

# Letters to the Editor

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## Hepatocellular carcinoma in Najran

Sir,

Primary hepatocellular carcinoma (HCC) is one of the most common malignancies in the world and is responsible for an estimated one million deaths annually. It is the most common malignancy in men in sub Saharan Africa and Southeast Asia and third most common in men in China. Hepatocellular carcinoma is the most common gastrointestinal carcinoma in Saudi Arabia.<sup>1</sup> The prevalence differs from province to province supposed to be correlating closely with hepatitis B pattern although hepatitis C also been shown to have a causal association with HCC. Al-Faleh reported an HBsAg prevalence of 9% in southwestern province.<sup>2</sup> Within the Kingdom, the highest prevalence of HCC is seen in Najran Province.<sup>3</sup> Liver cancer was responsible for 18% of gastrointestinal (GIT) cancer in Gizan<sup>4</sup> and 11% of GIT malignancies in Abha.<sup>5</sup> In this study, we decided to look at the natural history of hepatocellular carcinoma and its relation to hepatitis B and hepatitis C markers in this southern province of Saudi Arabia called Najran.

We have reviewed the records of the hospital (Najran General Hospital, a Ministry of Health Hospital with its well-defined catchment area) in the last five years and found a total of 24 patients of HCC seen here. Patient data was retrieved and recorded under the following headings: Serial number, name, age, sex, nationality, symptoms at presentation, duration of symptoms, signs at presentation, the various investigations, performed associated diseases, complications, number of admissions to hospital after diagnosis, and time and cause of death. In all our cases complete blood count, biochemistry including liver and kidney function tests, x-ray chest, ultrasound abdomen, CT scan abdomen, coagulogram, total protein and albumen, and alpha-fetoprotein was carried out. Hepatitis B and C markers and schistosomal serology was carried out in all patients. Liver biopsy was carried out here in a few cases and the remainder had it in tertiary care hospitals. All were followed here till death or otherwise.

We studied a total of 24 patients retrospectively. Nineteen of these patients have already died. Others are still under follow up. Twenty-three cases were Saudis and one was Yemeni, 23 males and one female. The age ranged from 46-103 years with a mean age of  $76 \pm 7$  years. The majority of our cases were between the age range of 60-90 years. The youngest patient was 46 years old and had fibrolamellar carcinoma. All others were above 60 years of age. None of the patients was alcoholic. The main symptoms at presentation were pain

abdomen (83%), loss of appetite (67%), loss of weight (21%), and vomiting (8%). The mean duration of symptoms was one month and most of the patients were already registered in the hospital previously for diabetes, cardiac diseases, hypertension or chronic liver disease. Hepatomegaly was seen in 75%, splenomegaly in 37%, ascites in 50% jaundice in 41% and anemia in 33% of patients. Severe itching was noted in 12% and one presented with spontaneous rupture of HCC and shock. Investigations at presentation revealed anemia (hemoglobin < 11 gms/dl) in 25%, 17% had thrombocytopenia (platelets <100000), 42% had elevated SGOT and SGPT, 25% had high alkaline phosphatase, 37% had abnormal coagulogram, and low protein was found in 8%. Hyponatremia (serum sodium < 130 mmol/L) was seen in 66% cases. HbsAg was positive in 25%, anti-HCV in 29% and Bilharzial serology in a total of 41%. One of the patients had both HbsAg and anti-HCV positive. Twenty five percent patients had only Bilharzial serology positive and other 25% were negative for all the three serological markers. Alpha-fetoprotein was within five times normal range in 50%, 5-10 times normal in 29% and >10 times normal in 21% of our patients. The range of survival after diagnosis was 60 days to 6 years with mean survival of 11 months (for 22 patients). The patient who lived only for 60 days was a male with an aggressive course of the disease and the one with survival to 6 years was our youngest patients who had a fibrolamellar carcinoma with recurrent ascites. Both of these were excluded while calculating the mean survival. Co-morbid states were associated in many patients with following frequency:- Ischemic heart disease with arrhythmias in 71%, chronic bronchitis 12%, diabetes mellitus 25%, hypertension 25% chronic gastritis and hiatus hernia 25%, chronic calculous cholecystitis 8%, benign prostatic hyperplasia 8% and one had previously treated nasopharyngeal carcinoma. Most of the patients were repeatedly admitted to the hospital till their death. The pattern of admission was as follows: refusal to eat 33%, tense ascites for drainage 33%, cardiac disease 20%, repeated hepatic encephalopathy 16%, upper GI bleed and diabetes related causes in 8% each. The cause of death was massive GI bleed in 2 patients, hepatorenal syndrome in 2, spontaneous bacterial peritonitis, myocardial infarction, and spontaneous cardiac arrest in 1 each. Twelve of the patients died due to a combination of hepatic encephalopathy, coagulopathy and severe hypoproteinemia. Five of our patients are still alive and following regularly.

