Nutritional assessment of patients with chronic hepatitis c treated with Sofosbuvir combined with Daclatasvir.

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Abstract: *Malnutrition is common in patients with chronic hepatitis C. Well nourished patients have a more successful outcome than others, as they tolerate treatment adverse effects, require less disruption of treatment, or dose reductions, therefore the study aimed at assessing the nutritional status of patients with chronic hepatitis C treated with Sofosbuvir combined with Daclatasvir. Research design: A descriptive exploratory study. Sample: A convenience sample of 102 adult patients. The study was conducted at Sovaldi clinics at the National Hepatology and Tropical Research Institute from January to June 2016. Patients were assessed before, one month after, and during third month of the medical regimen using socio-demographic data tool, medical related data tool and the 7-point Subjective Global Assessment scale (SGA). Results: There were statistically significant differences of the mean BMI and overall score of SGA throughout the three times of assessment. According to SGA, study subjects lying in category A were 83.3%, 63.7% and 75.5% in the 1st, 2nd, and 3rd assessment respectively, and the rest lying in category B. Conclusion: Nutritional assessment is imperative for patients with chronic hepatitis C treated with combination therapy for better clinical outcome.*
Key words: *chronic hepatitis C, malnutrition, nutritional assessment, Subjective Global Assessment.*

I. Introduction

Hepatitis C is the most common blood borne infection worldwide; it is caused by the hepatitis C virus (HCV) which is single-stranded Ribonucleic Acid (RNA) virus that attacks the liver causing either acute or chronic inflammation of the liver which may lead to diminished of all liver functions including the metabolic function and/orfinally liver failure. Unfortunately, about 55-85% of the cases will develop chronic hepatitis C (CHC) infection [1].

Treatment for hepatitis C infection has been evolving at a rapid rate. In late 2013 the U.S Food and Drug Administration (FDA) approved Sofosbuvir (Sovaldi) which is direct – acting antiviral (DAA) drug that blocks a specific protein needed by the HCV to replicate [2]. Sovaldi has many advantages which include an oral single daily dose, shortened treatment duration, limited potential for drug interactions, potent antiviral with excellent tolerability and pan-genotypic with a high barrier to resistance. Therefore, Sovaldi has become the cornerstone antiviral agent for treatment of CHC [3,4].

Actually, Sovaldi is to be used as a component of a combination antiviral treatment regimen for chronic HCV infection. Recent study revealed that because of the high efficacy and improved tolerability, Sofosbuvir combined with Daclatasvir (Sov+Dac) is an important treatment for hepatitis C [5]. Sofosbuvir combined with Daclatasvir (Sov+Dac) is currently the most effective pangenotypic combination treatment [6], and successfully the costs of the generic production of Sov+Dac, are rapidly decreasing. Despite, the safety of the new combination therapy compared with the classic treatment regimen, there are commonly reported adverse effects associated with Sovaldi which include headache, fatigue, and nausea that may lead to reduced oral intake. Therefore, the nutritional status of patients treated with combination therapy may be affected [7].

The liver is an important regulator of metabolism, synthesis, storage, and absorption of nutrients. Patients with CHC frequently become malnourished; they have an inability to meet their nutritional requirements [8]. The pathogenesis of malnutrition in chronic liver disease is multi-factorial and includes reduced oral intake due to anorexia, nausea, dietary restrictions, altered nutrient biosynthesis, malabsorption, abnormalities of carbohydrate, lipid and protein metabolism and a hypermetabolic state [9].

Poor nutritional status contributes to fatigue, anemia, and infection, all of which impair successful HCV treatment, as well nourished patients are more likely to tolerate treatment' adverse effects, require less disruption of treatment, or dose reductions, and, consequently, have a more successful outcome than those who are nutritionally depleted [7]. Therefore, nurses as a member of multidisciplinary team have a major role in accurately assessing the nutritional status, early detecting and treating malnutrition of all patients with HCV especially who are treated with Sov+ Dac to optimize their nutritional status and prevent complications, and consequently improve the treatment response.

