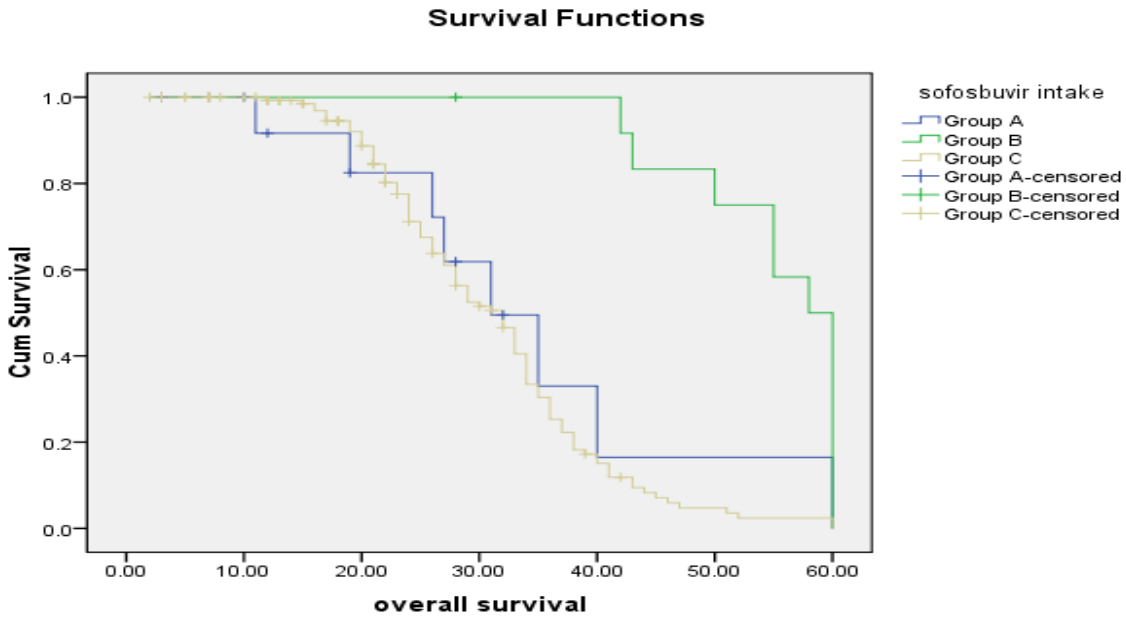

Figure (2): overall survival.

Chemotherapy toxicity was not different between the 3 groups except an increase in G1/2 thrombocytopenia in patients who received sofosbuvir either concomitant or sequential with chemotherapy (33.3 % for group A, 53.8% for group B compared to 8.2% in group C, P = 0.000). Also, there was a G1/2 increase in the creatinine level in patients who received sofosbuvir /daclatsvir concomitant with chemotherapy (26.7 % in group A compared to 0% and 1.4% in groups B and C respectively, P= 0.000). Patients who received sofosbuvir/daclatasvir concomitantly with chemotherapy (group A) have a higher rate of G1/2 fatigue compared to other patients (group B and C), (60% for group A, 30% for group B and 24% for group C, P= 0.01).

Table (7): Toxicities:

	Complication	**Group A [n (%)]**	**Group B [n (%)]**	**Group C [n (%)]**	***P* value [n (%)]**
Anemia	No G1,2 G3,4	6 (40) 7 (46.7) 2 (13.3)	4 (30.8) 9 (69.2) 0 (0.0)	91 (62.3) 49 (33.6) 6 (4.1)	0.089
Neutropenia	No G1,2 G3,4	6 (40) 5 (33.3) 4 (26.7)	9 (69.2) 3 (23.1) 1 (7.7)	88 (60.3) 46 (31.5) 12 (8.2)	0.385
Thrombocytopenia	No G1,2 G3,4	9 (60) 5 (33.3) 1 (6.7)	6 (46.2) 7 (53.8) 0 (0.0)	130 (89) 12 (8.2) 4 (2.8)	0
Liver enzyme	No G1,2 G3,4	14 (93.3) 0 (0.0) 1 (6.7)	10 (76.9) 1 (7.7) 2 (15.4)	138 (94.5) 5 (3.4) 3 (2.1)	0.686
Bilirubin	No G1,2	14 (93.3) 1 (6.7)	12 (92.3) 1 (7.7)	139 (95.2) 7 (4.8)	0.864
Creat	No G1,2	11 (73.3) 4 (26.7)	13 (100) 0 (0.0)	144 (98.6) 2 (1.4)	0
Vomiting	No G1,2 G3,4	9 ((60) 6 (40) 0 (0.0)	11 (84.6) 2 (15.4) 0 (0.0)	113 (77.4) 33 (22.6) 0 (0.0)	0.107
Fatigue	No G1,2 G3,4	6 (40) 9 (60) 0 (0.0)	9 (69.2) 4 (30.8) 0 (0.0)	111 (76) 35 (24) 0 (0.0)	0.01
FN	No Yes	13 (86.7) 2 (13.3)	13 (100) 0 (0.0)	138 (94.5) 8 (5.5)	0.276

DISCUSSION

In this study, we investigated the effect of sofosbuvir/daclatasvir (a new interferon free DAAs combination used widely in Egypt in the recent few years for the eradication of chronic HCV infection) on the outcome of different types of lymphoid malignancies in patients with concurrent HCV infection and lymphoid malignancies and if the timing of administration of these drugs in relation to chemotherapy (either concomitant or sequential) would give different outcomes.

