ejpmr, 2021,8(4), 462-468

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

SUCCESSFUL AYURVEDIC MANAGEMENT OF END STAGE LIVER DISEASE PREVENTING LIVER TRANSPLANT-A CASE STUDY

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Article Received on 29/01/2021 **Article Revised on 19/02/2021** **Article Accepted on 09/03/2021**

ABSTRACT

Introduction:- Liver Cirrhosis is a chronic progressive liver disease. Portal hypertension and Ascites indicate progress of Chronic liver disease to End Stage Liver Disease (ESLD). Once ESLD is developed the damage is said to be irreversible and then there is no remedy other than Liver transplant to save life. One year mortality in cases of Liver cirrhosis with Portal vein thrombosis, Portal hypertension, Refractory Ascites and SBP is high up to 90%. **Case study:** This 46 year old male patient with Chronic Liver Disease with portal vein thrombosis, Portal hypertension with Ascites, Hepato-Renal syndrome and severe sarcopenia was treated by Modern line of treatment for several months but liver damage remained progressive. Large Volume Paracentesis of Ascitic fluid was done several times and later he developed refractory Ascites. Spontaneous Bacterial Peritonitis developed two times during modern line of treatment, which confirmed that it was not adequately treated.

Patient was listed for liver transplant but the cost of the surgery was beyond the financial capacity of the patient. The case was referred to the author for further management. Case was treated with Ayurvedic line of treatment and within two months there was marked improvement in his clinical condition. His Refractory ascites and SBP was totally disappeared. The case is still maintained on Ayurvedic treatment for last 15 months and a destined liver transplant was prevented, saving life, money and maintaining quality of life. **Conclusion:** Ayurved has strength and ability to treat End Stage Liver Disease, showing a distinct ray of hope to thousands of sufferers listed for liver transplantation.

KEYWORDS: Liver cirrhosis, End Stage Liver Disease, Portal Vein Thrombosis, Spontaneous Bacterial Peritonitis (SBH), Ayurvedic management, Jalodar.

INTRODUCTION

Liver is the vital organ for its important role in metabolic, detoxifying and immune functions. A continuing or relapsing hepatic disease with symptoms for more than 6 months may be termed as Chronic hepatic disease. Chronic Hepatic disease may occur due to infection due to Hepatotropic viruses viz. Hepatitis B, Hepatitis C, Combined Hepatitis B and Hepatitis D; Alcohol-related liver disease, Non-alcoholic steato-hepatitis (NASH), and other causes including Cryptogenic and Autoimmune type of hepatitis. Chronic hepatic failure is mostly due to cirrhosis.[1] It is estimated that around 10 lakh patients of liver cirrhosis are newly diagnosed every year in India. Liver disease is the tenth most common cause of death in India as per the World Health Organization. Liver disease related mortality in India is reported to be 22/100,000 population. Due to Liver cirrhosis, 2.4% deaths occurred globally (2017).[2] Liver cirrhosis per se is compensated or decompensated depending on the stage it was diagnosed. There has been significant increase reported in Age standardised prevalence rate of decompensated liver cirrhosis cases between 1990-2017.[2] Decompensated liver cirrhosis progresses to End Stage Liver Disease which is absolutely irreversible. Liver transplant is the only life saving remedy for the subjects who land in to End Stage Liver Disease or Liver Failure. Jain M et al reported Liver transplant waitlisted mortality at 1 year was 27.7%, and the waitlist mortality rate was 33.8 deaths/100 patient-years.[3]

Case study: This 46 year old male had H/o Anorexia, nausea, vomiting, Easy fatigability and abdominal distension almost 9 months back and was investigated in an outside hospital of Pune and later referred to one corporate hospital in Pune (India). He was diagnosed to be a case of Chronic Liver Disease with almost complete Portal vein thrombosis. Patient was admitted in one

corporate hospital in Pune from 10 March to 22 March 2019 for the C/o Pain in abdomen, fever, distension of abdomen and bilious vomiting since one month and was referred from one outside hospital with the diagnosis of **Chronic Liver disease with Portal vein thrombosis with severe sarcopenia**.

