

STUDY OF ETIOLOGY OF HEPATOMEGALY WITH SPECIAL EMPHASIS ON NON ALCOHOLIC FATTY LIVER DISEASE AT A TEACHING HOSPITAL

*Ritu Karoli, Jalees Fatma, Vijay Singhal, Almas Qureshi,
Pragya Mishra, Pushker Singh, Ashok Chandra
Department of Medicine*

Era's Lucknow Medical College and Hospital, Lucknow, Uttar Pradesh India- 226003.

ABSTRACT

Hepatomegaly may be a presenting sign or symptom of the patient's illness or it may be an incidental finding in patients being examined for various other reasons. At present, many patients are diagnosed with liver disease who are asymptomatic and who have been found to have hepatomegaly or abnormalities in biochemical liver tests. These asymptomatic or undiagnosed liver diseases are of great concern so as to prevent various life threatening complications and better future outcome of patients. The present study was planned to explore of spectrum of causes of hepatomegaly from common to rare in a teaching hospital.

In our cross-sectional study all consecutive patients >18 years old with hepatomegaly detected on clinical examination and/or in ultrasonographic assessment (liver span >15cm) attending as medical outpatient department were enrolled. Depending on the clinical diagnosis based on detailed history and clinical examination, patients were subjected to hematological and biochemical investigations as required. Both infective and non infective causes constituted two equal halves. Acute viral hepatitis and dengue fever (15% each) were the commonest infective causes of hepatomegaly. Among non-infective causes NAFLD was the most common (21%) followed by congestive heart failure (18%). Seasonal variation showed increased prevalence of infective causes during the rainy season while non-infective causes were more common in winter and autumn.

Liver diseases are common in our population with diversified etiology, many are asymptomatic or may present only with liver enzyme abnormalities. There is almost equal prevalence of infective and non infective causes for hepatomegaly and nonalcoholic fatty liver disease has emerged as an important cause of hepatomegaly.

Keyword: Hepatomegaly, NAFLD, Liver diseases

INTRODUCTION

The liver holds a position of singular importance in the system, performing numerous metabolic functions. Hepatomegaly, a very obvious clinical marker of underlying liver pathology, was derived from Greek word hepar (liver)+ megas (large). It is abnormal enlargement of the liver that is usually a sign of disease, often discovered by percussion and palpation as part of a physical examination. Causes of liver enlargement are many. Liver size is determined by several factors, including volume of portal blood flow, amount of hepatic venous pressure and resistance, presence of infiltrative processes (e.g., inflammatory, metabolic, neoplastic, and cystic processes), and patency of bile flow. Hepatomegaly may be a presenting sign or symptom of the patient's illness or it may be an incidental finding in patients being examined for various other reasons.

Hepatomegaly occurs in liver diseases per se, systemic infections, systemic venous congestion, infiltrative diseases such as lymphoma, amyloidosis, storage diseases and in immune mediated diseases as part of reticuloendothelial hyperplasia. Nonalcoholic fatty liver disease (NAFLD) in recent years has shown tendency to shift up in the list of causes of hepatomegaly. According to the available studies fatty liver affect 20-25% of Indian population (1-2). NAFLD being asymptomatic in most of the patients encompasses a histological spectrum ranging from steatosis to steatohepatitis, advanced fibrosis and cirrhosis in absence of consumption of significant alcohol (3-4). NAFLD is the most common cause of liver disease in the western world (5-7).

NAFLD is now believed to be an integral part of metabolic syndrome which comprises a cluster of

Address for correspondence

Prof. Ritu Karoli

Department of Medicine,
Era's Lucknow Medical College &
Hospital, Sarfarazganj, Hardoi Road,
Lucknow-226003, India
Email: ritu.karoli@rediffmail.com
Phone no: +919415547894

abnormalities (abdominal obesity, atherogenic dyslipidemia, hypertension, elevated plasma glucose, prothrombotic state and insulin resistance (8-9).

