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TREATMENT OF INCURABLE LIVER CANCER (HEPATOMA) BY FOUR TRADITIONAL HERBAL MEDICINES

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ABSTRACT

Prognosis of Hepatocellular carcinoma (HCC) is very poor. Chemotherapeutic agents in allopathic medicines are hardly effective. Long time of survival is possible only in cases of full surgical excision or liver transplantation. Use of herbal medicine in the treatment of liver cancer and other cancers has a long tradition. A total of 30 HCC patients (66% were chronic hepatitis patients) treated with four well known herbal aqueous extracts (viz *Bergenia ciliata*, *Nigella sativa*, *cassia fistula* and *Picrorhiza scrophulariflora*) in which 17 patients were females and 13 males in age group ranges from 42-72 years. Over all six cases were HBV positive, 11 cases were HCV positive and one case with co-infection HBV and HCV viruses. All others were HBV/HCV negative. All individuals were diagnosed as HCC and further monitored on ultrasound, CT scan and alpha fetoprotein; some of them were confirmed additionally with MRI and tissue biopsy. Their liver function tests and serological tests, to determine the status of HBV and HCV were also performed. Out of 30 confirmed HCC patients 10 showed hundred percent improvements displaying no evidence of mass in liver. Ten patients showed remarkable reduction in their size of tumor/mass and are still on medication. Eight patients were having non compliance who had started treatment but either left in the mid of treatment or lack of follow up while the two patients were passed away. All on medication patients showed remarkable improvement and reduction in the size of tumor. However, no adverse effects were observed. To obtain a convincible data it is proposed to treat all the patients approximately for a minimum period of 5 years.

Keywords: Hepatocellular carcinoma, Traditional herbal medicines, Hepatoma

INTRODUCTION

Liver cancer (Hepatocellular carcinoma, HCC) is considered as one of the most challenging tumors with high incidence, prevalence and mortality rates [1]. According to WHO, 2010 report, it is the sixth most common cancer worldwide, accounting for 7% of all cancers and an estimated incidence that is almost identical to the mortality rate. Moreover, it represents the third cause of cancer related deaths [2]. HCC used to be described as a tumor with an ultimately poor prognosis. This poor prognosis is related to its rapid progression and its aggressive biological behavior that leads usually to the diagnosis at an advanced stage [3]. Hepatitis B (HBV) and Hepatitis C (HCV) infections are the main causes of liver disease worldwide. The incidence of HCV infection is hard to quantify as large number of patients are asymptomatic and no vaccination is effective yet [4]. Human hepatocellular carcinoma (HCC) is one of the most common malignancies all around the world, especially in Asia [5, 6]. It occurs with great frequency and is becoming more common as a complication of chronic Hepatitis B or Hepatitis

C [4, 7, 8]. Though the hepatitis B virus (HBV) is still the main etiological agent for HCC in many Asian Pacific countries, hepatitis C virus (HCV) related disease is the single largest cause of HCC in Pakistan [9, 10, 11]. In a country of about 200 million, 4.8% of general population is positive for anti-HCV antibody and 2.5% for HBV surface antigen [9, 10, 11]. HCV HCC dominance appears to be related to this higher prevalence of hepatitis C. HCV related HCC is seen in about 60 – 70% of cases. Only about 20% of cases are positive for HBV and 10 – 15% is non-B non-C. High contamination rates with aflatoxin in Pakistan also contribute to liver carcinogenesis [9, 10, 11]. The age-standardized rate of HCC in Pakistan is about 7.6 per 100,000 persons per year for males and 2.8 for females.13-16. The male to female ratio for HCC is 3.6:1. Most of the patients present in their 5th and 6th decade. Genotype 3a of HCV, and genotype D of hepatitis B, which is the most common genotypes in Pakistan, are also seen in the majority of HCC patients [9, 10, 11]. Other significant factors associated with HCC were older age, male gender and higher alkaline phosphatase.

Many therapeutic approaches have been applied clinically such as surgery, interventional or micro-traumatic techniques, physical or chemical methods [12]. HCC prognosis is very poor. Classical chemotherapeutic agents are barely effective. Long time of life is possible only in cases containing surgically full-excision or liver transplantation.