Our patients from Najran show certain unique features that have not been reported from other regions. For example, out of 24 patients that we have studied, there is only one single female. This gives us a male: female ratio of 23:1. The ratio reported from

elsewhere is between 4 to 6:1. We do not know the exact reasons for the male preponderance of HCC in this region and it needs to be re-confirmed by studies on a large scale and from cancer registers. Only six of our patients were HbsAg positive and seven were anti-HCV positive. One among these had both. The other 12 were negative for both these viral markers. HBV DNA is not available in Najran and we could not collect the result regarding this from patients returning from higher centers. Six other patients had only Bilharzial (anti-schistosomal antibodies by indirect hemagglutination) serology positive whereas the remaining six had all three serology tests negative. None of the patients were alcoholic. Hemachromotosis and Wilson's disease was ruled out where found necessary. Alpha-1-anti-trypsin deficiency was not considered in view of the age of the patients and lack of other concomitant clinical features. So, hepatitis B, hepatitis C, bilharzial liver disease or alcohol was not the underlying etiological factor for HCC in 25% of our cases. As this form one fourth of our cases, other possible etiological factors like aflatoxin need to be studied.

The mean survival of patients with HCC after diagnosis is reported to be around 2 months.<sup>6</sup> In our patients the mean survival was 11 months, which is far longer. Although our cases were inoperable at the time of diagnosis but despite this, the mean survival was not short as could be expected. Alpha-fetoprotein (AFP) levels were not very high in our patients. Around 50% of the patients had AFP that was just under five times the normal value. Elsewhere it has been reported that AFP levels were greater than five times normal in 80% of patients.<sup>6</sup> Keeping in view the longer survival and a low level of AFP, it may be postulated that the hepatocellular carcinoma seen in this part of the world may have a different natural history than presumed so far. In conclusion HCC is one of the common malignancies in southwestern provinces of Saudi Arabia. The prevalence of hepatitis B and C is also high in these regions. It is being presumed that high rates of HCC reflect the high occurrence of hepatitis B and C. However, a close look at patients in our study reveals that 50% of these are negative for both HbsAg and anti-HCV suggesting some other etiological factors for this malignancy. The malignancy is relatively slowly progressive as reflected by the mean survival of 11 months after diagnosis in these relatively elderly patients. Also AFP levels are not very high and male predominance is far more than reported elsewhere. It may be worthwhile to conduct a study to look into the epidemiology of HCC in this region in particular and rest of the country in general and its link with HCV and other possible causes as yet unknown.

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## **An experience with rigid oesophagoscopy**

Sir,

Rigid oesophagoscopy is a well-established endoscopic procedure for both diagnostic and therapeutic indications. Ritchie et al<sup>1</sup> studied the efficacy and safety of rigid oesophagoscopy in diagnostic and therapeutic setting in a consecutive series of 404 patients with oesophageal carcinoma and compared to that for flexible oesophagoscopy in the same group. They concluded that rigid oesophagoscopy in the presence of carcinoma retains an important diagnostic and therapeutic role which can be achieved with low incidence of perforation in high-risk patients. In another study<sup>2</sup> the same authors compared diagnostic rigid and flexible oesophagoscopy in carcinoma of the oesophagus and concluded that diagnostic oesophagoscopy can be achieved without perforation with either instrument, but the chance of diagnosing carcinoma was significantly greater with the rigid instrument. Manara et al<sup>3</sup> their experiences lead them to reject abandoning the rigid oesophagoscope for the flexible optical fibres also because even those ENT Departments with vast experience in the use of fibres are not always able to remove all kind of foreign bodies. Foreign body perforation of the oesophagus is a rare but important subentity of oesophageal

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**Table 1** - Indications number of patients and percentages.

Indication	No. of patients (%)
Oesophageal foreign body	110 (37)
Oesophageal carcinoma	84 (29)
Sideropenic dysphagia	59 (20)
Reflux oesophagitis	16 (5)
Oesophageal stricture	9 (3)
Neurological dysphagia	7 (2)
Cervical osteophytes	6 (2)
Pharyngeal pouch	3 (1)
Total	294 (100)