1.1. Significance of the study

World Health Organization reports that hepatitis C virus (HCV) infection is considering a major public health problem. The highest burden of HCV infection in the world is in Egypt, with a prevalence of 14.7% among individuals aged 15–59 years carrying the infection compared to a worldwide 3% prevalence. The widespread of chronic HCV infection in Egypt is thought to be largely due to needle re-use during mass-treatment programs for schistosomiasis in earlier decades (during the late 1950s through the early 1980s) [10]. Unfortunately, transmission continues to occur as nosocomial transmission has been and probably still is the most common route for new infections [11]. The virus can be spread unknowingly, as many people are not aware they are infected with the virus, consequently, more than 500, 000 Egyptians getting infected annually [12].

The prevalence of malnutrition in patients with CHC ranges from 65 to 100% depending upon the methods used for nutritional assessment and the severity of liver disease [13]. Different studies have shown that early detection and treatment of malnutrition is imperative to improve patient outcomes as well as to prevent the complications of chronic liver disease and to establish effective nutritional education programs for these patients [14]. Once, Sovaldi is a new promising drug started to be used in Egypt in the second half of 2014 for treatment of HCV infected population and literature review suggested that there are minimal adverse effects of the combination therapy for treatment of CHC infection that may affect the dietary intake. Beside, the investigator's observation in Sovaldi clinics at the National Hepatology and Tropical Research Institute (NHTMRI) that many patients were asking about the dietary recommendation during the treatment for better treatment response as they were having hope to cure completely from HCV infection. Reviewing literature revealed that there was an informational gap in the area of nutrition for those who are treated with the new promising agents despite its important effect on the treatment response.

II. Subjects and Methods

The current study aimed to assess the nutritional status of patients with chronic hepatitis C treated with Sofosbuvir combined with Daclatasvir. With this in mind, the following research question was postulated:

Q1- What is the nutritional status of patients with chronic hepatitis C treated with Sofosbuvir combined with Daclatasvir?

2.1. Design

A descriptive/exploratory research design was utilized in the current study.

2.2. Setting

This study was conducted at Sovaldi outpatient clinics at the National Hepatology and Tropical Research Institute (NHTMRI) in Cairo, affiliated to the Egyptian Ministry of Health.

2.3. Sample

A convenience sample of 102 adult male and female patients, their age ranged from 30 to less than 60 years old as HCV is common among individuals aged 30 years and above as reported by WHO, having prescription to start the treatment regimen that includes Sovaldi combined with Daclatasvir (dual therapy) was recruited to participate in the study over a 3 months period from January 2016 to March 2016.

2.4. Data collection tools:

Data was collected using the following tools: -

2.4.1. Tool (1): Socio-demographic data tool covering questions related to age, gender, level of education, occupation, nature of the exerted effort during work, marital status, income, etc., it was developed by the researcher.

2.4.2. Tool (2): Medical related data tool which include questions related to disease and medical history.

2.4.3. Tool (3): The 7-point Subjective Global Assessment (SGA) scale: is a valid and reliable nutritional assessment tool that is developed in the mid-1980's by Allan S. Detsky et al., [15], and it is a widely used tool to determine an individual's current nutritional status and the risk for malnutrition also this tool is sensitive to changes in nutritional status over a time period. The 7-point SGA includes two major

categories: the history and physical examination. Overall 7- point SGA score was determined based on a combined subjective and objective. An overall score is categorized into 3 levels; category A (very mild malnutrition risk to well-nourished score from 6 to 7), category B (mild to-moderate malnutrition score from 3 to 5), and category C (severe malnutrition score from 1 to 2) [16].

2.5. Pilot study

A pilot study was conducted on 10 patients (about 10% of the study sample); to ensure objectivity, clarity and feasibility of the study tool and to determine the time required filling the different data collection tools. There are no modifications needed. The pilot study was included in the actual research subject.

2.6. Ethical considerations

Primary approval obtained from the Research Ethics Committee of Faculty of Nursing. An ethical approval obtained from research ethics committee of NHTMRI in addition to obtaining official permission from institute administrators to conduct the study. Each patient was informed about the nature, purpose and importance of the study and its importance. Informed written consent was obtained from the subjects. Anonymity and confidentiality were assured through coding the data; every participant had the right to withdraw from the study at any time without any effect on the provided treatment. Subjects were assured that this data will not be reused in another research without permission. At the end of data collection final approval was obtained from the faculty ethical committee.

2.7. Procedure for data collection:

Data collection was conducted through implementing the following three phases:

2.7.1. Preparatory phase

Once obtaining the formal approval, the study participants who met the selection criteria were recruited and interviewed individually to explain the nature and purpose of the current study. The interview was conducted in the waiting area of Sovaldi clinics. Then the researchers obtained a written consent from patients who were willing to participate in the study.

