

Current Practices in Management of Hepatocellular Carcinoma in India: Results of an Online Survey



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Background: Prior to INASL guidelines, there were no Indian guidelines for management of hepatocellular carcinoma (HCC) in India. The guidelines given by other societies like AASLD, EASL etc are not uniform and not tailored for Indian patients. Hence management practices for HCC in India largely depended on physicians' individual preferences. This survey aimed to study current practices in management of HCC in India. **Methods:** An online survey was conducted from the platform of a survey portal (www.surveymonkey.com), from December 2012 to April 2013. Invitation to participate in the survey was sent to 1383 doctors of India who were expected to be involved in management of patients of HCC. The survey was of 10 min duration and consisted of questions on how the respondents diagnosed and managed patients of HCC. **Results:** Three hundred and seventy-seven doctors answered the survey questions (72% gastroenterologists, 95% working in India). The important points which emerged from the survey are following: (i) The incidence of HCC is increasing in India; (ii) The most common etiologic agent is Hepatitis B responsible for 43% cases; (iii) Only 14% patients present in early stage when curative treatment is possible (BCLC-A); (iv) 90% of these respondents screen for HCC when they first evaluate a cirrhotic patient; (v) While following a patient of cirrhosis most respondents screen for HCC by ultrasound and AFP at every 6 months to 1 year; and (vi) Most (82%) respondents follow some international guideline for staging and treatment of HCC. The respondents also suggested that there is a need for spreading awareness about HCC in public as well as in medical fraternity, and there is a need for a national registry of HCC. **Conclusions:** This is the first survey on management practices on HCC. With the publication of the INASL guidelines on HCC, the diagnosis and treatment of HCC will be more uniform and protocol based. Further such surveys should be carried out at periodic interval to track increasing awareness and better management practices for HCC in India. (J CLIN EXP HEPATOL 2014;4:S140-S146)

Hepatocellular carcinoma (HCC) is one of the major causes of mortality among patients with chronic liver disease. The incidence of HCC is rising in India and is poised to become the leading GI cancer.¹ Prior to INASL guidelines,² published in the present issue,

there were no Indian guidelines for management of hepatocellular carcinoma (HCC) in India. The guidelines given by other societies like AASLD, EASL etc are not uniform and not tailored for Indian patients. Hence management practices for HCC in India largely depended on physicians' individual preferences. This survey aimed to study current practices in management of HCC in India. This survey is the first of its kind done in India, and the results of this survey were presented and discussed during the round table discussion that was held on 9th and 10th February, 2013 at Puri, Odisha, to discuss, debate, and finalize the consensus statements.

Keywords: liver cancer, survey, guidelines, hepatocellular carcinoma, management practices

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Abbreviations: AASLD: American Association for the Study of Liver Diseases; AFP: alpha-fetoprotein; BCLC: Barcelona clinic liver cancer; CECT: contrast enhanced computerized tomography; CTP: Child Turcotte Pugh; EASL: European Association for the Study of the Liver; ESDO: European Society of Digestive Oncology; FNAC: fine needle aspiration cytology; GI: gastro-intestinal; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; INASL: Indian National Association for the Study of Liver; MBBS: Bachelor of Medicine, Bachelor of Surgery; SOL: space occupying lesion; TACE: transcatheter arterial chemoembolization

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METHODS

Survey Platform

An online survey was conducted from the platform of a survey portal (www.surveymonkey.com), from December 2012 to April 2013. The survey was of 10 min duration and consisted of questions related to the topics how the respondents diagnosed and managed patients of HCC. The

questions and their response options are given in Table 1. The survey consisted of 24 questions, mostly in objective response format, and each question appeared as separate screen on clicking 'next'.

Sample Size Calculation

There are approximately 2000 qualified gastroenterologists in India and almost all of them are life members of The Indian Society of Gastroenterology.³ This comprised of the target population for the survey. For the survey to adequately represent the target population ($n = 2000$), with a confidence level of 95% and a confidence interval of 5, a sample of 322 responders are needed. Expecting a 25% response from invitees, invitation to participate in the survey was sent to 1383 doctors of India who were expected to be involved in management of patients of HCC.

