# Body mass index and waist circumference in non-alcoholic fatty liver disease

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## Abstract

**Objective** To evaluate the association of anthropometric indexes (body mass index and waist circumference) in patients with non-alcoholic fatty liver disease (NAFLD), and its association with insulin resistance (IR), metabolic syndrome (MS) and histological findings.

**Methods** From August 2003 to July 2004 a case series of 81 outpatients with clinic and/or histological diagnosis of NAFLD were selected at the Bahia University Gastro-Hepatology Clinic, Brazil. Liver function tests, lipid profile, glucose and insulin were performed in all patients. Body mass index (BMI) and waist circumference (WC) were determined according to WHO criteria. IR was measured by means of the homeostasis model assessment (HOMA) and IR was considered with HOMA ≥3. MS was defined according to the Adult Treatment Panel III (ATP III). Liver biopsy was performed in 37 cases.

**Results** Body mass index ≥ 30 kg $m^{-2}$ (obesity) was found in 39% of the cases and BMI ≥ 25–29.9 kg $m^{-2}$ (overweight) in 53%. BMI was correlated with IR ($r = 0.29$; $P = 0.02$) and WC with ALT ($r = 0.02$; $P = 0.03$). Increased WC also was related to IR and to MS. The presence of steatohepatitis with fibrosis on liver biopsy was associated with overweight (68%) and increase of WC (41%).

**Conclusions** Body mass index and WC are frequent associated with MS, IR and histological findings (steatohepatitis and fibrosis) in patients with NAFLD.

## Introduction

Alterations in anthropometric measurements, such as body mass index (BMI) and waist circumference (WC) are associated with metabolic conditions (hyperinsulinaemia, hypertriglyceridaemia and type 2 diabetes) and non-alcoholic fatty liver disease (NAFLD). These indexes also have been related to the severity of steatosis and steatohepatitis (Scheen & Luyckx, 2002).

Non-alcoholic fatty liver disease is a clinicopathological condition characterized by lipid deposition in the hepatocytes of the liver parenchyma. The pathological picture is similar to those of alcoholic-induced liver injury, but it occurs in individuals without history of chronic alcohol

ingestion. NAFLD has a large spectrum, that includes steatosis, steatohepatitis with and without fibrosis (NASH), cirrhosis and it can progress to the end stage liver disease (Matteoni *et al*., 1999). This liver condition is a frequent diagnosis in cases of cryptogenic cirrhosis and has been associated to hepatocellular carcinoma (Caldwell *et al*., 1999).

Non-alcoholic fatty liver disease is a multifactorial condition, however most frequently associated to obesity, diabetes and hyperlipidaemia. It also has been associated to insulin resistance (IR) and metabolic syndrome (MS). The prevalence of NAFLD in obese adults is estimated from 39 to 95% (Álvarez-Martínez & Pérez-Campos, 2002). Some studies have suggested that individuals with obesity or overweight and with central distribution of fatty are more likely to develop NAFLD (Ruhl & Everhart, 2003; Hu *et al*., 2004).

Lifestyle has been considered essential to the development of NAFLD/NASH and modifications in individual habits, and diets combined with physical activity have been recommended to these patients. Gradual weight loss with diet and exercise have been associated with control of risk factors of NAFLD, decrease of IR indexes and improvement of liver enzimes and histology (Luyckx *et al*., 2000; Okita *et al*., 2001).

Body mass index and WC are considered important parameters to evaluate the grade of obesity and to the follow-up of patients who are in treatment (Luyckx *et al*., 2000). The present study aimed to evaluate the importance of these anthropometric measurements in patients with NAFLD and its association with IR, MS and histological findings.

## Materials and methods

### Study design

A case series study.

### Study population

Eighty-one outpatients with clinical and histological diagnosis of NAFLD were selected from August 2003 to July 2004 at the Gastro-Hepatology Clinic, Federal University of Bahia, Brazil.