2.7.2. Implementation phase

Data collection tools were filled out by the researchers in the waiting area of Sovaldi clinics in the NHTMRI or inside the Sovaldi clinics throughout the period from January 2016 to June 2016 (1st assessment ended at March 2016 as recruitment of new participant was over three months period, however the end of the study was in June 2016 as each participant was assessed three times). The first or the initial assessment was conducted before starting the medical regimen, second assessment was conducted one month after initial assessment and the third assessment was carried out during the 3rd month from starting the first dose of the treatment regimen. Data collection was fulfilled according to the patient response to structured interview.

2.7.3. Data analysis phase

The collected data was scored, tabulated and analyzed by personal computer using Statistical Package for The Social Science (SPSS) program version 20. Descriptive as well as inferential statistics was utilized to analyze data pertinent to the study. Level of significance will be adopted at $p < 0.05$.

III. Results

Results of the study are presented in two major sections; the first section is descriptive statistics that included the description of the personal and medical background information through two parts; the first part is devoted to describe the socio-demographic data as age, gender, residence, educational level, employment status and income. The second part represented medical related data such as past history of CHC, presence of comorbidities, and family history. The second section is inferential statistics that presents results related to nutritional parameters of the study (BMI and overall score of SGA) to answer the research question.

Table (1): Illustrating that the study subjects consisted of 102 adult patients with age ranged from 30 years to less than 60 years with a mean age of 44.25 ± 8.88. As regard to gender 56.9% were females. In relation to, marital status, 68.6% of them were married while 13.7% were widowed. Additionally, regarding place of residence 54.9% of them were residing in rural region and the rest were residing in urban region. As regard to occupation 66.7% of them were not working as 52% were housewives and 14.7% stopped working because of inability to make effort while the rest of the study subjects (33.3%) were doing free work. In relation to nature of the exerted effort during work, 42.2% of them were performing a simple muscular effort, 33.3% were performing a severe muscular effort and 24.5% did not make any effort. In relation to the educational level,

37.3% of them had completed secondary schools, while 28.4% of them could not read or write 22.5% had finished elementary school, 6.9% had finished bachelor's degree and 4.9% were able to read and write. Finally, this table showed that 71.6% of the study subjects' income was not enough.

Table (1): Frequency and percentage distribution of socio-demographic data among the study subjects (n= 102).

Variable	N	%
Age		
30-	41	40.2
>40-	22	21.6
>50-<60	39	38.2
X±SD 44.25 ± 8.88		
Gender		
Male	44	43.1
Female	58	56.9
Marital status		
Single	11	10.8
Married	70	68.6
Divorced	7	6.9
Widowed	14	13.7
Place of residence		
Urban	46	45.1
Rural	56	54.9
Occupation		
Working	34	33.3
Not working	68	66.7
House wife	53	52.0
Stop working	15	14.7
Nature of the exerted effort		
No muscular effort	25	24.5
Mild muscular effort	43	42.2
A severe muscular effort	34	33.3
Level of education		
Cannot read or write	29	28.4
Can read and write	5	4.9
Elementary school	23	22.5
Secondary school	38	37.3
Bachelor's degree	7	6.9
Income		
Enough	29	28.4
Not enough	73	71.6

Table (2) showed that 42.2% of the study sample had HCV infection for one year to five years and 40.2% of them have HCV infection for more than five years but 17.6% had HCV infection for six months and less than one year. Regarding presence of co morbidities, 53.9% of the study subjects had no co-morbidities and the rest had co-morbidities. However, 38.3% had diabetes mellitus only, 27.7% had hypertension only, while 8.5% had diabetes mellitus and hypertension, 14.9% had a cardiac disorder and the rest 4.3% had other disorders. The table also showed that 55.9% of the study sample had no family history of chronic HCV and 44.1% had a positive family history. All of the study subjects received Sovaldi 400mg combined with Daclatsvir as a treatment protocol.

Table (2): Frequency and percentage distribution of medical related data among the study subjects (n= 102).