perforations, which responds well to surgical treatment.<sup>4</sup> The risk of iatrogenic perforation of the oesophagus was greatest in old patients who had a lump of meat stuck in the distal third of the oesophagus.<sup>5</sup> The objective of this study is to review the indications and complications of rigid oesophagoscopy in Sudanese patients (n=294) who had rigid oesophagoscopy from January 1995 to December 1999 at the ENT Department, Wad Medani Teaching Hospital Sudan. All these patients were clinically diagnosed and investigated before endoscopic examination by plain radiograph, Barium swallow and 10 patients who had rigid oesophagoscopy for the first time. All patients who had repeat endoscopy for stricture dilatation were excluded. All patients had the procedure performed under general anaesthesia with suxamethonium muscle relaxation using a Negus oesophagoscope. The author performed all procedures. Hospital records of these were studied 157 cases were females and 137 were males. Female to male ratio was 1.1:1. Patients' ages ranged from 8 months to 80 years. Table 1 shows the indications for rigid oesophagoscopy, number of patients and percentages. In 178 cases (60.5%), the procedure was performed for therapeutic indications such as foreign body removal or oesophageal dilatation for a stricture or rupture of a postcricoid web. In 116 patients (39.5%) the procedure was carried out for diagnostic purposes in cases presenting with dysphagia. Only 2 patients (0.7%) had oesophageal perforation due to difficult sharp foreign body extraction which resulted in mediastinitis, septicaemia and death. The slight increase in the female to male ratio 1.1:1 is most due to a relatively high incidence of oesophageal carcinoma and sideropenic dysphagia in female Sudanese patients. Manara et al<sup>3</sup> also noticed a

female preponderance in a study of foreign body extraction with rigid oesophagoscopy. In this study oesophageal foreign body accounted for 110 cases (37%). Descriptive features of oesophageal foreign body by age, site and symptoms were largely compatible to those reported in the literature. Coins were the most frequent foreign body in children and meat was the most common offender in the material taken as a whole. Oesophageal carcinoma accounted for 84 cases (29%). the efficacy and safety of rigid oesophagoscopy in the diagnosis of oesophageal carcinoma is well-established.<sup>1,2</sup> In 10 cases (12%) of these carcinoma patients, initial biopsy with flexible endoscope failed to prove malignancy. In all carcinoma patients (100%) who had rigid oesophagoscopy histopathology reports confirmed the diagnosis. Sideropenic dysphagia or Plummer-Vinson syndrome was encountered in 59 patients (20%). The high incidence of this condition among Sudanese patients was previously noticed by the author and reported. All these patients underwent endoscopic dilation and good results without any complications were achieved. In 16 patients (5%) who presented with dysphagia, there was evidence of reflux oesophagitis and no other pathology was detected. This low number of patients with reflux oesophagitis may be explained by ethnic differences in gastro-oesophageal reflux disease. Nine patients (3%) had benign oesophageal strictures, which were successfully dilated without any complications. In 7 patients (2%) with dysphagia of neurological nature, rigid endoscopy was carried out to exclude a concomitant malignancy. In 6 patients (2%) dysphagia was due to prominent anterior cervical osteophytes pressing on the upper oesophagus and the hypopharynx. The diagnosis of these cases may be established by conventional x-ray of the spine, oesophagogram and CT. Severe forms of this condition are encountered less commonly with Forestier's disease, which is diffuse idiopathic skeletal hyperostosis. Three patients (1%) had pharyngeal pouch as a cause for their dysphagia and rigid endoscopy was considered to exclude an associated carcinoma. Pharyngeal pouch usually occurs in people over 70 and endoscopic stapling is the method of choice for its treatment. Two patients (0.7%) had oesophageal perforation at the cervical oesophagus and died as a result of mediastinitis and septicaemia. These two patients were elderly poorly controlled diabetic females and they had difficult sharp foreign body extraction. Very early post-operative surgical emphysema of the neck and earache were the presenting symptoms. Perforation was confirmed radiologically. Parenteral antibiotics were started, naso-gastric tube was inserted but both patients died of septicemia within the first 48 hours. Iatrogenic perforation of a normal oesophagus with

foreign body manipulation is a known complication.<sup>4,5</sup> In this series no instrumental oesophageal perforations were encountered in patients with carcinoma of the oesophagus. Rigid oesophagoscopy is a cheap, useful and a safe procedure for both therapeutic and diagnostic purposes.

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## Ten tips for writing fair multiple choice questions

Sir,

Multiple choice questions (MCQs) are used successfully for many years in evaluation of under and postgraduate training. However, it has been noticed that keeping MCQs fair is difficult. No matter how enthusiastically they are made, there still remain some flaws. How to rectify these problems? In this letter a few tips are presented that may help in keeping the MCQs fair.