Investigations: TLC 22000/ccm; HAV, HEV, HCV, HbsAg, IgM negative. JAK2 mutation absent.

Triphasic CT scan of abdomen & Pelvis dated 11 Mar 2019:- "Multiple hypodense wedge shaped peripheral non enhancing areas are noted in the liver in segments II,III and VI, more likely of Acute infarcts. Filling defects are noted in entire main portal vein and its right, left branch and also in SMV suggestive of thrombosis, near complete luminal occluding in all these areas for extrahepatic main portal vein. Non visualisation of splenic vein is noted in its entire extent suggestive of old thrombosis. SMV measures 7.4 mm. Multiple tortuous Porto-systemic collaterals at periportal, perigastric, pericholecystic, pericholedochal, peri pancreatic and perimesentric locations".

Upper G.I. endoscopy done on 12 Mar 2019 showed Grade I x2 columns of oesophageal varices.

Color Doppler abdomen study dated 16.3.2019 revealed, "Portal vein thrombosis proximally and showed minimal patchy flow distally. Splenic vein is small and does not show any flow. Multiple collaterals seen in peri- Gall bladder, perisplenic regions.

USG abdomen dated 16 Mar 2019 showed, "Liver is enlarged in size, shows heterogeneous echogenecity. Portal vein does not show any flow. Gall bladder is collapsed and shows varices in its walls. Spleen is marginally enlarged in size measuring 12.3 cm. Moderate loculated ascites is seen with multiple septation. Largest pocket of about 400 cc seen in the pelvis. Basal non tappable bilateral pleural effusion is seen.

Impression

- **Diffuse fatty infiltration in liver**
- **Portal vein thrombosis likely**
- **Marginal Splenomegaly**
- **Moderate loculated ascites with multiple septations and minimal free fluid is noted**
- **Basal non tappable bilateral pleural effusion"**

Ascitic fluid examination:- Asctic fluid showed neutrophils-1164, RBC-2000 S/o Spontaneous Bacterial Peritonitis. Culture isolated E.coli ESBL. He was treated with Inj. Meropenam, Inj Tagocid, Inj. Piperacillin Tazobactum, Inj Albumin 20% 100 ml I/V and advised on discharge a course of Inj. Clexane 60 mg BD S/C, Tab Rifagut 550 mg BD, Tab Feronem Er 300 mg 1BD, Tab Udiliv 300 mg, Tab Optineuron 1 OD, Tab Lasilactone 50 mg at 7 AM, Inj Albumin 20% 100 ml I/V weekly for 15 days.

USG dated 18 Jul 2019 showed Diffuse fatty infiltration, moderate ascites and reported it as Liver parenchymal disease. Color Doppler study done on the same day demonstrated Portal vein thrombosis, partial recanalisation with portal cavernoma formation.

Due to modern line of treatment, his pain in abdomen reduced but distension in abdomen remained. Repeatedly Paracentesis of Ascitic fluid was done but of no avail. His Ascites remained as refractory. Refractory ascites is defined as ascites that does not recede or that recurs shortly after therapeutic Paracentesis, despite sodium restriction and diuretic treatment. The predicted survival rate is as low as 50% at 1 year.[4] He was again admitted in to the same corporate hospital from 30.10.2019 to 3.11.2019 for similar complaints. This time ascitic fluid tapping was done twice; Polymorphonuclear leukocyte (PMN) count of > 250 cells/mcL is diagnostic of SBP; ascitic fluid showed nucleated cells-4891, RBCs-3900, Protein-0.85, Sugar-74, this time SBP was more severe and same line of treatment was continued. He was advised for Liver transplant and was waitlisted. The quotation for the estimate for Liver transplant was of Rs 20 Lacs excluding cost of postoperative complications. Cost of anticipated complications after surgery mentioned was approximately Rs. 5 Lacs; further the cost of treating infection/ rejection was anticipated to be approximately Rs. 3 Lacs. Thus the total cost of Liver transplant surgery was to the tune of Rs 28 Lacs. The patient was from middle income group, a shop vendor, did not afford to raise the huge cost of the Liver transplant surgery. He was referred to the author by one of the friend of the patient in Nov 2019.