Herbal medicine and their extract in the treatment of liver cancer have a long tradition [13]. The compounds derived from the herb and herbal composites are of considerable interest among oncologists [14]. Natural products, herbs and spices have been used as remedies for various diseases, including Cancer since ancient times. The bioactive constituents of various herbs seem to be promising targets for isolation, cancer activity screening and clinical evaluation. Finally, herbal preparations may offer a cost effective protective alternative to individuals known to have a high risk for HCC and possibly other cancers, through maintaining cell integrity, reversing oxidative stress and modulating different molecular pathways in preventing carcinogenesis [15]. The current trend of cancer research is the investigation of medicines of plant origin because of their affordability and accessibility with minimal side effects. In this study we have specifically selected the following four herbs Bergenia ciliate, Clongi (Nigella sativa), Cassia fistula linn and Picrorhiza scrophulariflora. All of these plant(s) have been tried and reported individually for cancer treatment and mostly tested earlier by herbalists, botanists and traditional Hakeems for the cancer treatment either for specific cancer or group of cancers.

B.ciliata bears potent anti-neoplastic activities that may have prospective clinical use as precursor for preventive Medicine [16, 17, 18]. Methanolic and aqueous *B. ciliata* rhizome extracts were found to possess antioxidant activity, including reducing power, free radical scavenging activity and lipid peroxidation inhibition potential. The methanolic extract displayed greater potential in all antioxidant assays. It is, however, interesting to note that the aqueous extract demonstrated considerably higher DNA protection, although lagging behind its methanolic counterpart as an antioxidant [16]. The major chemical constituents of plant include tannic acid, gallic acid, glucose, metarbin, albumen, bergenin, (+)-catechin, gallicin. *Bergenia ciliata* was subjected to bioactivity analysis. The plant has antitussive, antiulcer, antioxidant, antibacterial, hypoglycemic, toxicological activity. It was observed that root and leaves extract were promising as antifungal agent. The root and leaves extract were effective against *Microsporum canis*, *Pleuroetus oustreatus* and *Candida albicans*[17]. Methanolic and aqueous extract of *Bergenia ciliate* rhizome were found to have promising potential towards the development of drug that might be used to target tumors for chemoprevention/chemotherapy to check neoplastic growth and malignancy.

Nigella sativa, also known as black cumin, black seed, Kalonji and Haba al-barakah (Arabic name) has been proven with countless peer reviews to effectively treat cancer. There have been more than 450 peer reviews in the past 40 years for a wide range of diseases, such as diabetes, MS, Alzheimer's disease, hepatitis C and more. Originally, Nigella sativa was used to treat migraines and allergies, but recent discoveries have shown that this little black seed is effective in destroying cancer cells. For thousands of year, the seeds, oils and extracts of *N. sativa* have been used as an anticancer agent by Unani, Ayurveda and the Chinese system of medicine that have originated from the Arab, Ind-Bangla and China, respectively. The modern scientific research with the investigation of anticancer activity of *N. sativa* is a comparatively recent affair (for the last 2~3 decades) [19].

Ingredients of *N. sativa* have beneficial effects against many diseases, including cancers. For example, it is effective in the diminishing the risk of atherosclerosis by decreasing the serum low density lipoprotein cholesterol level and increasing the serum high density lipoprotein cholesterol levels[20, 21]; it exerts therapeutic and protective effect in diabetes by

decreasing morphological changes and preserving pancreatic beta-cell integrity[22] and by beneficially changing the hepatic enzyme activities[23], it is effective against hypertension[24, 25], its oil protects kidney tissue against oxygen free radicals, preventing renal dysfunction and morphological abnormalities[26, 27, 28]. The cytotoxic activity of *N. sativa* seed was tested on the human hepatoma HepG2 cell line by Thabrew *et al.,* (2005) [29], and 88% inhibitory effect on HepG2 was found after 24-hr incubation with different concentrations (0–50 mg/ml) of the *N. sativa* extract. Nagi and Almakki (2009) reported that oral administration of Thymoquinone (TQ) is effective in increasing the activities of quinone reductase and glutathione transferase and makes TQ a promising prophylactic agent against chemical carcinogenesis and toxicity in hepatic cancer [30].