Variable	N	%
Duration of illness		
6 months –	18	17.6
one year –	43	42.2
≥ 5 years	41	40.2
Co morbidities		
No	55	53.9
Yes	47	46.1
Hypertension	13	27.7
Diabetes mellitus	18	38.3
Cardiac disorders	7	14.9
Renal disorders	3	6.4
Combined (DM+ HTN)	4	8.5
Others	2	4.3
Family history		
No	57	55.9
Yes	45	44.1
Aunt or / and uncle	16	15.7
Mother or / and father	17	16.7
Sister or / and brother	12	11.8

Table (3) showed that the percentage of the BMI during the 1st assessment 39.2% of the study subjects were obese followed by 31.4% pre-obese, and 29.4% normal BMI. But during the 2nd assessment 38.2%, were obese followed by 32.4% normal BMI and 29.4% were pre-obese .In the 3rd assessment 39.2% were obese, 29.4% normal BMI, also 29.4% were pre-obese and the rest 2.0% were underweight. There were a statistically significance difference in BMI ($p = 0.00$) at F= 11.61 throughout the three times of assessment using repeated measures ANOVA with a Greenhouse-Geisser correction.

As regard to the overall score of SGA, the means of the overall score of SGA during 1st, 2nd and 3rd assessment were as the following 6.10±.86, 5.81±.94, and 5.96±.88 respectively. The percentage of the study subjects lying in category A (very mild risk to well-nourished SGA score 6-7) followed by category B (mild to moderate malnutrition SGA score 3-5) were as the following; 83.3% and 16.7% in the 1st assessment, 63.3% and 36.3% in the 2nd assessment and 75.5% and 24.5% in the 3rd assessment. Also, this table presented that there was a statistical significant difference in the mean overall score of SGA (($p = 0.00$) at F = 14.26 throughout the three times of assessment.

Table (3): Comparison of parameters of nutritional status (BMI and overall score of SGA) throughout the three times of assessment among the study subjects (n= 102).

Variable	1st Assess.	2nd Assess.	3rd Assess.	F	Sig.
Body mass index					
X± SD	28.59±5.04	28.21±5.02	28.17±5.17		
<18.5 kg/m²	0 (0)	0 (0)	2 (2.0)		
18.5-24.9 kg/m²	30 (29.4)	33 (32.4)	30 (29.4)	11.61	.000*
25-29.9 kg/m²	32 (31.4)	30 (29.4)	30 (29.4)		
≥30.0 kg/m²	40 (39.2)	39 (38.2)	40 (39.2)		
Overall SGA score					
X ± SD	6.10±.86	5.81±.94	5.96±.88		
(SGA score 1-2) N (%)	0 (0%)	0 (0%)	0 (0%)	14.26	.000*
SGA score 3-5) N (%)	17 (16.7)	37 (36.3)	25 (24.5)		
SGA score 6-7) N (%)	8 (83.3)	65 (63.7)	77 (75.5)		

* The mean difference is significant at p≤ 0.05 probability level.

IV. Discussion

Based on the current study a total of 102 patients with CHC treated with combination therapy were recruited from the outpatient Sovaldi clinics affiliated to NHTMRI. In relation to study subjects' age it was

revealed that their age ranged from 30 years to less than 60 years with a mean of 44.25 ± 8.88. This finding was affected by the inclusion criteria of the study subjects that included patients whose age was from 30 to ≤ 60 years. These findings were supported by WHO as chronic hepatitis C affects people at any age but it is common among individuals aged 30 years and above. Regarding gender it was found that more than half of the study subjects were females. However, this finding was in disagreement with [17] in a nationwide survey about HCV burden of infection in Egypt who found that in subjects older than 30 years of age, HCV was higher in males compared to females (17.4% versus 12.2%, respectively, P < 0.001) who reported that the difference might be partly related to the higher exposure of males to the past anti-schistosomiasis treatment campaign.

In relation to place of residence approximately over half of the study subjects were living in rural area. This might be related to the fact that hepatitis C is prevalent in rural areas. This finding is in agreement with [18] in their systematic review about the epidemiology of hepatitis C virus in Egypt which revealed that prevalence of chronic HCV infection is higher in people from rural areas than those from urban areas, it might be because more poverty and decrease level of education were found more in rural compared to urban. Regarding occupation, less than two thirds of the study subjects were not working as more than half of the patients were housewives and less than one fifth stopped working as a result of inability to make effort, one third of the patients were doing free work; these findings of the study were in agreement with [19] in their study which revealed that 53.4% of the study subjects were housewives, whereas 39% had stopped working because of their inability to work as a result of liver disease.