He presented with the complaints of abdominal distension, Loss of appetite, nausea, extreme weakness, Inability to walk without support, Dyspnoea on slightest exertion, Slurred speech & reduced urine output.
No H/o Alcoholism, smoking, drugs
No H/o Blood transfusion
No H/o Jaundice in the past
HBA, HBV, HCV, HEV, HIV negative, JAK2 negative

Personal history: Appetite poor, Constipated, Non alcoholic, Urine output- 400 ml/24 hours

Occupation: Shop vendor of readymade clothes in Pune.

On examination:- Patient Afebrile, Pulse 100/min, low volume/*Kshin and Vata-pradhan* Respiration-28/min, Pallor+, Sunken eyes, Dejected look, Digital clubbing +, Loss of muscle mass (Sarcopenia) ++ (Fig. No.6) Bilateral oedema over feet and legs ++ (Fig.No.4)

RS:-Air entry reduced at bases on both sides.
CVS-S_1, S_2 normal P/A- Liver 1 finger palpable, Spleen just palpable Ascites+++ (Fig No.1 and 2)

CNS- Conscious but not well oriented, Flapping tremors present. Deep reflexes elicited. Speech-Slurred, feeble voice. not enough strength to speak.

Table No. 1. Comparative Investigation chart of important indicators.*

Blood Test	15.3.2019	30.10.2019	17.12.2019	27.10.2020	28.2.2021
Bilirubin total mg/dL Direct	1.19 0.81	1.60 1.16	0.46 0.15	0.44 0.12	0.53 0.17
AST units/L	16	19	18	17	20
ALT units/L	28	21	25	12	22
Total Proteins g/dL Albumin	5.93 2.81	4.15 1.41	6.07 2.0	6.83 3.01	6.90 3.12
S.Creatinine mg/dL	0.93	3.2	2.75	0.68	0.66
Blood urea mg/dL	31.13	60	48	22.4	21.1
Hb g/dL	11.6	9.2	9.2	10.0	10.3
Prothrombin time Sec	14.96	18.20	14.90	15.40	14.08
TSH units/dL	10.1	10.6	9.64	5.84	5.5

*Last 3 reports are when patient was on Ayurvedic treatment.

Treatment

Treatment of this challenging case was based on the sound principles of Ayurved viz. Nidan-Parivarjan, Deepan, Pachan, Virechan, Shaman and Rasayan chikitsa (Apunarbhav-chikitsa).

Nidan-parivarjan:-Patient had habit of Atyambupan (Excessive drinking of water) including Usha-pan for number of years. He used to have fermented food-Idly-Wada /Dosa, *Sheet* food Ice-cream, curd, food preserved in refrigerator. He was advised to take warm water only when thirsty. *Ushapan, Nishapan Bhojanpoorva jalapan* was asked to avoid. *Abhishyandi* aahar as described above was asked to avoid. He was asked to consume freshly prepared light food; *Laghu/supachya aahar*.

Deepan and Pachan were accomplished by a course of *Erand-patra swaras* (freshly prepared juice from leaves of Ricinus communis) followed by Piper longum churna 700 mg daily on empty stomach for 5 days. Sitopaladi churna further boosted *Deepan* process and hepled in *Pachan* process. *Virechan/ Anulomn* was carried out by Avipatikar churna.

Shaman chikitsa was accomplished by Dashamool - Panchakoladi kashay, Phala-Trikadi Quath + Drakshadi Kadha/quath, Quath made from Maka/ Bhringaraj (Eclipta alba), Punarnava (Boerhaavia diffusa) and Palash (Butea monosperma), and Unani medicine named as Majun Dabidulward and Jawarish Jalinus (Hamdard) which is very effective in treating Ascites. Later Arjun was added to Maka+Punarnava+ Palash combination. Hingvastak churna along with Ghrita (medicated ghee) was prescribed for treating his constipation. Kumariasav was given to treat SBP infection and to correct Hepatic dysfunction. Kumari (Aloe vera) is known to be very useful in correcting liver fibrosis occurring in Liver cirrhosis.