It is well-known that different types of antiviral drugs especially acyclovir is given frequently in association with chemotherapy as a prophylactic antiviral in patient who receive highly aggressive chemotherapy protocols especially those with acute leukemia and during BMT without serious side effects and the combination is well tolerated but as regards sofosbuvir/daclatasvir (a new antiviral combination recently used) the added toxicity of giving these drugs concomitantly with chemotherapy was not well known [23]. The dilemma of whether giving the anti HCV with or after chemotherapy is also studied. Theoretically, treatment with chemotherapy without any anti HCV treatment will affect patient immunity and would increase the viral load and affect the liver function [24] and this already happened in our study in 2 patients who developed marked G3/4 increase in liver enzymes while on chemotherapy and we had to stop chemotherapy which would affect lymphoma outcome, but upon start of DAAs (sofosbuvir/daclatasvir) liver enzymes normalized within 1 week and DAAs continued concomitantly with chemotherapy safely without added toxicity just mild increase in G1/G2 fatigue.

As shown in table (1), patients with HCV positive lymphoma had a higher rate of being diagnosed with stage 3-4 disease (86.7 % in group A , 69.2 % in group B compared to 50.7 % in group C), extra nodal presentation and hepatosplenic infiltration, a finding that was confirmed in many previous studies [10].

Until now, only 7 studies examined the effect of DAAs given concurrently with chemotherapy in patients with different types of lymphoid malignancies and HCV infection (table 8).

Table (8): DAAs therapy concomitant with chemotherapy in patients with lymphoid malignancies

Authors, Year	Study Design	N. Pts	Lymphoma Histology	DDAs Therapy	Chemotherapy N. (%)	Sustained Virologic Response	NHL Response N. (%)	Follow Up (Mos.)
Carrier *et al.*, 2015 [25]	Case series	5	MZL: 3 (60) DLBCL: 2 (40)	SOF-based regimen	Concomitant: 1 (20) After chemotherapy: 2 (40)	5 (100)	CR: 5 (100);	9-12
Alric *et al.*, 2016 [26]	Prospective cohort	10	MZL: 6 (60) DLBCL: 3 (30) Other: 1 (10)	SOF-based regimen	Concomitant: 9 (90)	9 (90)	CR: 9 (90) PR: 1 (10)	12
Ewers *et al.*, 2016 [27]	Case report	1	DLBCL	SOF-based regimen	Concomitant	1(100)	CR	NO
Persico *et al.*, 2018 [28]	Prospective cohort	20	DLBCL: 20 (100)	SOF-based regimen: 20 (100)	Concomitant: 20 (100)	20 (100)	CR: 19 (95) PD: 1 (5)	12
Occhipinti *et al.*, 2019 [29]	Case series	7	DLBCL: 7 (100)	SOF-based regimen: 7 (100)	Before DAA: 2 (29) Concomitant: 5 (71)	7 (100)	CR: 7 (95) PD: 1 (5)	12
Merli *et al.*, 2019 [30]	Retrospective cohor	47	DLBCL: 45 (96) FL: 2 (4)	SOF-based regimen: 47 (100)	Before DAA: 38 (81) Concomitant: 9 (19)	45 (96)	CR: 46 (98) PD: 1 (2)	33.6
Nesterova E *et al.*,2020 [31]	Retrospective comparative study	11	FL	SOF-based regimen: 11 (100)	Concomitant: 11 (100)	9 (82)	CR: 9 (82) PD: 2 (18)	32

MZL, marginal-zone lymphoma; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; SOF, sofosbuvir; CR, complete response; PR, partial response; SD, stable hematological disease; PD, progressive disease.

In this study 15 patients (6 patients with DLBCL, 3 with CLL/SLL, 1 with SMZL, 2 with FL, 1 with HL, 1 with MM and 1 with lymphoblastic lymphoma) received DAAs concomitant with chemotherapy (group A), 11 patients out of 15 patients (73.3 5%) achieved CR or PR with 1st line chemotherapy. All patients (100%) had a SVR at the end of the antiviral treatment. Also, 13 patients (4 with DLBCL, 3 patient with FL, 3 with CLL/SLL,1 with SMZL, 1 with MALT lymphoma and 1 with MCL) received DAAs after the end of chemotherapy (group B) 12/13 patients (92.3%) achieved CR & PR with 1st line chemotherapy , all patients (100%) had a SVR at the end of antiviral treatment.

