Fatty liver in overweight and obese patients in Western part of Saudi Arabia

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Abstract:
The aim of the study is to determine the association of fatty liver diagnosed by ultrasound and obesity in patients presented to King Abdulaziz University Hospital.

Methods: A clinical notes review was performed of all patients undergoing evaluation for fatty liver associated with obesity over one year period between April 2005 and April 2004. Data included age, gender, nationality, BMI, serum level of alanine (ALT) and aspartate (AST) transaminases, bilirubin, albumin, HbA1c, cholesterol, triglyceride, LDL, and TSH, and clinical presentation of abdominal pain or the presence of hepatomegaly.

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Results - A total of 235 subjects were enrolled in the study. The mean age of the study group was 46 +/- 14.4 years with 82 males (35%) and 153 females (65%). Mean +/- SD aspartate aminotransferase level was 43.9 +/- 18.1 units/L, alanine aminotransferase was 56.2 +/- 5.1 units/L. Values of transaminase above the normal range was present in 15 (6.4%) patients only. Whereas values of cholesterol and triglyceride above normal range was seen in 17 (7.2%) patients. Over weight and obesity were the main risk factors in our study group. Mean BMI was 33.6 +/- 7.5 Kg/m2. Obesity with diabetes is the most important risk factor for fatty liver. 78 (33%) of our study group patients were diabetic. Other risk factors associated with fatty liver are metabolic syndrome which is reported in 14.9% and hypercholesterolemia in 3.8% subjects.

Conclusion and recommendations:
Overweight and obesity is the most important risk factor for fatty liver in Saudi Arabia. It is more prevalent in females. Ultrasound appears to be a useful non-invasive tool to determine liver involvement with fatty liver in obese adult cases in the absence of hypertransaminasemia.

We should encourage obese subjects for gradual weight reduction to improve the liver abnormalities.

Keywords: - Fatty liver, NASH, obesity, overweight, and abdominal ultrasound

Introduction
The term nonalcoholic fatty liver (NASH) was first used by Dr. Ludwig and colleagues in 1980 to describe a previously recognized clinicopathologic syndrome. The original syndrome was described predominantly in obese, diabetic women, who denied alcohol use, but in whom the hepatic histology was consistent with alcoholic hepatitis.

Nonalcoholic fatty liver disease is now recognized as the most common liver disease in the United States, with a prevalence of approximately 5% in the general population and reaching 25% to 75% in patients with obesity and type 2 diabetes mellitus. A prevalence of 7-10% has been reported in the general population of Saudi Arabia. 1,4

Nonalcoholic fatty liver disease covers a spectrum of disease ranging from simple fatty deposition in the liver to inflammation and finally to fibrosis and cirrhosis. 1,4 Although the exact etiology is not clear, it could possibly be part of large metabolic syndrome associated with insulin resistance, diabetes, obesity, and hypertension. Patients typically present with a symptomatic serum aminotransferase elevation of 2-3 times normal. Symptoms may include fatigue and abdominal pain. Physical examination may show hepatomegaly. 1,4 The gold standard test for diagnosis is liver biopsy. Although the procedure is effective as a prognostic indicator, but it is invasive and costly tool to diagnose fatty liver. 1,4

The imaging modalities most often used to identify hepatic steatosis include computed tomography and ultrasonography. Hyperdense (bright) liver indicates steatosis in ultrasonography 1,2. No medical treatment has been found to be totally effective. 1,4 Patients who are overweight or obese should be encouraged for gradual weight reduction which has been associated with improvement in liver abnormalities. 1,4 The prevalence of overweight and obesity is increasing in Saudi Arabia among Saudi and expatriates especially in females due to a change in dietary habit and sedentary life style. We studied the association of fatty liver diagnosed by ultrasonography and obesity in patients presented to King Abdulaziz University hospital.

Methods
A clinical notes review was performed on all patients undergoing evaluation for fatty liver with obesity over one year period between April 2003 to April 2004 at King Abdulaziz University Hospital. Fatty liver was diagnosed by ultrasonography using an ATL HDI 5000 abdominal probe at 20-3 MHz. Longitudinal, subcostal, supine, and oblique scans were performed. The ultrasonographic criteria of liver, kidney, echo discrepancy, Presence of hypertrophy (bright), echo penetration into the deep portion of the liver, and clarity of liver blood vessels structures were used to diagnose fatty liver. In most patients' medical charts serum level of alanine (ALT) aspartate (AST) transaminases, bilirubin, albumin, cholesterol, triglyceride, LDL,
and TSH were documented. Obesity was defined as body mass index (BMI > 30 Kg/m²), overweight (BMI =25-29.9 Kg/m²) Records data from study participants obtained at initial clinic visit included age, gender, nationality, weight, height, BMI, and clinical presentation of abdominal pain or presence of hepatomegaly.