Since Nov 2019 he is on Ayurvedic treatment. Patient responded very well to the Ayurvedic line of treatment and within 2 months his Ascites was completely disappeared (Fig 1, 2 and 3), oedema over feet disappeared (Fig. 4 and 5); Change in the sickly look to Normal look (Fig. 6 and 7). His appetite improved and bowel habits became regular. Urine output was increased to more than one litre per day. Now, he has enough strength to walk without support and doing routine work. This is the testimony of quality of life he is enjoying due to Ayurvedic line of treatment. Biochemically, first time his Serum Albumin level crossed 3 g/dL limit. Creatinine and Blood urea values became normal as kidney function restored. His condition is biochemically as well as clinically stable, without undergoing liver transplant surgery.

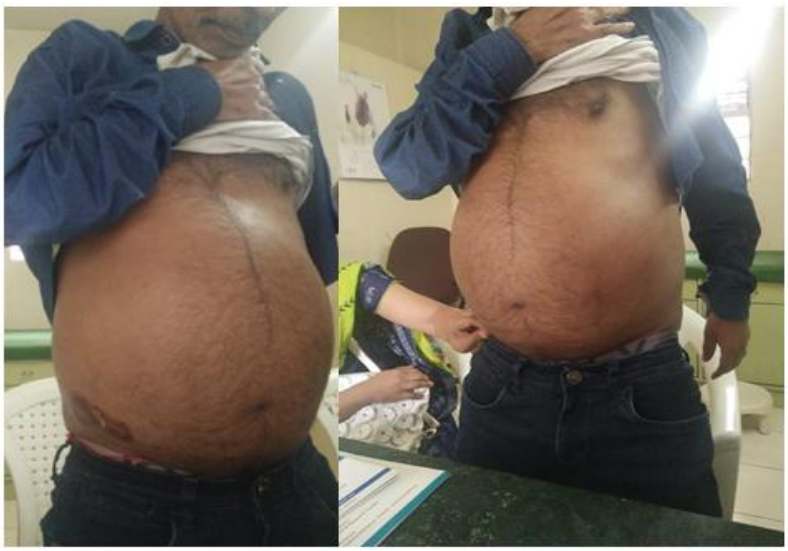

Fig. 1 & 2: Before treatment.

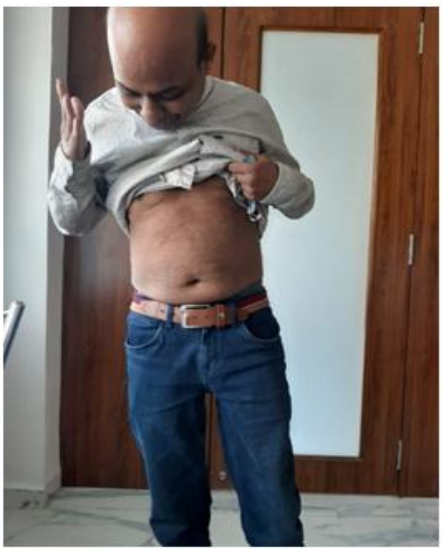

Fig. 3: Within 3 months of Ayu. Treatment.

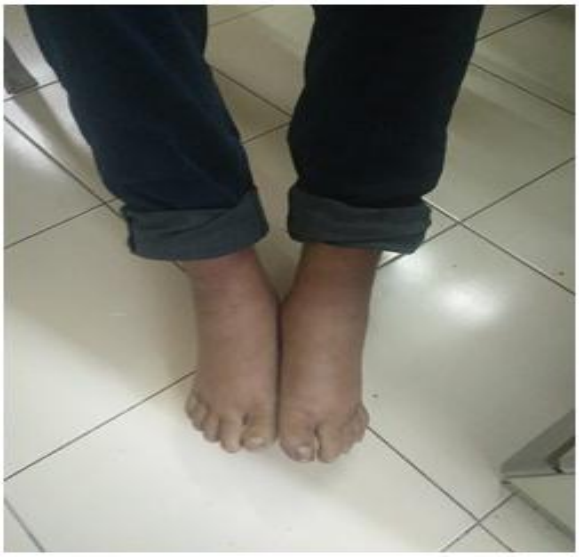

Figure. 4: Before. .