Cassia fistula belonging to the family Leguminosae Casesalpinaceae is commonly called as Amaltas an Indian Laburnum and is native to India, the Amazon, and Sri Lanka and is extensively diffused in various countries [31]. Main property of Cassia fistula is mild laxative and also used as a purgative due to the wax aloin and has been used to treat many intestinal disorders like ulcers. The plant has a high therapeutic value and it exerts antipyretic and analgesic effects. It has been reported to possess antitumor, hepatoprotective, antifertility, and antioxidant properties. Cassia fistula plant organs are known to be an important source of secondary metabolites, notably phenolic compounds [31]. The herb contains anthraquinones, flavonoids and flavan-3-ol derivatives. The seeds are rich in glycerides with linoleic, oleic, stearic and palmitic acids as major fatty acids together with traces of caprylic and myristic acids. Besides phenolics and their derivatives, a certain amount of alkaloids have also been reported in the flowers, while traces of triterpenes have been observed in both flowers and fruits. Four new compounds, 5-(2-hydroxyphenoxymethyl) furfural, (2'S)-7- hydroxy-5-hydroxymethyl-2-(2'-hydroxypropyl) chromone, benzyl-2- hydroxy-3, 6-dimethoxybenzoate, and benzyl 2β-O-D-glucopyranosyl- 3,6-dimethoxy benzoate, together with four known compounds,5-hydroxymethylfurfural, (2'S)-7-hydroxy-2-(2'-hydroxypropyl)-5- methylchromone, and two oxyanthraquinones, chrysophanol and chrysophanein, were also isolated from the seeds of *Cassia fistula* [32].

Picrorhiza scrophulariiflora extensively used in traditional as well as modern medicinal system in India, China, Tibet, Nepal and Sri Lanka for the treatment of various immune-related diseases. It is used as antidiabetic, antiasthmatic, cardioprotective, anti healing, antioxidant and antiradical activities, antiulcer and anticancer activity, and a selective enhancer of neuron growth [33]. A wide range of biological activities have been attributed to iridoids, such as antihepatotoxic, choleretic, hypolipidemic, anti-inflammatory, antispasmodic, antitumor, antiviral, purgative, immunomodulatory, antioxidant, antiphosphodiesterase, neuritogenic, antidiabetic, antiasthmatic, cardioprotective, molluscicidal and leishmanicidal activities. Similarly, the hepatoregenerative and hypolipidemic effects of Picroliv, the preparation was shown to have similar or more potent activities than silymarin, a purified fraction of *Silybum marianum* (Asteraceae), commonly used in the treatment of liver disorders [33].

MATERIAL AND METHODS

Patient samples: A total of 30 HCC/and or hepatoma confirmed patients in which 13 males and 17 females were selected for this study. The male age group was 50 to 72 years, while, the female age group was in the range of 42 to 70 years. All individuals were diagnosed with HCC and/or hepatoma on histopathology, ultrasound, CT scan and Alpha fetoprotein, some of them were confirmed additionally with, MRI and Tissue Biopsy. These persons opted to be treated with herbal remedy. Their liver function tests and serological tests, to determine the status of hepatic virology were also performed. In some cases Bone Scan was also performed. After registration of all subjects a repeat liver function test, CBC and an ultrasound was also performed before initiating the herbal treatment. On follow up (minimum 6 months) all patients were monitored by either ultra sound or C.T scan or both.

The samples of patients were further divided into three groups viz; A, B and C. Group A (Hepatitis C Reactive) Group B (Hepatitis B Reactive) and group C (Hepatitis C and Hepatitis B Non-Reactive).

Herbal Drugs Used: To achieve this goal a survey of ancient medical literature (manuscripts) regarding herbal medicinal plants used as therapeutic intervention was undertaken at Department of Botany, university of Karachi and Hamdard University Karachi. Following four candidate traditional herbal plants viz., Bergenia ciliate, Clongi (Nlgella sativa), Cassia fistula linn and Picrorhiza scrophulariflora were finally selected for this study.