Exclusion criteria for the study included primary liver disorders other than fatty liver that could account for steatosis including Wilson disease and hemochromatosis. Study patients denied alcohol consumption or use of drugogenic medications.

Results were expressed as mean +/- standard deviation. Using Student’s t test assuming equal values. Chi-square test, performed statistical analysis. Test considered being significant if p value is less than 0.05.

Results -

A total of 215 overweight and obese adult patients were enrolled in the study. The mean age of the study group was 46 +/-4.4 years with 82 males (35 %) and 133 females (65 %) with male to female ratio of 1:1.9. (49 %) 115 of them were Saudi and (51) 120 were non-Saudis (chart 1).

Table - 1: Laboratory data in obese patients with fatty liver

<table>
<thead>
<tr>
<th>Laboratory tests</th>
<th>Mean +/-SD</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT</td>
<td>43.9+/-6.18</td>
<td>31</td>
<td>17-519</td>
</tr>
<tr>
<td>AST</td>
<td>36.2+/-5.1</td>
<td>25</td>
<td>19-536</td>
</tr>
<tr>
<td>HbA1c</td>
<td>8.4+/-1.6</td>
<td>8</td>
<td>6-12.5</td>
</tr>
<tr>
<td>Albumin</td>
<td>38+/-4.6</td>
<td>39</td>
<td>16-47</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>12.4+/-18</td>
<td>8</td>
<td>2-144</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>5.3+/-1.4</td>
<td>5.2</td>
<td>2-14.2</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>5.3+/-1.4</td>
<td>1.6</td>
<td>0.1-12.1</td>
</tr>
<tr>
<td>TSH</td>
<td>6.64+/-13.5</td>
<td>3.31</td>
<td>0.2-95</td>
</tr>
</tbody>
</table>

ALT = alanine aminotransferase NR (7-53 IU/L)  
AST= aspartate aminotransferase NR (11-47 IU/L)  
HbA1c=glycated hemoglobin  
Albumin =36-50 g/L  
Bilirubin=1-18 mmol/L  
Cholesterol=1-5-5.2 mmol/L  
Triglyceride=0.6-3.3 mmol/L  
TSH = 0.27-4.2 IU/L

Biochemical Abnormalities
Mean serum aspartate aminotransferase level was 42.9+/- 3.18 units/L, alanine aminotransferase was 36.2+/- 5.1 units/L and bilirubin 12.4+/-18 mmol/L. Values of transaminase above the normal range was present in 15 patients (6.4%) only. Hyperbilirubinemia was seen on the same patients with hypertransaminasemia. The incidence of hypertransaminasemia was statistically not significant in relation to BMI or age of patients.

Four of the patients who had high levels of both enzymes (ALT, AST) above four fold of the normal value were mainly due to secondary diseases involving the liver, two patients had hemolytic anemia, one had congestive heart failure and the fourth had glycogen storage disease.

Values of cholesterol and triglyceride above normal range was present in (7.5%) 17 patients, 13 of them were diabetics. Mean cholesterol level was 5.3+/-1.4 mmol/L and mean triglyceride level was 5.3+/-1.4 mmol/L. The incidence of hypercholesterolaemia and hypertriglyceridaemia was not correlated to hypertransaminasemia in patients with fatty liver reported by ultrasound.

TSH was done in 68 patients (29%) to rule out hypothyroidism as a cause of obesity, overt hypothyroidism was noted in nine (3.8%) cases who were obese and who had fatty liver by ultrasound.

(Table-1)

Risk Factors-Over weight and obesity were the main risk factors in our study group. Mean BMI was 33.6 +/- 7.5 Kg/m². The mean BMI in females was 33.5 +/- 7.2 Kg/m². And in males 33.5 +/- 7.7. There was statically significant difference in the BMI between males and females with p value <0.005. Significant different in BMI between Shudi and non Shudi was also observed as illustrated in table 2.