RESULTS

Participants

Invitation to participate in the survey was sent to 1383 doctors of India. Of them, 377 (27%) responded to the questionnaire; in 11 (0.8%) the email bounced; 5 (0.4%) opted out; and 990 (72%) did not respond. Among the 377 who responded to the survey questionnaire, 313 (83%) answered all the 24 questions, while rest 64 (17%) answered some of the questions, but not all.

Most respondents (273/377, 72%) were gastroenterologists; followed by gastro-surgeons (47/377, 12%); and general physicians (18/377, 5%). Ninety-five percent (359/377) respondents were working as consultants or faculty. Eighty-five percent (322/377) respondents had completed their medical school (MBBS) between 1977 and 2003. Ninety-five percent respondents (360/377) were working in India.

The survey was designed in such a way that it proceeded further only if the respondent answered "Yes" to the question "In your practice do you come across patients of HCC?". Ninety-seven percent (367/377) respondents answered "yes" to this question.

Epidemiology of Hepatocellular Carcinoma

For the question "On an average, how many NEW patients of HCC do you see every month?" 40% of respondents answered as 0-1 patients per month; 30% respondents answered as 2-3 patients per month; and 20% respondents answered as 4-6 patients per month. Less than 10% respondents see 7 or more patients per month.

For the question "Is the number of new HCC patients increasing in your practice?" most (64%) respondents answered "Yes"; while 18% responded as "No" and another 18% were unable to comment.

Respondents were asked about the approximate etiological break-up percentage of HCC patients they see. The result is shown in Figure 1. According to the respondents the most common etiologic agent for HCC in India is Hepatitis B (43%), followed by Hepatitis C (22%), unknown or cryptogenic (17%), and alcohol (15%).

Apart from HCC, 78% of the respondents also come across intrahepatic cholangiocarcinoma in their practice, which resembles HCC.

Screening for Hepatocellular Carcinoma and Diagnosis

When asked how many of the respondents ROUTINELY screen for HCC when evaluating a patient of cirrhosis for the first time, more than 90% respondents answered that they do screen for HCC. The modalities of screening for HCC on their first evaluation of cirrhotic patients is shown in Figure 2. The most frequently used modality for screening for HCC is a combination of AFP and ultrasound abdomen.

While following a patient of cirrhosis 55% respondents screen for HCC once in every six months and 30% screen once a year (Figure 3).

When asked "What is the value of AFP in your opinion for screening for HCC?", 79% responded that they USUALLY order it recognizing its limitations because it is cheap and readily available.

Figure 4 shows the answers to the question "What will make you suspect HCC in a known patient of cirrhosis and will lead you to investigate for HCC?". Development of new portal vein thrombosis, worsening of ascites, worsening of CTP score, and pain abdomen were the most commonly encountered clinical pointers to HCC.

On detection of SOL in the liver in a cirrhotic patient, 90% of the respondents order triple phase CECT abdomen and AFP for diagnosis of HCC. Only 7% resort to FNAC for diagnosis of HCC.

Staging

Once HCC is diagnosed 76% (257/337) respondents will do staging and follow established guidelines for treatment as per the stage; while 16% (53/337) respondents will refer the patient to higher center for further management.

When asked, "Do you use the BCLC classification to treat HCC?" only 43% (143/336) respondents answered that they classify all their patients; while 30% (100/336) respondents classify some of their patients (Figure 5).

It was asked what is the approximate break-up of BCLC stages of new HCC cases they encounter. Three hundred and seventeen respondents answered and results are shown in Figure 6. About 40% of patients of HCC they see for the first time are already in the BCLC stage D when curative or palliative treatment is

Table 1 The Survey Questionnaire.