DISCUSSION

The RR to 1st line chemotherapy in groups A and B was slightly lower than the previous results [25-31] but was not statistically different between the 2 groups or HCV negative lymphoid malignancies (group C 84.9 %) (P= 0.245), and as old studies showed lower response rate of HCV positive lymphoma compared to HCV negative lymphoma [10], so it's reasonable to say that DAAs plus chemotherapy given either concomitantly or after the end of chemotherapy improved the outcome of lymphoid malignancies (RR, DFS, OS) to be statistically non significantly different from HCV negative lymphoid malignancies compared to old literatures before the use of DAAs. The slightly higher response rate in other studies [25-31] in which sofosbuvir-based DAAs was given concomitant with or after chemotherapy compared to our study may be explained by the higher rate of low grade lymphoma in some of these studies while in our study 53% in group A diagnosed with aggressive and highly aggressive lymphoma (1 case with lymphoblastic lymphoma) and also 30.8% in group B diagnosed with DLBCL (aggressive lymphoma). Also, these studies [25-31] combined patients who receive DAAs either concomitantly or after chemotherapy, while in our study the combined CR & PR in both group A and B was 82.14%. Another explanation may be the different HCV genotypes prevalent in western countries than in Egypt, which would affect the treatment results. Also, in these studies different DAAs combinations are given according to different genotypes while in our study only one DAAs combination was given (sofosbuvir/daclatasvir).

In our study, 2 patients from group A died during treatment, 1 with febrile neutropenia after the 1st cycle chemotherapy (65 years old male patient with highly aggressive lymphoma) and the other patient died of uncontrolled lymphoid malignancy (disease progression). In both cases, the cause of death was unrelated to DAAs, no patient died during the period of chemotherapy or DAAs treatment in group B. The combination of chemotherapy and DAAs (sofosbuvir and daclatasvir) was well tolerated with no serious acute side effects, which is the same in the previous studies in which DAAs was given concomitantly with chemotherapy [25-31]. Only slight increase in G1/2 fatigue (P= 0.010), G1/2 increase in the serum creatinine (P= 0.000) and G1/2, G3/4 thrombocytopenia (P= 0.000). Only 2 patients had febrile neutropenia (FN) (13.3 %, P= 0.276) which was not statistically different from the other groups and the 13 living patients completed the planned chemotherapy and antiviral drugs. More importantly, there was no increase in liver toxicity (only 1 patient had G1/2 increase in total bilirubin and 1 patient had G3/4 increase in liver enzymes), no added toxicity was observed in group B except a slight increase in G1/2 thrombocytopenia compared to patients with HCV negative lymphoid malignancies (group C).

This study was the first prospective comparative study in Upper Egypt comparing DFS and OS between patients with HCV positive and HCV negative lymphoid malignancies and the first prospective randomized study in Upper Egypt to evaluate if the timing of DAAs given either concomitant or after the end of chemotherapy would give different lymphoid malignancy outcomes.

During a median follow up period of 33.5 months, the lymphoid malignancy outcome (median DFS and OS) was highly significant for group B (P= 0.000), which means that the highest DFS and OS was for patients with lymphoid malignancies who were HCV positive and received DAAs combination after the end of chemotherapy and lymphoma resolution. This observation might be explained by the higher prevalence of low grade lymphoid malignancy in this group (69.2%), longer median follow up period or the claim that DAAs might have a role in the affection of cell mediated immunity [32-34] but this explanation can't be confirmed in this study and actually even in group A (patients who received DAAs concomitantly with chemotherapy) the lymphoid malignancy outcome (RR, DFS and OS) was not statistically different from group C (patients who have lymphoid malignancies and HCV negative), which is a marked improvement in the outcome compared to the old literatures, which showed lower RR , DFS and OS of the HCV positive lymphoid malignancies in the period before DAAs approval. **Nesterova *et al*.** [31] found a non-significant difference in the outcome of 11 patients with FL and HCV infection who received sofosbuvir-based combination concomitant with immune-chemotherapy compared to patients with FL without HCV infection, which is the same in our study. The old studies demonstrated that the HCV-positive vs HCV-negative FL patients had significantly worse outcome (3-year OS 40% vs 90%, $P < .0001$ and relapse-free survival 30% vs 60%, $P = .006$) [35]. The only comparative study [31] conducted to

compare the outcome of HCV positive lymphoid malignancies treated using DAAs concomitantly with chemotherapy versus HCV negative lymphoid malignancies had the same results as our study. Other non-comparative studies mentioned an excellent outcome using DAAs either concomitantly or after the end of chemotherapy in HCV positive lymphoid malignancies without adding serious toxicity [25-30].

It is observed in this study that the HCV PCR level markedly increased at the end of chemotherapy if anti HCV treatment delayed after the end of chemotherapy (group B) compared to group A but clinical liver toxicity was only observed in 2 patients , this increase in HCV PCR level didn't affect HCV outcome as all patient had SVR.

CONCLUSION

DAAs mainly sofosbuvir/daclatasvir improved the outcome of different types of lymphoid malignancies (RR, DFS, OS) in patients with HCV infection associated with lymphoid malignancies when given either concomitant or after the end of chemotherapy to be non-significantly different from HCV negative lymphoid malignancies. The DFS and OS were markedly improved even better than HCV negative lymphoid malignancies when DAAs was given after the end of chemotherapy.

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