



CORRELATION OF CALF CIRCUMFERENCE WITH INSULIN RESISTANCE AND NAFLD

Dr Asha Maria Xavier

Specialist in Internal Medicine, NMC Royal Hospital, Sharjah, UAE.

Dr Damodar Shenoy

HOD and Professor of Medicine, Kasturba Medical College

ABSTRACT Non-Alcohol Fatty Liver Disease is strongly linked to insulin resistance. Calf circumference is a substitute for lower body adiposity and an inexpensive credible screening measure for the identification of subjects with aberrant adipose distribution. Recent studies have shown that lower body subcutaneous fat also plays a pivotal role in accumulation of free fatty acids indicating it is a risk factor in the pathogenesis of various metabolic disorders. Several studies have established that calf circumference may be a risk factor for metabolic disorders independent of waist hip ratio and Body mass index. One of the goals in this study is to look into the fact whether an infrequently used anthropometric parameter like calf circumference which represents both lean mass and peripheral fat has any correlation with Non-Alcohol Fatty Liver Disease.

KEYWORDS :**INTRODUCTION**

NAFLD is a chronic liver disease that may lead to liver cirrhosis and hepatic cellular carcinoma. It is the abnormal accumulation of lipids primarily in the form of triglycerides in individuals who do not consume significant amount of alcohol (<20g of ethanol/day).

The disease can be associated with other co-morbidities and affects 50 to 87% of diabetics¹, 44 to 57% of obese people⁸.

Definition

Non-alcoholic Fatty Liver Disease (NAFLD): Indicates the presence of fatty infiltration of the liver, defined as fat exceeding 5%–10% of liver weight and frequently taken as fat in >5%–10% macrosteatotic hepatocytes in biopsy specimens.

The obesity epidemic and increasing prevalence of the metabolic syndrome is predicted to be paralleled by an increasing prevalence of NAFLD in the future.³⁶

Steatosis in NASH is typically macro vesicular and inflammation of steatohepatitis is predominantly lobular, whereas intense portal inflammation with interface activity is more potent in other causes e.g. chronic viral, autoimmune or drug induced hepatitis.² In some patients of burnt out cirrhosis, features of steatosis and necroinflammatory activity may be absent.²⁴

Diagnosis

The diagnosis of NAFLD requires that (a) there is hepatic steatosis by imaging or histology, (b) there is no significant alcohol consumption, (c) there are no competing etiologies for hepatic steatosis, and (d) there are no co-existing causes for chronic liver disease.

Non-contrast enhanced CT is the most accurate CT technique to detect and characterize hepatic steatosis.³¹ Magnetic resonance imaging provides an accurate and rapid assessment of hepatic steatosis to a lower limit of 3%. MRS provides a sensitive, quantitative, non-invasive method to measure HTGC (hepatic triglyceride content).³² An MR equivalent of transient elastography (TE) has recently demonstrated excellent diagnostic accuracy with sensitivity and specificity of 98% and 99% respectively for detecting all grades of fibrosis.³³ Transient elastography (Fibroscan) is a non-invasive method of assessing liver fibrosis which can be performed at the bedside or in the outpatient clinic, it employs ultrasound-based technology to measure liver stiffness and had shown good results in patients with NAFLD.³⁴

Management

As patients with NAFLD without steatohepatitis have excellent prognosis from a liver standpoint, treatments aimed at improving liver disease should be limited to those with NASH.⁶

Participants with NAFLD have higher calf circumference than in those

without NAFLD (36.1 vs. 34.2 cm) which was statistically significant. The NAFLD risk elevated progressively from the lowest to the highest quartiles of calf circumference with the odds ratio of 1.84, 3.01, and 5.59, respectively after control for sex and age. Calf circumference was positively correlated with ALT, AST, GGT, diastolic blood pressure, systolic blood pressure, and total cholesterol, triglycerides, and inversely correlated with HDL-cholesterol in both simple and multiple adjusted linear regression analyses. There were positive associations of calf circumference with Homeostatic model assessment and insulin resistance (HOMA-IR) and fasting insulin levels in the all study population, after adjustment for potential risk factor. The multivariate- adjusted geometric mean of HOMA-IR was 0.83 higher and fasting insulin was 2.65 μ U/ ml higher for the subjects in the highest quartile compared with subjects in the lowest.⁽¹⁰⁾

In a univariate correlation analyses, all anthropometric measures evaluated the arm circumference (AC), thigh circumference (TC), and calf circumference (CC), Waist circumference (WC), Hip circumference (HC,) found to be positively correlated with lean body mass in men and women.

A study done by Boemeke L et al.,²⁰ in the year 2014-15, with an objective to evaluate the association between Neck Circumference (NC) and metabolic alterations in patients with non- alcoholic fatty liver disease on 82 patients, at Brazil, it was found that patients with altered NC had increased body mass index, abdominal circumference, insulin and HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) when compared to those with adequate NC.