Q. No.	Question	Options
1	Tell us about yourself	<ul style="list-style-type: none"> • Specialty • Current position • Year of passing MBBS • Country of practice
2	In your practice do you come across patients of HCC?	<ul style="list-style-type: none"> • Yes • No
3	On an average, how many NEW patients of HCC do you see every month?	<ul style="list-style-type: none"> • 0–1 • 2–3 • 4–6 • 7–10 • 11–15 • >15
4	Is the number of new HCC patients increasing in your practice?	<ul style="list-style-type: none"> • Yes • No • Unable to comment
5	Do you feel that there is a need for a Registry for HCC?	<ul style="list-style-type: none"> • Yes • Maybe • No need • Doesn't matter
6	If a National Registry for primary liver cancers were to be set up by INASL, are you willing to contribute your patients' details to this registry?	<ul style="list-style-type: none"> • All my patients • Some of my patients • Not sure • No I don't want to report
7	In your experience of all patients of HCC you see in your practice what is the approximate etiological break-up percentage?	<ul style="list-style-type: none"> • Hepatitis B • Hepatitis C • Alcohol • Unknown or cryptogenic • Others (e.g. Budd Chiari, hemochromatosis etc.)
8	When you are evaluating a patient of cirrhosis for the first time, do you ROUTINELY screen for HCC?	<ul style="list-style-type: none"> • Yes, by doing AFP and triple phase CECT • Yes, by doing AFP and USG abdomen • Yes, by doing USG alone • Yes, by doing AFP alone • No, I do not routinely screen for HCC
9	What is the value of AFP in your opinion for screening for HCC?	<ul style="list-style-type: none"> • I ALWAYS order it because it is an excellent modality with good sensitivity and specificity • I USUALLY order it recognizing its limitations because it is cheap and readily available • I OCCASIONALLY order it because it is neither excellent nor poor • I NEVER use it because it is a useless investigation with poor sensitivity and specificity
10	When you are following a patient of cirrhosis, how frequently do you screen for HCC?	<ul style="list-style-type: none"> • Never, unless there are clinical pointers to HCC • Once in three years • Once in a year • Once in six months • Once in three months • Every time he visits
11	What will make you suspect HCC in a known patient of cirrhosis and will lead you to investigate for HCC?	<ul style="list-style-type: none"> • Development of new portal vein thrombosis • Development of refractory variceal bleeding • Worsening of ascites • Deteriorating CTP score • Pain abdomen • Thrombocytopenia
12	When you detect a SOL in liver on USG/CT abdomen how do you proceed further?	<ul style="list-style-type: none"> • Refer the patient to higher center for evaluation/treatment • Order AFP and triple phase CECT abdomen • Do FNAC • Do only AFP • Don't do anything

Table 1 (Continued)

Q. No.	Question	Options
13	Once HCC is diagnosed, what do you do?	<ul style="list-style-type: none"> • Refer the patient to higher centre • Do staging and follow established guidelines for treatment as per the stage • Do TACE without staging • Do local ablation by alcohol/acetic acid/RFA without staging • Give Sorafenib only • Other (please specify)
14	Do you use the BCLC classification to treat HCC?	<ul style="list-style-type: none"> • No because I don't know about BCLC classification • No because although I am aware of BCLC classification, but I don't know how to do it • No because BCLC classification is not relevant in my practice • Yes I classify some of my patients • Yes I classify all my patients
15	BCLC classification refers to the stage of HCC, where BCLC-A is early HCC while BCLC-D is terminal HCC. In your practice what is the approximate break-up (%) of new cases you see according to stage? Note: the total must add up to hundred.	<ul style="list-style-type: none"> • BCLC-A • BCLC-B • BCLC-C • BCLC-D
16	Do you strictly follow clinical practice guidelines (e.g. AASLD, EASL) for staging and treating HCC in your practice?	<ul style="list-style-type: none"> • Yes • Usually yes • Usually no • No
17	Does the hospital where you work has any of these facilities for treating HCC? (Tick all those which apply)	<ul style="list-style-type: none"> • Liver transplantation • Resection • Trans Arterial Radio Embolization (TARE) • TACE • RFA • Percutaneous alcohol injection • Sorafenib • None
18	Which patients of HCC do you refer for TACE?	<ul style="list-style-type: none"> • Size <ul style="list-style-type: none"> ❖ Small size ❖ Large size ❖ Any (small or large size) • Location <ul style="list-style-type: none"> ❖ Located in single lobe ❖ Located in both the lobes ❖ Any • Number <ul style="list-style-type: none"> ❖ Single ❖ Up to two ❖ Multicentric ❖ Any
19	Do you feel that targeted therapy for liver cancer will be better managed by	<ul style="list-style-type: none"> • Gastroenterologists (or Hepatologists) • Oncologists • Both
20	Are you comfortable in prescribing Sorafenib?	<ul style="list-style-type: none"> • Yes, I am comfortable and prescribe it if required • No, I hesitate in prescribing it • Other (please specify)
21	Do you put patients on HBV related HCC on anti-virals before starting their HCC treatment to prevent flares?	<ul style="list-style-type: none"> • Yes • No • Others (please specify)
22	Do you use opioid medication for pain control in HCC patients who are terminally ill?	<ul style="list-style-type: none"> • Yes in titrated doses • Never as it will precipitate encephalopathy • Other (please specify)
23	In your practice do you come across patients with intrahepatic cholangiocarcinoma?	<ul style="list-style-type: none"> • Yes • No • Never checked for it
24	In your opinion, how can INASL help in prevention or better management of HCC in India?	<ul style="list-style-type: none"> • Textual response