At present, many patients are diagnosed with liver disease who are asymptomatic and who have been found to have hepatomegaly or abnormalities in biochemical liver tests as a part of a routine physical examination or screening for blood donation or for insurance or employment. These asymptomatic or undiagnosed liver diseases are of great concern so as to prevent various life threatening complications and better future outcome of patients. The present study was planned to explore of spectrum of causes of hepatomegaly from common to rare in a teaching hospital.

MATERIAL AND METHODS

In a cross-sectional study all consecutive patients >18 years old with hepatomegaly detected on clinical examination and/or in ultrasonographic assessment (liver span>15cm) attending as medical outpatient department of Era's Lucknow Medical College between January 2010 to December 2010 were enrolled (10-11). Exclusion criteria included pregnancy or patients who were not willing to participate. A written informed consent was taken from all the participants and study protocol was approved by the Institutional Ethics Committee.

Each patient of the study population had been subjected to detailed history that included symptomatology, history of alcohol consumption, drug history, high risk behavior (illicit/intravenous drug abuse, sexual promiscuity, tattooing) blood/blood product transfusion, needle prick or other modes of blood borne transmission, history of travel, consumption of contaminated food and water, systemic illness and detailed family history of significant systemic illnesses. Detailed general examination including anthropometric measurements and systemic examination was done in each patient.

Depending on the clinical diagnosis based on detailed history and clinical examination, patients were subjected to hematological and biochemical investigations as required and when feasible. Hematological parameters included hemoglobin, complete blood counts, coagulation profile, peripheral blood smear for parasites, stool examination, widal, viral markers for hepatitis, serology for dengue and amoebiasis, blood urine sputum cultures were done. Abdominal ultrasonography was performed in all the patients while chest skiagram, electrocardiography and echocardiography were done when required. Biochemical tests comprised of plasma glucose, electrolytes, lipid profile, renal and liver function tests. The diagnosis of NAFLD was based on presence of hepatic steatosis as bright/echogenic liver on

abdominal ultrasound (12). Hepatic steatosis was defined as diffuse increase in fine echoes in liver parenchyma with impaired visualization of intrahepatic vessels and the diaphragm after exclusion of alcohol consumption, smoking, positive hepatic markers of viral hepatitis, autoimmune hepatitis, Wilson's disease, hemochromatosis alpha-1 anti-trypsin deficiency and medications known to cause fatty liver (methotrexate, estrogens, amiodarone, tamoxifen). Ultrasonography was performed by the same radiologist who was blinded for subjects's medical history and diagnosis. A high resolution B-mode scanner of General Electric Logic 5 with a 3.5 MHz convex-array probe was used.

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (SPSS version 15.0, SPSS Inc., Chicago, IL) was used for statistical analysis. Data were expressed as percentages, mean values (with standard deviations), or Differences between groups were analyzed with chi-square test for proportions, and the Students *t* test for means. Results were defined as statistically significant when the *P* value (2-sided) was less than 0.05. Chi square test of goodness of fit has been applied for seasonal variation.

RESULTS

In present series, the causes of hepatomegaly were broadly categorized into infective and non-infective. (Table 1), interestingly both infective and non-infective causes constituted two equal halves. Acute viral hepatitis and dengue fever (15% each) were the commonest infective causes of hepatomegaly followed by malaria, enteric fever and liver abscess (6%, 5% and 4% respectively). All the other infective causes together contributed for the rest of 5% of all cases. Among non-infective causes NAFLD was the most common (21%) followed by congestive heart failure (18%) (as shown in Table 2).