### Patient evaluation

Criteria to NAFLD were: negative or occasional ($\leq 20$ g day$^{-1}$) history of alcohol consumption; exclusion of other chronic liver diseases (hepatitis B, hepatitis C, genetic haemochromatosis and autoimmune conditions, drugs use); ultrasound evidence of hepatic steatosis.

Body mass index and WC were evaluated in all cases, according to the World Health Organization (WHO) criteria (WHO, 1997). Weight was measured in light clothing, without shoes, in kilograms and height was measured in centimetres, using a scale-integrated stadiometer. BMI was calculated as body weight (kg)/height$^2$ (m$^2$) and patients were categorized as normal weight (<25.0 kg m$^{-2}$), overweight (≥25.0 and $\leq$ 29.9 kg m$^{-2}$) and obese (≥30.0 kg m$^{-2}$). The obesity was classified in grade I (30.0–34.9 kg m$^{-2}$), grade II (35.0–39.9 kg m$^{-2}$) and grade III (≥40.0 kg m$^{-2}$) (WHO, 1997).

Standing WC was measured at the midway between the lowest rib and the iliac crest with a flexible tape. WC was classified according to the risk of metabolic complications: low (men <94 cm, women <80 cm); slightly increased (men 94–101 cm and women 80–87 cm) and increased (men ≥102 cm and women ≥88 cm). The last cut-off point was also taken to define central obesity (Lean *et al*., 1995; WHO, 1997).

Metabolic syndrome was defined according to the Adults Treatment Panel III (2001) and three or more criteria were considered: plasma glucose concentration of at least 110 mg dL$^{-1}$, WC ≥102 cm in men and ≥88 cm in women, serum high-density lipoprotein (HDL) cholesterol concentration <40 mg dL$^{-1}$ in men and <50 mg dL$^{-1}$ in women, blood pressure of at least 130/85 mmHg, and serum triglyceride concentration of at least 150 mg dL$^{-1}$.

The biochemical analyses included: liver enzymes as alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltranspeptidase (GGT), lipid profile, plasma glucose and serum insulin. Enzymes alterations were defined as an elevation above the upper limit of normal of the reference levels. The insulin resistance index (IRI) was measured by the homeostasis model assessment method (HOMA)

(Matthews *et al.*, 1985), and IR was considered when HOMA was ≥3.0 (Siqueira *et al.*, 2005).

Liver biopsy was performed in 37 of the 81 cases. Criteria for biopsy included serum ALT/AST determinations greater than 1.5 the normal level in more than two occasions, separate by at least 1 month, after attempt to control the risk factors. Histopathological classification was made according to Matteoni *et al.* (1999).

This study was approved by the Ethics Committee for Medical Research at Universidade Federal da Bahia, Brazil.

### Statistical analysis

Data were expressed as mean values ± standard deviation (SD), percentage and absolute values. Pearson's correlation coefficient was used to estimate linear relationship between variables. Categorical variables were tested by the chi-square test. Pearson's correlation coefficient was considered statistically significant at $P < 0.05$. The *Statistical Package for the Social Science* program (SPSS, Chicago, IL, USA, version 9.0, 1998) was used.

## Results

The mean age of the 81 cases was 44.6 ± 10.5 years; 60% were male.

### Body mass index

The Table 1 shows the clinical and serological data of 81 patients with NAFLD according to BMI. Thirty-two patients 32 (40%) were obese, 43 (53%) were overweight. Obesity grade I was observed in 24 (30%) and obesity grade II in 8 (10%).