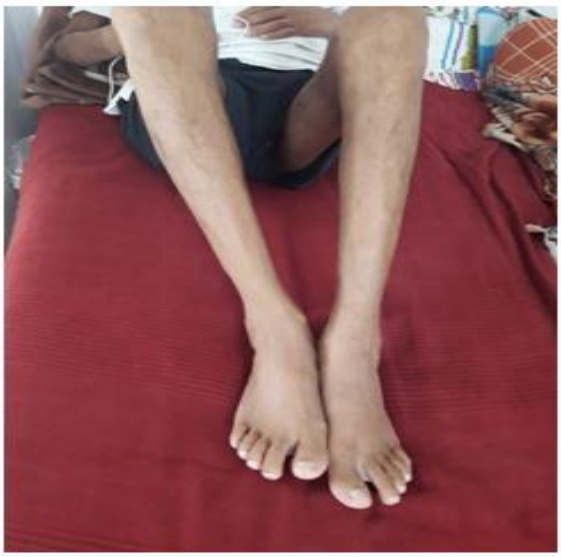

Fig. 5: Within 2 months of Ayu treatment.

Figure 6. Before.

Figure 7. After.

DISCUSSION

This patient of Chronic Liver disease was diagnosed and treated by modern line of treatment of Sodium restriction, diuretics, anticoagulants, antibiotics for treating SBP, preventive drugs for Hepatoencephalopathy and protein supplements for treating hypoproteinemia, for nealy 9 months. Patient had hypoalbuminemia and Albumin Globulin ratio was reversed. His prothrombin time was slightly elevated. Biochemical LFT were within normal limit. The cause of concern was his deteriorating health, refractory ascites and severe Sarcopenia. Sarcopenia in cirrhosis is seriously affected by changes in protein turnover, energy disposal, and hormonal and metabolic changes which lead to muscle depletion. Sarcopenia may be considered one of the most common and significant complication of liver cirrhosis, yet not commonly mentioned, and has been associated with adverse outcomes and increased morbidity and mortality.[5]

Liver receives 20% of its blood supply from Hepatic artery while its 80% nutrient blood supply comes from Portal vein arising from stomach, Intestines, pancreas and spleen.[6] In this case Patient had complete Portal Vein Thrombosis (PVT) but gradually collaterals were developed and portal cavernoma was formed. Reasons for the high incidence of PVT in advanced cirrhosis might be the simultaneous presence and effect of the three components of the Virchow's triad: venous stasis, endothelial injury, and hypercoagulopathy.[7] Causes of PVT in cirrhosis include reduced portal blood flow velocity, multiple congenital or acquired thrombophilic factors, inherited or acquired conditions, and derangement of liver architecture.[8]

Aikaterini Mantaka et al reported that PVT is a relatively frequent event in advanced cirrhosis with severe portal hypertension. PVT formation in cirrhosis is multifactorial. Increased intrahepatic vascular resistance in combination with reduced portal flow velocity are considered important risk factors for PVT in liver cirrhosis. Other possible factors are male sex, low platelet count, and advanced liver failure.[9] Bagheri et al reported the overall prevalence of PVT in Liver cirrhosis as 15.9%,[10] similarly E A Tsochatzis et al mentioned the same prevalence as 10-25%.[11] As per scale proposed by Yardel et al,[12] case was graded as Grade 3 with complete portal vein thrombosis and thrombosis of proximal superior mesenteric vein. A causative relationship between liver fibrosis and PVT in cirrhosis has been documented. According to this, micro-infarcts resulting from thrombosis of the hepatic and PV branches may cause ischemia and cell death that activates the hepatic stellate cells, which trans-differentiate into myofibroblasts and ultimately replace these areas with fibrous tissue, aggravating cirrhosis[13] D'Amico *et al* reported a more than threefold higher risk of failure to control active variceal bleeding in cirrhotic patients with PVT, irrespective of the use of endoscopic hemostasis or surgical shunting.[14] Subjects with advanced liver failure are not benefitted by TIPS (Transjugular Intrahepatic Porto Systemic shunt) and there are increased chances of Hepatic Encephalopathy in such cases. There are studies which indicate that though it reduces Ascites, it does not improve survival and is associated with significant mortality.[15] Probably, that was the reason; the treating physician did not use this option for treating refractory Ascites. SBP is the most common source of infection in liver cirrhosis. Mortality due to SBP ranges between 30% and 90% within the first year of diagnosis.[16] In the present case, patient had developed SBP twice during 9 months of Modern treatment, but could not be treated adequately by modern line of treatment, there were high chances of death; but patient survived only because of Ayurvedic line of treatment.