**Tip 1.** Stem should be a statement (scenario even better) rather than a single word. Example. Shock. A. May be cardiogenic or septic depending upon the etiology. B. Manifests as tachycardia and hypotension when uncompensated. C. Needs invasive monitoring including pulmonary wedge pressure. D. Needs broad spectrum antibiotic coverage when infection is suspected. E. Is usually

treated with colloids rather than crystalloids. As seen in the example that a single word is followed by long sentences. The question can be redrafted as a scenario. A 2 month old infant with 3 days history of diarrhea, presented to the A & E with oliguria. His vital signs revealed a BP of 50/34 mm of Hg with pulse of 190 mins. The most likely cause for his condition is (options:- A, B, C ...) or the appropriate intervention at this point include (options:- A, B, C ...).

**Tip 2.** Place all common elements in the stem of the item. Example. Double bubble sign on plain abdominal x-ray. A. Is consistent with pyloric stenosis. B. Is consistent with duodenal atresia. C. Is consistent with gall bladder tumors. D. Is consistent with cancer of pancreatic head. E. Is consistent with small gut obstruction. The phrase "in consistent with" is better included in the stem.

**Tip 3.** Arrange numerical order. Example. The incidence of twin pregnancy in UK is:- A. 1:4000, B. 1:10000, C. 1:5000, D. 1:12000, E. 1:8000. The options are not in any order (ascending or descending).

**Tip 4.** Make sure about the homogeneity of the distracters. Example. The incidence of same illness is higher in the next generation, it holds true for A. Sickle cell anemia, B. Hemophilia, C. Gullian-Barre syndrome, D. Down syndrome, E. Diabetes mellitus. The options are not homogenous. Option C is neither a chromosomal disorder nor inherited disorder. Same with option E, the exact mode of inheritance is not clear.

**Tip 5.** Avoid use of absolutes such as "always", "only", or never. Try not to use "none of the above" or all of the above" as options. Example. Neonatal jaundice. A. Always presents as unconjugated hyperbilirubinemia, B. Never occurs in breast fed infants, C. Occurs only in preterm infants, D. None of the above, E. All of the above. Medicine is a changing science so "never or always" are not good distracters. Similarly, when one of the options (A, B or C) are wrong, the choice "all of the above" can be easily eliminated.

**Tip 6.** Use plausible or logical distracter. Example. A patient with signs of heart failure should get: A. Cardiac consultation, B. Echocardiogram, C. EEG, D. Chest x-ray, E. Physiotherapy. Option C should be ECG, an electroencephalogram (EEG) is irrelevant to heart failure. Similarly, Option E does not make sense and it looks out of context. The word "chest physiotherapy" is more appropriate.

**Tip 7.** Avoid clues to the correct answer. Example. The non-pulmonary causes of respiratory distress in newborn include. A. Meconium aspiration syndrome, B. Respiratory distress syndrome, C. Pneumothorax with fractured ribs, D. Diaphragmatic hernia without pulmonary hypoplasia, E. Congenital heart disease. The options A and B

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**Table 1** - Checklist for fair multiple choice questions.

Checklist for fair multiple choice questions
Stem: No single words
All common elements in the stem
Numerical in order
Distracters should be homogenous
No use of always, never, all or none of the above
Distracters should be logical or plausible
No clues to the correct answer
Check the syntax and grammar
No double negatives in the stem and negative word underlined
No abbreviations, eponyms or acronyms

are wrong as the stem indicates non-pulmonary causes. Similarly option C has two components so cannot be the right choice. D is long one with two components. so by exclusion one could easily pick up E as a right response.

**Tip 8.** Check the syntax and grammar. Example. Which of the following is a well-known complication of obstructed labor? A. bleeding and anemia, B. Use of forceps, C. Cesarean section, D. Neonatal asphyxia, E. Increasing mortality. Option A contains two parts while the stem says “a well-known complication”, so can be easily eliminated. Option B when read with the stem does not seem to be in correct syntax, use of forceps is not a complication of obstructed labor. Similarly obstructed labor is an indication rather than a complication of cesarean section. In option E, the stem is not in syntax with the word “increasing”.

**Tip 9.** Avoid negative statements or underline it. Example. Vomiting is not uncommon in each of the

following except. A. Peptic ulcer, B. Food poisoning, C. Meningitis, D. Head trauma, E. Anemia. The stem contains double negatives “not uncommon”. Also the word except is not underlined. Such statements confuse the examinees.

**Tip 10.** Avoid using abbreviation, eponyms and acronyms. Example. UTI is common in A. Edward syndrome, B. Vater’s association, C. SCID, D. Prune-belly syndrome, E. Males than females. UTI is urinary tract infection. Edward syndrome is trisomy 18. Prune-belly syndrome is also called triad syndrome or Eagle-barrett syndrome. SCID is abbreviation for severe combine immune deficiency. Better avoid using these.

In summary, MCQs should be fair, with least flaws. A checklist (Table 1), should be followed before qualifying MCQ for examination.

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