The association between liver enzymes (AST, ALT and GGT) and IR in obese and overweight

**Table 1** Clinical and serological data according to body mass index (BMI) of 81 patients with NAFLD

| Variable | BMI | | | Total ($n = 81$) |
|---|---|---|---|---|
| | Normal ($n = 6$) | Overweight ($n = 43$) | Obese ($n = 32$) | |
| Sex | | | | |
| Male | 3 (50) | 28 (65) | 18 (56) | 49 (61) |
| Female | 3 (50) | 15 (35) | 14 (44) | 32 (39) |
| Age (years) | | | | |
| ≥45 | 4 (67) | 22 (51) | 12 (37) | 28 (47) |
| <45 | 2 (33) | 21 (49) | 20 (63) | 43 (53) |
| Occupational exposure to hepatotoxins | | | | |
| Yes | 2 (33) | 10 (23) | 4 (12) | 16 (20) |
| No | 4 (67) | 33 (77) | 28 (88) | 65 (80) |
| Serum AST | | | | |
| Elevated | 0 (0) | 16 (37) | 9 (28) | 25 (31) |
| Normal | 6 (100) | 27 (63) | 23 (72) | 56 (69) |
| Serum ALT | | | | |
| Elevated | 2 (33) | 27 (63) | 16 (50) | 45 (56) |
| Normal | 4 (67) | 16 (37) | 16 (50) | 36 (44) |
| Serum GGT | | | | |
| Elevated* | 2 (33) | 24 (57) | 13 (41) | 39 (49) |
| Normal | 4 (67) | 18 (43) | 19 (59) | 41 (51) |
| Insulin resistance† | | | | |
| Yes | 2 (40) | 11 (30) | 11 (42) | 24 (35) |
| No | 3 (60) | 26 (70) | 15 (58) | 44 (65) |
| Metabolic syndrome | | | | |
| Yes | 2 (33) | 5 (12) | 18 (56) | 25 (31) |
| No | 4 (67) | 38 (88) | 14 (44) | 56 (69) |

Values in parenthesis are percentages.
*Missing 1.
†HOMA (homeostasis model assessment method ≥3) in 68 patients.
AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transpeptidase.

patients were not significant ($P > 0.05$). The MS was found in 12% of overweight and in 56% of obesess ($P = 0.001$).

The correlation of BMI levels and serum AST ($r = 0.11$), ALT ($r = 0.10$) and GGT ($r = 0.02$) levels were not significant, however they showed a moderate positive linear correlation with HOMA levels ($r = 0.29$; $P = 0.02$).

*Waist circumference*

Waist circumference was low in 22 (27%) patients, slightly increased in 25 (31%) and increased in 34 (42%) cases (Table 2). Increased WC was strongly associated to IR ($P = 0.01$) and to MS ($P = 0.001$). Increased WC was not associated with increased serum AST, ALT and GGT ($P > 0.05$).

Waist circumference levels were linearly correlated with serum ALT levels ($r = 0.24$, $P = 0.04$), but not with AST ($r = 0.16$), GGT ($r = 0.01$) and HOMA ($r = 0.16$).

### Histopathological assessment

Liver biopsy was performed in 37 of the 81 patients. Simple steatosis was observed in eight (22%) patients, non-alcoholic steatohepatitis (NASH) in 23 (62%); 22 of these had fibrosis. Among the 22 patients with NASH with fibrosis, IR was observed in nine (41%), overweight (BMI ≥25.0 and ≤ 29.9 kg $m^{-2}$) in 15 (68%), obesity (BMI ≥30.0 kg $m^{-2}$) in six (27%) and increased WC in nine (41%).

## Discussion

In this case-series study, obesity was the most frequent risk factor to NAFLD, affecting 40% of the cases. Increased BMI (obesity and overweight) was associated with MS. These data are similar to others studies (Scheen & Luyckx, 2002; Álvarez-Martínez & Pérez-Campos, 2002).