As per Ayurved, The cause of *Udar-rog* (Abdominal diseases) is due to *Prakupit*/ vitiated *vata* and *Mala-sanchay*. Charakacharya mentioned the Samprapti (etiology) of Udar-rog, in this verse:
Rudhwa Swedambuvahini Doshah Strotansi Sanchitah IPranagnyapanan Sandushya Janayantyudaram Nrunan II Charak Chikitsa sthan 13/19[17]

Sanchit (Accumulated) *Vata* and other doshas in *Udar-pradesh* (Abdomen) stop the circulation of *Swedavahi and Jalavahi Srotasa* which vitiates *Pranvayu, Jathargni and Apanvayu*, producing *Udar-rog*. Charakacharya nearly 3000 years back mentioned the lakshnas (symptoms) of Udar rog in this verse:
Kuksheradhamantopa Shophah Padkarasya cha I
Mandoagnih Shlakshnagandatwam Karshya Cha Udar lakshanam II
Charak Chikitsa sthan 13/20[17]

It means abdominal distension, pain in abdomen, *Shoph* (oedema) over feet and hands, *Mandagni* (Loss of appetite), sweatiness of scalp, *Krushata* (loss of muscle mass/ Sarcopenia) are the symptoms of *Udar-rog*.

As mentioned earlier most of these symptoms were present in this patient.

Samprapti:- Consumption of *Madhur, Guru, Sheet,* fermented, *Abhishyandi aahar, Ushna, Lawan, Kshar, Ruksha, Viruddha anna* leads to increase in *Kapha* formation causing *Jatharagnimandya* (Anorexia) and it is the cause of *Strotorodh* (Obstruction), that was noticed in the form of *Malasanchay (Sweda-Mala-Mutra)*, causing *Saam Rasa-Rakta dushti* resulting in to portal vein thrombosis, Splenic vein thrombosis and SMV thrombosis which badly affected the functioning of *Yakrut* and *Pleeha* which are the *Mool-sthan* of *Raktavah-srotas*. *Yakrut* secretes *Rankak pitta* which has important role in formation of *Rakta dhatu*. The color of *Rakta*/Blood and RBCs is due to *Rajak pitta*. In liver diseases formation of *Ranjak pitta* is deficient causing anemia. Once *dushti* /vitiation of *Rasa-Raktavah srotas* occurred that further *Poshan* (nourishment) of *Uttarottar*

srotasa/Dhatu in line/chronology, i.e. *Mauns, Meda, Asthi, Majja and Shukra dhatu* were badly affected. *Mauns dushti* was visible in the form of Sarcopenia, i.e. loss of muscle mass. Vitiation of *Meda dhatu* affected fatty tissue formation. Kidney is made of Sar-bhag of *Rakta and Meda* dhatu. Vitiation of *Rakta dhatu* affected *poshan of Meda dhatu* which is reflected in malfunctioning of Kidneys seen as Hepato-renal syndrome. Vitiation of *Asthi dhatu* caused decalcification of bones and Hypocalcemia. Slurred speech, flapping tremors point out towards vitiation of *Majja dhatu*. Vitiation of *Shukra dhatu* caused lack of energy, inability to move without support and dejected look. In Ayurved, Ascites is called as *Jalodar*. Various types of Udar-rog namely *Vataj, Pittaj, Kaphaj, Tridoshaj and Jalodar* are termed as *Uttarottar Kastasadhya*; i.e difficult to treat, in the order as mentioned in classical literature.