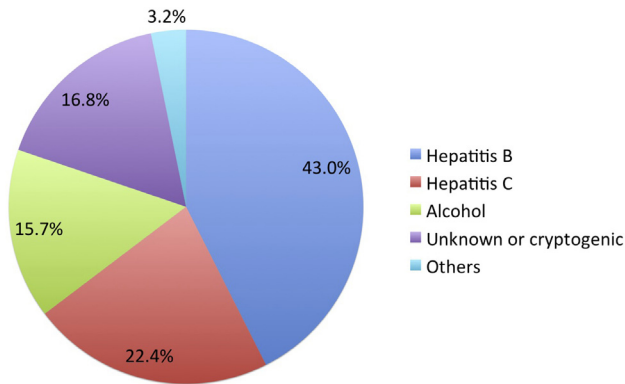


Figure 1 Etiological break-up of HCC in India according to 334 respondents of the survey.

not possible. Only 14% patients present in BCLC stage A when curative treatment is possible.

Treatment of Hepatocellular Carcinoma

Various international societies like EASL, AASLD, ESDO etc. have given their guidelines for treatment of HCC depending on the stage of HCC. Most (82%, 271/329) respondents agreed that they do follow these guidelines.

Availability of various treatment options was asked from the respondents at their hospital. Their responses are shown in Figure 7. Sorafenib was the most commonly available treatment and 88% respondents said that it was available at their hospital. The second most commonly available treatment modality was resection, which 72% respondents said it was available in their hospital.

According to 320 respondents, the most common indication for TACE was when the tumors were of large size, up to two in number, and located in the single lobe (Table 2).

Most survey participants were in the favor that targeted therapy for liver cancer will be better managed by either Gastroenterologists (48%, 154/320) or by a team of Gastroenterologist and Oncologist (47%, 149/320); while only 5%

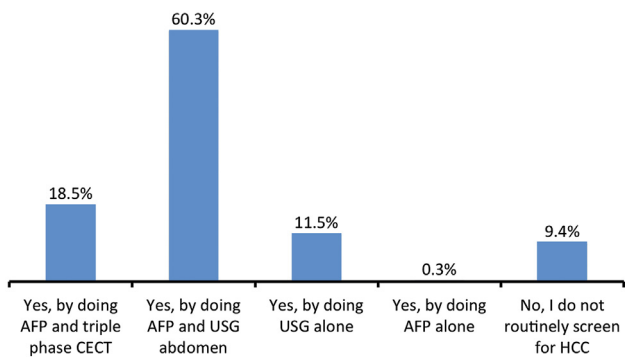


Figure 2 Answer of 340 respondents for the question "When you are evaluating a patient of cirrhosis for the first time, do you ROUTINELY screen for HCC?".