**Table 2** Clinical and serological data according to waist circumference (WC) of 81 patients with NAFLD

| Variable | WC | | | Total ($n = 81$) |
|---|---|---|---|---|
| | Low ($n = 22$) | Slightly increased ($n = 25$) | Increased ($n = 34$) | |
| Sex | | | | |
| Male | 20 (91) | 16 (64) | 13 (38) | 49 (60) |
| Female | 2 (9) | 9 (36) | 21 (62) | 32 (40) |
| Age (years) | | | | |
| ≥45 | 10 (45) | 10 (40) | 18 (53) | 38 (47) |
| <45 | 12 (55) | 15 (60) | 16 (47) | 43 (53) |
| Occupational exposure to hepatotoxins | | | | |
| Yes | 9 (41) | 4 (16) | 3 (9) | 16 (20) |
| No | 13 (59) | 21 (84) | 31 (91) | 65 (80) |
| Serum AST | | | | |
| Elevated | 6 (27) | 9 (36) | 10 (29) | 25 (31) |
| Normal | 16 (73) | 16 (64) | 24 (71) | 56 (69) |
| Serum ALT | | | | |
| Elevated | 15 (68) | 13 (52) | 17 (50) | 45 (56) |
| Normal | 7 (32) | 12 (48) | 17 (50) | 36 (44) |
| Serum GGT* | | | | |
| Elevada | 13 (62) | 8 (32) | 18 (53) | 39 (49) |
| Normal | 8 (38) | 17 (68) | 16 (47) | 41 (51) |
| Insulin resistance† | | | | |
| Yes | 3 (16) | 6 (29) | 15 (54) | 24 (35) |
| No | 16 (84) | 15 (71) | 13 (46) | 44 (65) |
| Metabolic syndrome | | | | |
| Yes | 3 (14) | 1 (4) | 21 (62) | 25 (31) |
| No | 19 (86) | 24 (96) | 13 (38) | 56 (69) |

Values in parenthesis are percentages.
*Missing 1.
†HOMA (homeostasis model assessment method, ≥3) in 68 patients.
AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transpeptidase.

Obesity is a worldwide problem of public health and several studies have showed association of obesity and liver diseases (Naveau *et al.*, 1997; Nakao *et al.*, 2002). BMI and WC have been helpful to define obesity, overweight and central obesity.

Waist circumference measurement has been used to diagnose and to define central obesity. This type of obesity is related to visceral fat, IR, increased free fatty acid levels (Wajchenberg, 2000; Marchesini *et al.*, 2003) and to MS. We observed WC increased in 42% of our NAFLD patients. Another similar study (Marchesini *et al.*, 2003) reported WC increased in 44% among NAFLD patients.

Insulin resistance was frequently associated to central obesity in our patients with NAFLD. This result is compatible with other studies that have described this association (Marchesini *et al.*, 1999; Ruhl & Everhart, 2003; Hsiao *et al.*, 2004).

Elevated ALT levels in patients with NAFLD have been associated with accumulate components of the MS: obesity, central obesity and high levels of triacylglycerol (Marceau *et al.*, 1999; Clark *et al.*, 2003).

Body mass index and WC have been considered as predictors of NAFLD severity (Marceau *et al.*, 1999; Fassio *et al.*, 2004). Central obesity has been considered an independent predictor of steatosis (Clouston & Powell, 2004) and an independent risk factor to elevated aminotransferases levels in patients with NAFLD (Ruhl & Everhart, 2003). Among our patients, elevated levels of aminotransferases were not related to increased WC. However, central obesity was observed in 41% of the patients who presented steatohepatitis with fibrosis on liver biopsy.

Liver biopsy is considered the golden standard to NAFLD/NASH diagnosis, however hepatic steatosis on ultrasound or others image methods and exclusion of others liver diseases in patients without history of alcohol intake can define NAFLD diagnosis. Liver biopsy can be indicated in selected cases or in protocols. Ratziu *et al.* (2000) have suggested that obesity, overweight, age, ALT and triglycerides levels may define the best indication and time for liver biopsy in a NAFLD patient.

This study presented 37 NAFLD cases that underwent liver biopsy. Hepatic fibrosis was associated with increased measurements of BMI and WC.

In summary, BMI and WC are frequent associated with MS, IR and histological findings (steatohepatitis and fibrosis) in patients with NAFLD and may be helpful to evaluate risk and prognostic factors in these patients.

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