A significant relationship was found between the presence of fatty liver and female sex (p value was 0.05). No significant relationship was found between the presence of fatty liver and age.

Diabetics were an important risk factor associated with obesity and fatty liver. 78 (33 %) of our study group patients were diabetics. The mean duration of diabetic was 136+/- 3.3 years and mean HbA1C was 8.4 +/-1.6, which was done in 13 patients only.

There were 25 cases (14.9%) of metabolic syndrome associated with non-alcoholic fatty liver. Metabolic syndrome is characterized by obesity, hyperinsulinemia, peripheral insulin resistance,
diabetes, hypertriglyceridemia and hypertension. Hypothyroidism was another risk factor associated with obesity and fatty liver, which comprised of 10 cases (4.2%). Almost all patients had abdominal pain as clinical indication to have abdominal ultrasound. Hepatomegaly with fatty infiltration as assessed by ultrasound was reported in 78 cases (33%) with mean liver size of 18.5±4.3 cm.

Discussion

Obesity, defined by a body mass index (BMI) 30 Kg/m2 is clearly associated with NASH. Furthermore, it was associated moderately overweight 10-to 40 percent more than their ideal body weight. We had found in this study that NASH to be very common in over weight and obese adults in western part of Saudi Arabia (Jeddah), and commonly observed in females of childbearing age. Previous epidemiological surveys have shown high prevalence of overweight and obesity among Saudi subjects. The prevalence of obesity in Saudi females subjects was the highest reported all over the world and a report of increasing obesity in females from different Arab community. The incidence of hypertransaminasemia in patients with fatty liver diagnosed by ultrasound is similar to other reports in the literature.

Obesity and type 2 diabetes often clusters together, hence 33 % of our subjects were diabetics. However, our study did not show any relationship between duration of diabetes or glycemic control with the severity of fatty liver. This could be biased result and explained by rather small sample size and the fact that Hb A1C was measured in 13 subjects only because this test was rarely available in the hospital.

Other risk factors associated for fatty liver like metabolic syndrome, which is characterized by obesity, hyperinsulinemia, peripheral resistance, diabetes, hypertriglyceridemia and hypertension was reported in 14.9% of our study group which was similar to other reports in the literature. Hypothyroidism was one of the risk factors associated with obesity and fatty liver which has been observed in 3.8% of our study group. Hypertransaminasemia was observed in patients with severe fatty liver; two patients had hemolytic anemia due to a deficiency of red cell Mg 2+ adenine triphosphatase, and one young adult patient had glycogen storage disease. The fatty liver could be discovered incidentally during routine abdominal ultrasound as workup of abdominal pain which is typically vague, non-descript aching in character. The common clinical findings of fatty liver was hepatomegaly, however no other stigmata of chronic liver disease like spider nevi, palmar erythema were noted in our study. A fourteen year old boy who had sickle cell anemia developed symptoms of hepatic encephalopathy which indicated decompensated liver disease due to fatty liver after evolution of other causes of liver cirrhosis.

Liver biopsy to assess stages of the disease and histological changes of steatosis were not carried out in any patient enrolled in the study because of the risk of the biopsy and also because the findings will not contribute to future management.

In conclusion

Overweight and obesity is coexisting risk factors for fatty liver in Saudi Arabia, and it is more prevalent in females. Ultrasound appears to be a useful non-invasive tool to determine liver involvement with fatty liver in obese adults even in absence of hypertransaminasemia. No medical treatment has been found to be totally effective. Patients who are overweight or obese should be encouraged for gradual weight reduction which has been associated with improvement in liver abnormalities.

Table 2: Comparison of BMI in Kg/m2 between sex and nationality in patients with fatty liver

<table>
<thead>
<tr>
<th>Character</th>
<th>Mean ±SD</th>
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<th>Range</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male BMI</td>
<td>33.5±7.7</td>
<td>32</td>
<td>25-63</td>
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<tr>
<td>Females BMI</td>
<td>33.5±7.4</td>
<td>32</td>
<td>25-71</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Saudis BMI</td>
<td>33±7.2</td>
<td>31</td>
<td>25-61</td>
<td></td>
</tr>
<tr>
<td>Non-Saudis BMI</td>
<td>31.9±7.7</td>
<td>32.5</td>
<td>25-71</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>
References


2. Adler M, Schiffner F. Fatty liver hepatitis and cirrhosis in obese patients. In J Med 1979; 67: 811-816.3-