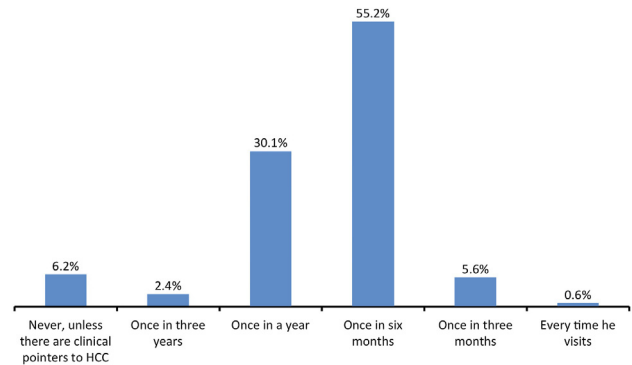


Figure 3 Screening interval for HCC for a patient of cirrhosis on follow up, according to 339 respondents of the survey.

(17/320) favored that it should be managed by oncologists alone. Most (62%) respondents were comfortable in prescribing sorafenib if required. Seventy-nine percent of respondents (251/319) agreed that they put patients of HBV related HCC on anti-virals before starting their HCC treatment to prevent flares. Eighty percent (253/318) of respondents agreed that they used opioid medication in titrated dose, for pain control in HCC patients, who are terminally ill.

Future Directions for Indian National Association for the Study of Liver

When it was asked whether they felt that there was need for a registry for HCC, 88% (316/360) responded in 'yes'; and most (87%, 312/358) said that they will contribute their HCC patients details to the registry if such a registry is set up by the INASL.

The last question of the survey was "In your opinion, how can INASL help in prevention or better management of HCC in India?" and the response was in text format. Three hundred and thirteen respondents answered this question, and the most frequent responses are shown in Table 3.

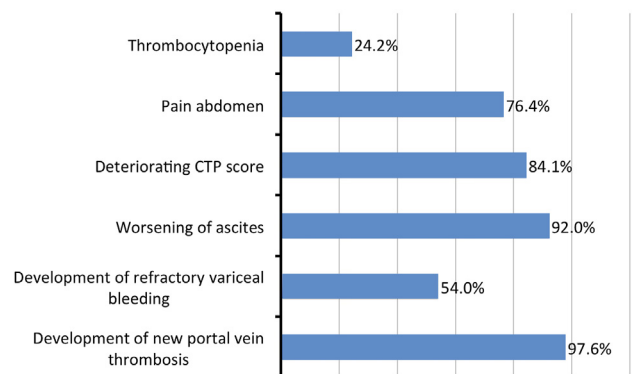


Figure 4 Clinical pointers to HCC in a patient of cirrhosis which lead to investigation for HCC, according to 339 respondents.

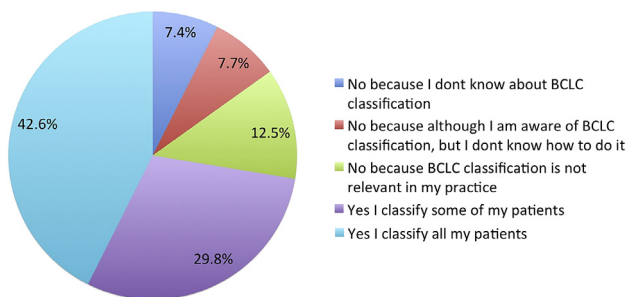


Figure 5 Responses of 336 survey participants to the question “Do you use the BCLC classification to treat HCC?”

DISCUSSION

This is the first survey on management practices on HCC in India. The important points which emerged from the survey are that the incidence of HCC is increasing in India; the most common etiologic agent is Hepatitis B responsible for 43% cases; only 14% patients present in early stage when curative treatment is possible (BCLC-A); 90% of these respondents screen for HCC when they first evaluate a cirrhotic patient; while following a patient of cirrhosis most respondents screen for HCC by ultrasound and AFP at every 6 months to 1 year; and most (82%) respondents follow some international guideline for staging and treatment of HCC.

One of the important and pleasantly surprising finding was that, most physicians managing HCC in India, were following some International guidelines like EASL, AASLD, ESDO etc for staging and treatment of HCC. Since there were no Indian guidelines that could cater to Indian needs, it was physicians’ personal choice which international guideline he or she followed. However, with the publication of the INASL guidelines on HCC in the present issue of the journal,² the diagnosis and treatment of HCC is expected to be more uniform and protocol based.