The crude extracts of plants were obtained in different solvents but water extract was found most effective in different clinical trials (According to ICH-GCP guidelines). Before starting the study, an

approval from ERB and patients informed consent was obtained.

Extraction of Plant Material: 5 gram of plant materials was extracted three times with 100 ml of distilled water, under reflux for three hours. The extract was than filtered and vacuum dried for use for further research investigations as a therapeutic interventions.

RESULTS AND DISCUSSIONS

Out of 30 confirmed Hepatoma or HCC patients 10 patients showed hundred percent improvements having no evidence of mass in liver confirmed by ultrasound, CT scan and Alpha fetoprotein (Table 1). Among these 10 patients six cases had diagnosed liver cancer (Hepatoma), one has liver mets from gall bladder one has liver mets from pancreas and two had liver mets but were basically breast cancer patients. Among these six hepatoma cases five were HCV positive and one was HBV positive while among patients having Mets either from GB, pancreas and both breast cancer patients were negative for both HCV and HBV. All of these patients responded very well soon after the start of treatment and on subsequent visits all of these patents reported that the therapy was effective in reducing their cancer-related pain, nausea and vomiting, fatigue, constipation and improving appetite, and weakness. These were also confirmed after examining the participants clinically. Improvements were also observed in the lab investigations like Complete Blood Count (CBC), Liver Function Test (LFT), Kidney function test, and AFP level. These lab investigations were done as a part of their routine clinical checkups (data not presented).

Other ten patients also showed remarkable reduction in size of tumor/mass monitored on ultrasound, CT scan and AFP and are still on medication. Their follow up results are evident of regression in size of tumor (Table 1). Although these patients are still on medication and responded very well and all are happy with treatment and reported similar results of reduction in pain, nausea, vomiting fatigue, constipation and improving appetite, and weakness. In these ten cases also two were breast cancer patients and both had no history of HBV and HCV. Among other eight cases of hepatoma one is HBV positive 4 were HCV positive, four were negative for both HBV and HCV while one case had both HBV and HCV positive report. Eight patients were having non compliance who have started treatment but either left in the mid of treatment or lack of follow up while two patients were passed away. All on medication patients showed remarkable improvement and reduction in size of tumor as is evident from their ultrasound, CT scan and AFP results (Table 1).

Many studies were published on the role of herbal medicines in treating liver cancer patients [14-18, 20- 23, 30,] some studies are on individual plant extracts[16-20, 31, 33] and very few on group of plants and their extracts [14, 15, 34, 35,]. Moreover, most of these studies are on animal models[23, 24, 26, 31] or on cell lines[17, 18, 29]. Among our study plants, all plants have been tried and reported earlier for cancer treatment and mostly tested by herbalists, botanists and traditional Hakeems for the cancer treatment either for specific cancer or group of cancers.

Chemotherapy as well as conventional treatment for the cure of cancer causes the adverse and toxic side effects therefore fails to control the cancer disease [34]. The alternate solution for the harmful effects of synthetic agents is the use of medicinal plants [36]. The plants have been used for the cure of cancer from a prolonged period of time. The medicinal plants contain chemical constituents of therapeutic value. These chemical substances produce physiological action on the human body. It has been shown currently by clinical studies and phytochemical investigation that many herbs exhibit anti tumor potential against various cancers [35]. In this study, no adverse side effects were observed however, very few patients reported to have mild oral and local stomach irritations which were successfully controlled by the supportive cares. Our herbal treatment was also effective in improving the disease symptoms and the quality of life of the participants. Almost all patients reported that the therapy was effective in reducing their cancer-related pain, nausea and vomiting, fatigue, constipation and improving appetite, and weakness. These were also confirmed after examining the participants clinically (data not presented). Improvements were also observed in the lab investigations like Complete Blood Count (CBC), Liver Function Test (LFT), Kidney function test, and AFP level. These lab investigations were done as a part of their routine clinical checkups. To obtain a convincible data it is proposed to treat all the enrolled persons approximately for a minimum period of 5 years.