As far as the symptomatology was concerned, infective causes were marked by fever, jaundice, anorexia and abdominal complaints while right hypochondrium pain was the most common complaint of patients with NAFLD

Seasonal variation showed increased prevalence of infective causes during the rainy season (Table 3), while non-infective causes were more common in winter and autumn. The presentation of NAFLD and infective disorders was at any early age. The prevalence of NAFLD was more common among those aged between 31 to 50 years (82.3%) and infectious disorders being more common in 21 to 40 years age group (n=32; 64%). Non-infectious non-NAFLD diseases were more common in elderly age group (>50 years; 72.7%). The prevalence of NAFLD was more common in females

than males. Significantly higher proportion of NAFLD patients were obese as compared to both non-infective non-NAFLD and infective disorders. Mean liver span of patients with NAFLD patients was significantly lower than those with non-infective non-NAFLD patients ($16.6 \pm 2.12\text{cm}$ vs $18.5 \pm 1.8\text{ cm}$, $p=0.03$). The derangement of liver functions was maximum in infectious diseases and minimum in NAFLD patients. Lipid parameters were more deranged in patients with NAFLD as compared to non-infective non-NAFLD group patients.

DISCUSSION

Hepatobiliary diseases are common in our population with diversified etiology, many are asymptomatic or may present only with liver enzyme abnormalities. Because of geographic variation etiology of liver diseases may be different in our population compared with western world. Investigating liver diseases in resource poor settings is difficult due to limited access to laboratory facilities and financial constraints. Therefore very few studies have addressed this issue of causes of hepatomegaly or liver diseases in tropical countries. In our study also we could perform investigations as required and whenever feasible basis. Maharaj et al had done a hospital based study way back in 1986 (13).

The present study was carried out to revisit the causes of hepatomegaly in view of changing lifestyle and health related awareness and to estimate prevalence of recent clinical entities such as NAFLD. An effort was also made to evaluate the incidence of indeterminate causes and effect of seasonal variations on etiology of hepatomegaly. Hepatomegaly is a non specific sign with many causes, which can broadly be broken down into infection, infiltrative diseases, direct toxicity, hepatic tumors, or metabolic disorders. Thus hepatomegaly is the reflection of an underlying disorder and it is essential to understand its cause and then prepare a strategy to manage it. In the present series, we categorized the causes of hepatomegaly broadly into two— infective and non-infective. The infective causes included acute viral hepatitis, dengue fever, malaria, enteric fever, liver abscess and abdominal tuberculosis and collectively accounted for 50% cases of hepatomegaly. Acute viral hepatitis remains a public health problem in India despite improving sanitation, health awareness and socio-economic conditions. Dengue fever emerged out to be another most important cause (15%). This might be due to an unprecedented outbreak of dengue fever in Northern India during the period of study. Abdominal tuberculosis, malaria and HIV were other less common causes observed in infective group of hepatomegaly. Among non-infective causes the commonest were non-alcoholic fatty liver disease and congestive hepatomegaly.

In the present study we had made an attempt to understand the prevalence of different causes of hepatomegaly over different seasons. It was as per expectation that the incidence of infective causes of hepatomegaly was maximum during the rainy season (36%) as compared to the other seasons (20% to 24%). Rainy season is traditionally considered to be a reason when epidemics and contagious diseases spread quickly. There was a significant association among different hepatic disorders as regards the age of affected patients. Association of non-infectious non-NAFLD diseases with elderly age group could be understood easily as most of the times these diseases are associated with some chronic or lifestyle disorders mainly involving cardiovascular disorders which are at their peak among elderly.

The important finding of the present study was non-alcoholic fatty liver disease in a substantial number of patients (21%). This less diagnosed liver disorder which is identified by raised liver transaminases or hepatic steatosis on ultrasonography is becoming a common entity.

Nonalcoholic steatohepatitis (NASH) emerged from an anecdotal disease first described by Ludwig et al in 1980 to the most common cause of incident chronic liver disease at the end of the current decade (14). It was thought to be a benign condition but is now increasingly recognized as a major cause of liver related morbidity and mortality. Non-alcoholic fatty liver disease (NAFLD) is commonly associated with components of the metabolic syndrome. This strongly supports the notion that NAFLD is the hepatic manifestation of the syndrome. Mishra et al (28) found the prevalence of metabolic syndrome and NAFLD to be 24% and 14.8%, respectively, in non-alcoholic North Indian men (15). The prevalence of NAFLD in the general population has been reported by Mohan et al (2) as 22% in normal glucose tolerance to 55% in patients with type 2 diabetes (16). Increasing recognition of the importance of NAFLD and its strong relationship with the metabolic syndrome has stimulated an interest in the possible role of NAFLD in the development of cardiovascular disease (CVD).