"*.....Vatapittaa Kapha Pleeha sannipato Udkodaram*," 'Ashtang Sangrah' Chapter 12. Udar-rog Nidanam verse 46.[18]

Deranged Liver function is noted by measurement of Serum Bilirubin, Serum Albumin and Prothrombin time. Serum Bilirubin level is the measure of hepatic conjugation and excretion while Serum Albumin level and prothrombin time is the measure of protein synthesis.[6] In this case Serum Bilirubin level was maintained within normal range or marginally increased. Serum Albumin level was reduced significantly so that Albumin: Globulin ratio was reversed. Prothrombin time was slightly raised. Despite giving I/V Inj. Albumin 20% solution -100 ml weekly for several weeks, his Albumin level never raised above 2g/dL.

However Ayurvedic treatment made the difference within 2 months of treatment. Serum Albumin level raised to > 3g/dL, RFT values were brought within normal range, TSH level brought to almost normal. Sodium, Potassium level were maintained within normal limits. The combination of **Maka/ Bhringaraj (Eclipta alba), Punarnava (Boerhaavia diffusa) and Palash (Butea monosperma),** was wonderful in restoring the balance. Maka is useful in *Yakrut vikaras* (Liver disorders) i.e. Hepatomegaly, Splenomegaly; improves functioning of Liver, Spleen, Stomach and intestines and removes the toxins, accumulated due to mal-functioning of liver. Punarnava is proved to be useful in treating enlargement of liver and spleen, being *Shothghna*, reduces Ascites. Palash (Butea monosperma) flowers act as diuretic, alkalizer and improve appetite due to its *Deepniya* properties to increase the *Jatharagni*. This herbal combination improved hepatic as well as renal function which was deranged due to Hepato-renal syndrome.

We prescribed **Phaltrikadi quath** which contained **Haritaki** (Terminalia chibula) **Bibhitak** (Terminalia bellirica), **Amalki** (Emblica officinalis), **Guduchi** (Tinospora cordifolia), **Vasa** (Justicia adhatoda) **Katuka** (Picrorhiza kurroa), **Chirayita** (Swertia chirata) and **Nimb** (Azadirachta indica), that was further useful in restoring the Liver function.

We successfully used **Majun Dabidulward and Jawarish Jalinus** (Hamdard) as ***Rasayan chikitsa***. Majun Dabidulward is Hepatoprotective, Antioxidant, corrects Liver and Spleen enlargement, and reduces inflammation of liver and stomach. Jawarish Jalinus gives strength to all the vital organs including Liver, Heart, Kidneys, Lungs and brain whose functioning was adversely affected in Chronic Liver disease.

Due to the combined and synergistic use of above mentioned treatment, the balance was restored. Within 2 months of Ayurvedic treatment Hepatic function was improved, Portal hypertension was reduced, Refractory Ascites and SBP were totally disappeared, Pleural effusion was cured and Kidney function was also restored. His latest Doppler abdomen revealed," Portal vein which was thrombosed earlier completely was normal in calibre (8 mm at Porta hepatis) showed partial recanalization & patchy flow established PSV 15cm/sec. Splenic vein which was thrombosed earlier was showing normal flow." Thus Ayurvedic treatment enabled flow in Portal vein and splenic vein; further multiple collaterals seen at periportal region that is confirmed by Doppler study and corroborated clinically. We added Arjun (Terminalia arjuna) later in the herbal combination to improve functioning of heart as well as to add strength to the muscles as due to severe Sarcopenia, muscle mass was lost significantly. Readers may note his physical condition of reduced Sarcopenia from Fig No. 7.

As mentioned above, the case is still maintained on Ayurvedic line of treatment for last 15 months and an End Stage Liver Disease case destined for Liver transplant, was spared off from the costly surgery, saving money (Rs 28 Lacs), sufferings and restoring quality of life.

CONCLUSION

This case study highlighted that Ayurved has strength and ability to treat End Stage Liver Disease, showing a distinct ray of hope to thousands of sufferers awaiting Liver transplantation.

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