Table 1: History of patients, clinical diagnosis, followup and status of tumor(s) on different stages of treatment

S.No.	Name of patient	Age Yrs.	Sex	1) Diagnosis & date	2) Viral profile	3) Status of Liver at prsentation	4) Tumor marker	5) CT/ Ultrasound /MRI on diff. stages & Follow up visits	6) Size of Tumor/ Hepatoma and on F/U stages	7) Remarks
1	Salma Bibi	60	F	Hepatoma 3-8-2013	HBV +Ve	Cirrhosis, Ascitis		1) u/s 3-8-2013 2) u/s 21-3-2014 3) 6-6-2014	1) 3x2.6cm 2) 2.2x1.9cm 3) Not seen	Focal mass not present
2	Surayya Qamar	55	F	Hepatoma 22-6-2004	HCV +Ve	CLD/Splenomegaly Cirrhosis	AFP 29-6-2004 31.5IU/ml	1) u/s 22-6-2004 2) CT 8-7-2004 3) u/s 26-8-2004 4) MRI 6-9-2004	1) 5.6mm 2) 1.7x1.2x1.2cm 3) 4) Not seen	No evidence of mass seen
3	Kishwer Sultanan	59	F	Neoplastic mass, GB to Liver	HBV/HCV negative	Liver Mets from GB		1) u/s 30-4-2010 2) CT 5-5-2010 3) u/s 6-8-2010 4) 10-2-2011	1) 2.8x2.0 cm 2) 3) 2.2x2.2 cm 4) Not seen	Focal mass not present
4	Nargis Kafeel	51	F	Hepatoma 7-5-2009	HCV +Ve	Liver cirrhosis/ portal hypertension	AFP 10-5-2009	1) CT 7-5-2009 2) u/s 9-9-2009 3) 1-6-2010 4) 13-1-2011 5) 14-11-2011	1) 2.2x2.0 cm 2) 1.4x1.0 cm 3) 1.4x1.0 cm 4) Not seen	Mass disappears
5	Naseem Akhtar	58	F	Hepatoma 25-4-2013	HCV +Ve	Cirrhosis, Ascitis Splenomegaly	AFP 24-4-2013	1) u/s13-12-2012 2) CT24-12-2012 3) u/s 4-4-2013	1) 2.0x1.2 cm 2) 2x1 cm 3) Not seen	No Obvious mass seen
6	Abdul Haleem	71	M	Hepatoma 01-2-2013 Mets from pancreas	HBV/HCV negative	Normal		1) CT 19-12-2012 2) CT 20-12-2012 3) ERCP 18-12-2012 4) u/s 26-8-2013 5) u/s 28-10-2013 6) u/s 3-3-2014	1) 22x16 mm 2) No mass seen 3) No mass seen 4) No mass seen	No Obvious mass seen
7	Saeeda	28	F	Hepatoma Mets from breast cancer	HBV/HCV negative	Normal		1) CT 18-8-2012 2) CT 30-1-2013 3) u/s 26-9-2013	1) 7x9 mm in right lobe 2) No mass seen 3) No mass seen	Focal mass not present