The limitations of our study were its small sample size and cross-sectional design. Though no such type of study based on hepatomegaly has been done earlier in this population.

CONCLUSION

Liver diseases are common in our population with diversified etiology, many are asymptomatic or may present only with liver enzyme abnormalities. There is almost equal prevalence of infective and non infective causes for hepatomegaly and nonalcoholic fatty liver

disease has emerged as an important cause of hepatomegaly which can have systemic consequences as it worsens insulin resistance.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

REFERENCES

1. Singh SP, Nayak S, Swain M, Rout N, Mallik RN, Agrawal O, Meher C, Rao M. Prevalence of nonalcoholic fatty liver disease in coastal eastern India: a preliminary ultrasonographic survey. *Trop Gastroenterol* 2004;25:76-79.
2. Amrapurkar D, Kamani P, Patel N, Gupte P, Kumar P, Agal S et al. Prevalence of non-alcoholic fatty liver disease: population based study. *Ann Hepatol*, 2007;6:161-163.
3. Farrell GC, Larter CZ, Nonalcoholic fatty liver disease: from steatosis to cirrhosis. *Hepatology*, 2006;43:S99-S112.
4. Bellentani S, Saccoccio G, Masutti F, Croce LS, Brandi G, Sasso F et al. Prevalence of and risk factors for hepatic steatosis in Northern Italy. *Ann Intern Med*, 2000;132:112-117.
5. Clark JM, Brancati FL, Diehl AM. The prevalence and aetiology of elevated aminotransferase levels in the United States. *Am J Gastroenterol*, 2003;98:960-7.
6. Clark JM, Diehl AM. Nonalcoholic fatty liver disease: an underrecognized cause of cryptogenic cirrhosis. *JAMA*, 2003;289:3000-3004.
7. Angulo P. Nonalcoholic fatty liver disease. *N Eng J Med*, 2002;346:1221-1231.
8. Targher G. Non-alcoholic fatty liver disease, the metabolic syndrome and the risk of cardiovascular disease: the plot thickens. *Diabet Med*, 2007;24:1-6.
9. Bellentani S, Bedogni G, Tiribelli C. Liver and heart: a new link? *J Hepatol*, 2008;49:300-302.
10. Michael Glynn. Gastrointestinal system. In *Hutchison's Clinical Methods*, 22nd edition Editors Michael Swash, Michael Glynn. Saunders Elsevier London UK pp.117-146.
11. Carol M. Rumack, Stephaun R Wilson, J W Charboneau. *The Liver in Diagnostic Ultrasound* 3rd edition. Editors Jo-Ann M. Johnson. Elsevier Mosby London UK. pp. 77-145.
12. Saadeh S, Younossi ZM, Remer EM, Gramlich T, Ong JP, Hurley M. The utility of radiological imaging in non alcoholic hepatic disease. *Gastroenterology*, 2002;123:745-750.
13. Maharaj B, Cooppan RM, Maharaj RJ et al. Causes of hepatomegaly at King Edward VIII Hospital, Durban. *South Afr Med Journal*, 1986; 69: 183-184.
14. Ludwig J, Viggiano T, McGill DB, Ott BJ. Non alcoholic steatohepatitis: Mayo clinic experiences with a hitherto unnamed disease. *Mayo Clin Proc*, 1980;55:434-438.
15. Mishra S. Hyperinsulinemia predisposes to NAFLD. *Indian J Clin Biochem*, 2008;23:130-135.
16. Mohan V, Farooq S, Deepa M, Ravikuma R, Pitchumoni CS. Prevalence of non-alcoholic fatty liver disease in urban south Indians in relation to different grades of glucose intolerance and metabolic syndrome. *Diabetes Res Clin Pract*, 2009;84:84-91.