The one disturbing finding of the survey was that most patients of HCC present very late especially in the BCLC stage C or D. Only 14% patients present early (BCLC-A) when curative treatment is possible. The main reason for this could be poor awareness about risk of HCC among

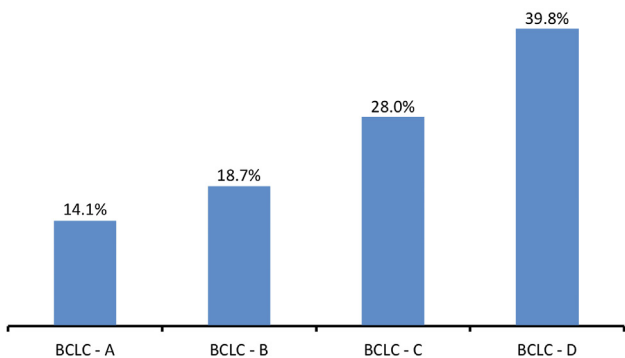


Figure 6 BCLC stage of HCC patients on their first presentation, according to 317 respondents.

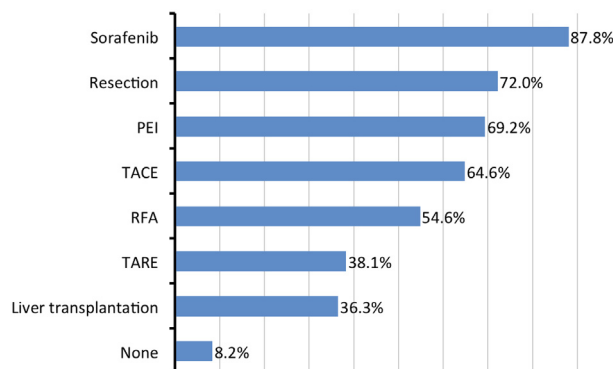


Figure 7 Availability of various treatment modalities for HCC at the hospital of 328 survey respondents.

Table 2 Responses to the Question “Which Patients of HCC Do You Refer for TACE?”.

Parameter	Tumor characteristics	Response count (n = 320)
Size	Small size	82 (26%)
	Large size	141 (44%)
	Any size	97 (30%)
Location	Located in single lobe	206 (64%)
	Located in both the lobes	36 (11%)
	Any	78 (24%)
Number	Single	54 (17%)
	Up to two	172 (54%)
	Multicentric	51 (16%)
	Any	43 (13%)

general physicians who were primarily managing cirrhotic patients. Although most gastroenterologists of India, who answered the survey, were regularly screening their patients of cirrhosis for early detection of HCC, the same may not be true for the general physicians, who may not be using regular and adequate screening practices as is necessary for early detection of HCC. Hence there is an urgent need, especially for INASL, to spread the awareness among the primary care physicians of India about regular and

Table 3 Most Common Text Responses to the Question “In Your Opinion, How Can INASL Help in Prevention or Better Management of HCC in India”. Total Response Count 313.

Increase public awareness about HCC
Education of medical fraternity involved in management of HCC by regular CMEs
Develop Indian guidelines on HCC based on Indian healthcare realities
Promote screening for HCC and early referral of HCC patients
Make HCC database/registry
Universal immunization for hepatitis B

Management Practices Survey

effective screening practices for HCC in the patients of cirrhosis they are managing.

According to this survey, the most important etiological agent for HCC in India is hepatitis B, which accounts for 43% of cases. Fortunately, the spread of hepatitis B can be effectively prevented by vaccination. Many survey respondents suggested that INASL should take lead in spreading the awareness of universal hepatitis B immunization.

In conclusion, this survey has highlighted the need for increasing the awareness about HCC in India, especially in the medical fraternity, so that HCC can be prevented or detected early at a curable stage. Further such surveys should be carried out at periodic interval to track increasing awareness and better management practices for HCC in India.

CONFLICTS OF INTEREST

The author has none to declare.

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