8	Qudsia Khalid	63	F	Hepatoma 2-4-2011	HCV +Ve	Liver cirrhosis/ portal hypertension/ Splenomegaly	AFP	1) CT 2-4-2011 2) CT 26-4-2011 3) u/s 1-4-2012	1) 2.9x2.9 cm 2) 3.0x3.0 cm 3) No mass seen	Focal mass not presen
9	Zulfiqar	52	M	Hepatoma 27-1-2012	HCV +Ve	Liver cirrhosis/ portal hypertension	AFP	4) CT 27-1-2012 5) CT 14-5-2012 6) u/s 16-11-2012	1) 2.3x2.0 cm 2) 2.1x1.9 cm 3) No hepatic mass	No hepatic mass seen
10	Johar Begum	50	F	Hepatoma METS from breast 20-4-2009	HBV/HCV negative	Normal	CA-15-3 22-3-2013	1) u/s 24-9-2009 2) u/s 13-8-2010 3) u/s 4-7-2012 4) u/s 15-11-2012 5) u/s 20-9-2013 6) u/s 28-3-2014	1) 9x5 cm 2) 10.3x5.8 cm 3) 9.0x3.6 cm 4) 8.2x3.4 cm 5) 6.7x4.9 cm 6) 0.9x0.9 cm	Remarkable reduction in size of hepatoma
11	Ishrat Murtaza	50	F	Hepatoma 14-05-2014	HBV +Ve	Normal	AFP 31.3 IU/ml 17-5-2014	1) u/s 14-5-2014 2) CT 20-5-2014	1) 2.3x2.1 cm 2) 2.4x2.7 cm	On medication
12	Raham Jan	50	F	Hepatoma 5-02-2014	HBV/HCV negative	Normal		1) u/s 5-2-2014 2) u/s 7-4-2014	1) 1.6 cm 2) 2.4x2.0 cm	On medication
13	Tanveer Raja	46	M	Hepatoma 3-05-2014	HCV +Ve	Liver cirrhosis/ Splenomegaly	AFP 883.0 IU/ml 23-5-2014	1) u/s 03-05-2014 2) CT 27-05-2014	1) 5.4x5.2 cm 2) 5.8x6.8 cm	On medication
14	Arifa	48	F	Hepatoma 31-08-2013	HCV +Ve	Liver cirrhosis/ Splenomegaly/ Ascitis	AFP 224.0 IU/ml 2-9-2013	1) u/s 31-8-2013 2) u/s 04-3-2014 3) u/s 20-6-2014	1) 4.4x4.1 cm 2) 7.5x6.5 cm 3) 8.7x7.4 cm	On medication
15	Hadia Samar	43	F	Hepatoma Mets from breast cancer	HBV/HCV negative	Hepatospleenomegaly		1) u/s 12-9-2013 2) u/s 28-2-2014 3) u/s 13-6-2014	Multiple nodules, consist with mets 1) 3.1 cm 2) 3.2 cm	On medication

16	Said Muhammad	62	M	Multifocal HCC 19-2-2014	HBV/HCV negative	Ascitis	AFP 200.0 IU/ml 18-9-2013	1) u/s 17-9-2013 2) CT 26-9-2013 3) u/s 3-10-2013 4) u/s 3-4-2014	1) 9.8x8.1 cm 2) 10.2x11.7 cm 3) 6.8x6.3 cm 4) 6.7x7.6 cm	Size reduced, On medication
17	Jan Muhammad Mahar	50	M	Hepatoma 5-05-2014	HCV +Ve	Enlarged liver	AFP 650.0 IU/ml 5-5-2014	1) CT 5-5-2014 2) u/s 19-6-2014	1) 10.0x8.5 cm 2) 8.9 cm	Size reduced, On medication
18	Muhammad Bux	47	M	Hepatoma HCC 10-6-2014	HBV/HCV positive	Hepatospleenomegaly	AFP 274.0 IU/ml 3-6-2014	1) CT 10-6-2014 2) CT 17-6-2014	1) 10.0x8.0 cm 2) 10x11 cm	On medication
19	M. Aslam Babu	65	M	Hepatoma HCC 3-9-2013	HCV +Ve	Liver cirrhosis/ Splenomegaly/ portal hypertension	AFP 9.8 ng/ml 13-6-2014	1) u/s 3-9-2013 2) CT 12-9-2013 3) CT 16-11-2013 4) u/s 15-2-2014 5) CT post TACE 14-6-2014	1) 3x3 cm 2) 2.8x2.5 cm 3) No change 4) No lesion seen 5) New lesion identified	Size increased after TACE Now on herbal medication
20	Saeeda Noor	30	F	Hepatoma Mets from CA breast	HBV/HCV negative	Normal		1) CT 24-6-2014 2) u/s 27-6-2014	3) 6.7.0x4.3 cm 4) 3.5x3.2 cm	On medication
21	Haji Zain	56	M	Hepatoma 8-11-2013	HBV +Ve	CLD, Splenomegaly, Ascitis	AFP 5-9-2013	1) CT 8-11-2013 2) CT 29-10-2013 3) CT 13-11-2013	1) 7.5x7.5 cm	Non compliance
22	Maqsood Bibi	60	F	Hepatoma 19-03-2013	HBV +Ve	Splenomegaly	AFP 1360 ng/ml 19-5-2013	1) u/s 19-3-2013	1) 10.3x8.8 cm	Non compliance
23	Arshad Ali	55	M	G.B mass infiltrating into Liver 1-12-2012	HBV/HCV negative	Normal		1) u/s 1-2-2012 2) CT 4-12-2012	1) 6.0 cm	Non compliance
24	Zainul Islam	53	M	Multifocal HCC 17-1-2013	HBV +Ve	Normal	AFP 71.0 ng/ml 15-6-2013	1) u/s 17-1-2013 2) CT 10-7-2013	1) 2x2 cm 2) 1x1 cm	Non compliance