Regarding level of education more than one third of the study subjects completed secondary school, followed by less than one third of them couldn't read and write, less than one fourth of them were educated till elementary school and minority of them could read and write; these findings were in agreement with [20] who announced that about 29.8% of Egyptians above age 15 years were illiterate and 39.9% were females. On the same line, these findings were in agreement with [17] who stated that lack of education was also strongly associated with HCV infection.

Regarding BMI as an indicator to the nutritional status, the highest of the study subjects were obese. These findings were in agreement with [21] who stated that in recent years, the rate of obesity in cirrhotic patients rose to approximately 30%. Also comparison of means between 1st, 2nd and 3rd assessment regarding BMI in the current study showed that there was a statistically significance difference. This might be because of the adverse effects of the combination therapy containing Sovaldi and Daclatasvir (Sov+Dac) reported by the study subjects including fatigue, nausea, headache and rarely constipation that lead to reduced oral intake, these findings were in agreement with [5] in their study about safety and tolerability of direct-acting anti-viral agents in the new era of hepatitis C therapy which revealed that Sofosbuvir was associated with no clinically significant adverse effects beyond headache, fatigue, nausea, insomnia, pruritus, anemia and dizziness. The most common adverse effects reported were headache, fatigue, nausea and joint pain.

Regarding the overall score of the 7-point SGA, approximately three fourth of the study subjects had score 6-7 and were classified as well nourished while the rest had score 3-5 and were classified as mild to moderate malnutrition throughout the three times of assessment. Study results also revealed that there was a statistically significance difference in means of the overall SGA. These results might be because of the adverse effects of the combination therapy (Sov+ Dac) as mentioned before which included fatigue, loss of appetite, abdominal pain, and nausea that were reported more commonly and frequently after one month from starting the treatment protocol than after that; these results were in agreement with [6,22] who reported that treatment with a combination therapy (Sov+Dac) is well tolerated with minimal adverse effects that may affect the dietary intake and subsequently affect the nutritional status.

V. Conclusion

Based on results of the current study, it can be concluded that there was a statistically significant difference in total means of BMI and total score of the SGA as indicators to the nutritional status therefore it is imperative to assess the nutritional status of patients with chronic hepatitis C treated with combination therapy for better clinical outcome.

VI. Nursing implications and recommendations

1) Multidisciplinary team should be collaborated in nutritional management of patients with CHC treated with Sofosbuvir combined with Dacalatsvir to prevent and manage complications of malnutrition.

2) Updating knowledge of nurses who are working in outpatient clinics at the NHTMRI through attending in services training program, seminar, workshop and scientific conference regarding the importance of nutritional management and early signs of malnutrition while dealing with these patients.

3) Establish effective nutritional education programs for patients with CHC treated with Sofosbuvir combined with Dacalatsvir and providing them with written booklet about the suggested nutritional guidelines before starting the treatment regimen.

4) Replication of the study using a larger probability sample acquired from different geographical areas.

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REFERENCES

[1] The World Health Organization. (2014). available @ http://www.who.int/csr/disease/hepatitis/whocdscsrlyo2003/en/#.VLDIy7TcvtI.google. Accessed at January 2015.

[2] Gaetano, J. N. (2014). Benefit–risk assessment of new and emerging treatments for hepatitis C: focus on Simeprevir and Sofosbuvir. Drug, Healthcare and Patient Safety, Vol. 31(6), PP. 37-45.

[3] Cholongitas, E., & Papatheodoridis, G. V. (2014). Sofosbuvir: A novel oral agent for chronic hepatitis C. Annals of Gastroenterology: Quarterly Publication of the Hellenic Society of Gastroenterology, Vol. 27(4), PP. 331-337.

[4] Bhatia, H. K., Singh, H., Grewal, N., & Natt, N. K. (2014). Sofosbuvir: A novel treatment option for chronic hepatitis C infection. Journal of pharmacology and pharmacotherapeutics, Vol. 5(4), PP. 278.

[5] Banerjee, D., & Reddy, K. R. (2016). Review article: safety and tolerability of direct acting antiviral agents in the new era of hepatitis C therapy. Alimentary pharmacology & therapeutics, 43(6), 674-696.

[6] Hill, A., Simmons, B., Gotham, D., & Fortunak, J. (2016). Rapid reductions in prices for generic sofosbuvir and daclatasvir to treat hepatitis C. Journal of Virus Eradication, 2(1), 28.