25	Haji M. Akram	71	M	Hepatoma 22-04-2014	HBV/HCV negative	Enlarged liver	AFP 58.7 IU/ml 9-4-2014	3) u/s 24-4-2014 4) CT 24-4-2014	1) 7.1x5.9 cm 2) 6.7x6.4 cm	Size reduced but Non compliance
26	M. Israael	64	M	Multifocal HCC 17-1-2013	HBV/HCV negative	Normal	AFP 20.6 IU/ml 28-1-2014	1) u/s 01-01-2014 2) CT 2-01-2014	1) 6.1x5.8 cm 2) 7.5x5.5 cm	Non compliance
27	Shahnaz Bibi	45	F	Hepatoma 8-01-2014	HBV +Ve	Hepatomegaly	AFP 372.8 IU/ml 8-1-2014	1) u/s 08-01-2014 2) CT 9-01-2014	1) 6.5x5.8 cm 2) 6.4x7.6 cm	Non compliance
28	Pinda Jan	50	F	Multifocal HCC 19-2-2014	HCV +Ve	Liver cirrhosis	AFP 200.0 IU/ml 24-3-2014	1) u/s 19-02-2014 2) u/s 24-03-2014 3) CT 27-03-2014	1) 2.5x2.4 cm 2) 6.0x4.0 cm	Non compliance
29	Najma Khatoon	70	F	Multifocal HCC 26-3-2014	HBV/HCV negative	Liver cirrhosis/ portal hypertension	AFP 820.5 ng/ml 28-3-2014	1) u/s 26-3-2014 2) CT 28-3-2014	1) 4.6x4.0 cm 2) 4.0x4.0 cm	Passed away
30	M. Riaz	61	M	HCC 15-6-2013 H/O post TACE HCC	HCV +Ve	Liver cirrhosis	AFP 39.0 IU/ml 23-9-2013	1) CT 15-6-2013 2) CT 30-9-2013 3) CT 29-5-2014	Patchy multiple mass 1) 2.8x4.4 cm 2) 2.0x4.9 cm 3) 10x2.5 cm 4) 1.5x1.7 cm	Passed away

1. All patients were already diagnosed based on Histopathology, Ultrasound, CT, MRI and tumor marker reports. Liver METS were also considered as Hepatoma
2. Serology reports (Anti HCV and HBs-Ag) of all patients and PCR reports of positive patients were recorded
3. Based on Ultrasound and CT scan interpretation
4. Tumor markers of only selected patients for diagnostic purpose were investigated, not for followup treatment
5. All radiological tests including X-rays, CT scan and MRI were from ARC, AKU, KIRAN, LNH or other well known registered departments. Ultrasound reports were also from these departments and usually followed up from same departments.
6. Size of tumor were recorded on each follow up usually estimated by radiologist or sonologist in comparison of previous reports
7. Remarks are copied from radiology reports. In cases of complete regression (disappearance of mass), five year followup is advised. Non compliance is not due to side effects of medication. Few patients were showed promising results but they could not follow up.

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