[7] Paterson, J. C., Miller, M. H., & Dillon, J. F. (2014). Update on the treatment of hepatitis C genotypes 2–6. Current Opinion in Infectious Diseases, Vol. 27(6), PP.540-544.

[8] Cheung, K., Lee, S. S., & Raman, M. (2012). Prevalence and mechanisms of malnutrition in patients with advanced liver disease, and nutrition management strategies. Clinical Gastroenterology and Hepatology, 10(2), 117-125.

[9] Juakiem, W., Torres, D. M., & Harrison, S. A. (2014). Nutrition in cirrhosis and chronic liver disease. Clinics in liver disease, 18(1), 179-190.

[10] The World Health Organization. (2014). available @ https://www.google.com.eg/search?q=WHO+2014+HEPATITIS+C&oq=WHO+2014+HEPATITIS+C&aqs=chrome..69i57j0.24896j0j8&sourceid=chrome&ie=UTF-8.

[11] Waked, I., Doss, W., El-Sayed, M. H., Estes, C., Razavi, H., Shiha, G., & Esmat, G. (2014). The current and future disease burden of chronic hepatitis C virus infection in Egypt. Arab J Gastroenterol, 15(2), 45-52.

[12] Breban, R., Doss, W., Esmat, G., Elsayed, M., Hellard, M., Ayscue, P., & Mohamed, M. K. (2013). Towards realistic estimates of HCV incidence in Egypt. Journal of viral hepatitis, 20(4), 294-296.

[13] Bémeur, C., & Butterworth, R. F. (2015). Reprint of: Nutrition in the Management of Cirrhosis and its Neurological Complications. Journal of clinical and experimental hepatology, 5, S131-S140.

[14] Shiraki, M., Nishiguchi, S., Saito, M., Fukuzawa, Y., Mizuta, T., Kaibori, M., & Moriwaki, H. (2013). Nutritional status and quality of life in current patients with liver cirrhosis as assessed in 2007–2011. Hepatology Research, 43(2), 106-112.

[15] Detsky, A. S., Baker, J. P., Johnston, N., Whittaker, S., Mendelson, R. A., & Jeejeebhoy, K. N. (1987). What is subjective global assessment of nutritional status?. Journal of Parenteral and Enteral Nutrition, Vol. 11(1), PP. 8-13.

[16] Lim, S. L., Lin, X. H., & Daniels, L. (2015). Seven-point subjective global assessment is more time sensitive than conventional subjective global assessment in detecting nutrition changes. Journal of Parenteral and Enteral Nutrition.

[17] Guerra, J., Garenne, M., Mohamed, M. K., & Fontanet, A. (2012). HCV burden of infection in Egypt: results from a nationwide survey. Journal of viral hepatitis, 19(8), 560-567.

[18] Mohamoud, Y. A., Mumtaz, G. R., Riome, S., Miller, D., & Abu-Raddad, L. J. (2013). The epidemiology of hepatitis C virus in Egypt: a systematic review and data synthesis. BMC infectious diseases, 13(1), 288.

[19] Youssef, N. F., El Kassas, M., Farag, A., & Shepherd, A. (2017). Health-related quality of Life in patients with chronic hepatitis C receiving Sofosbuvir-based treatment, with and without Interferon: a prospective observational study in Egypt. BMC gastroenterology, 17(1), 18.

[20] The Egyptian Central Agency for Public Mobilization. (2013). available @ https://www.google.com.eg/search?q=The+Egyptian+Central+Agency+for+Public+Mobilization+and+Statistics+CAMPAS+(2013)&oq=The+Egyptian+Central+Agency+for+Public+Mobilization+and+Statistics+CAMPAS+(2013)&aqs=chrome..69i57.2368j0j8&sourceid=chrome&ie=UTF-8.

[21] Shiraki, M., Nishiguchi, S., Saito, M., Fukuzawa, Y., Mizuta, T., Kaibori, M., & Moriwaki, H. (2013). Nutritional status and quality of life in current patients with liver cirrhosis as assessed in 2007–2011. Hepatology Research, 43(2), 106-112.

[22] Focaccia, R., Ferreira, R., & De Mello, P. S. M. (2016). Management of Hepatitis C Infection with Direct Action Antiviral Drugs (DAA). Arch Hepat Res, 1(1), 009-017.