In a study done by Saad M A N et al²¹., in the year 2011-13, at Brazil., with an objective to investigate the correlation of NC, other anthropometric measures, and body composition analysis with insulin resistance in individuals aged over 60 years attending a primary care center on 411 subjects, it was found that BMI, fasting blood glucose, fasting insulin, and HOMA-IR were not significantly different between the male and female groups. NC was positively correlated with WC, BMI and Waist Hip Ratio in men and women, respectively.

In a study done by Wang W et al²⁷, with an objective to evaluate whether neck circumference could be used as a valid and effective method for identifying obesity and insulin resistance in Chinese adults, on 3307 adults, it was found that NC correlated positively with BMI and WC in both sexes.

In a study done by Hu Y et al³¹., at China with an objective to analyze the correlation between neck circumference and non-alcoholic fatty liver disease and compare the predictive value of NC for NAFLD with that of other simple anthropometric measures, it was found that NC in women with NAFLD increased by 1 cm and fasting insulin (FINS) and homeostasis model assessment-insulin resistance (HOMA-IR) increased by 1.87 mIU/L and 1.43, respectively. Compared with other anthropometric measures, neck circumference-height ratio (NHR)

had a significant impact both on the incidence of NAFLD.

In a study done by Stabe C et al³⁴, with an objective to investigate the relationship of the neck circumference with the metabolic syndrome and insulin resistance in a large Brazilian population-based sample, within a wide range of adiposity and glucose tolerance, on 1053 Brazilian adults^{41,42}, it was found that T2DM diagnosis was present in 306 individuals, of whom 34% were men. NC correlated with WC and BMI in both men and women.

By reviewing some of the previously conducted studies, we get a glimpse of the relation between insulin resistance, calf circumference and NAFLD.

Aim and Objectives

Aim:

To analyse the correlation between Insulin Resistance and calf circumference in patients with Non Alcohol Fatty Liver Disease.

Objectives:

Primary Objectives:-

To assess whether calf circumference; representing lean mass & peripheral fat, is correlate with NAFLD.

Secondary Objectives:-

- To establish that calf circumference may be a risk factor for Insulin Resistance independent of waist circumference and BMI.
- To analyse whether Insulin Resistance is associated with NAFLD

Subjects

- All NAFLD patients attached to Kasturba Medical College, Mangalore who satisfy the inclusion/exclusion criteria were included in the study. The patients were included only after obtaining written informed consent.
- A questionnaire including the age, sex, history of chronic diseases and current use of medications were be recorded. Smoking habit, information of alcohol consumption and physical activity will be defined.
- Anthropometric information were collected by standardized protocol. Calf circumference will be collected on the lower right leg at the point of maximal circumference.
- Patient details such as height, weight, BMI, Waist-to-Hip ratio will be collected and all subjects will be defined as normal weight, overweight or obese.

Investigations and Clinical Assays to be Carried Out

- General Physical Examination and Systemic Examination
- FBS, Fasting Insulin
- AST, ALT, Fasting Lipid Profile
- Ultrasound abdomen
- HBsAgB, Anti HCV, ANA
- Serum Cerruloplasmin, Serum Ferritin
- Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)

MATERIALS AND METHODS

- Study Design :** Cross sectional study
- Period of Study :** August 2017 - August 2019
- Study Population :** Patients attending department of general medicine in Govt. Wenlock Hospital, KMC and allied hospitals, Mangalore
- Sample Size:** 150
- Sampling Method:** Convenient sampling with 95% confidence level and 7% absolute precision⁹, the sample size comes to be 148 for convenience made 150.

The study was started only after approval from the Institutional Ethics Committee (IEC) of Kasturba Medical College, Mangaluru.

Sample Size Calculation: The sample size was calculated using the formula:

= 1.96 at 95% Confidence level

= 0.84 at 7% precision,

= Combined SD, d = mean difference

Inclusion Criteria

- All NAFLD patients aged 18 years or older who consented to this study after NAFLD was diagnosed.
- NAFLD is categorised by excessive hepatic fat accumulation associated with insulin resistance and defined by the presence of

steatosis in more than 5% of hepatocytes according to histological analysis or after ruling out secondary diseases such as Alcoholic Fatty Liver Disease, Drug Induced Fatty Liver Disease, Hepatitis C, Autoimmune Hepatitis, Wilson's Disease, Haemochromatosis, Hypothyroidism, Hypopituitarism, Starvation, inborn errors of metabolism.³⁸

Exclusion Criteria

- Subjects with a medical history of known hepatic diseases such as Alcoholic Fatty Liver Disease, Drug Induced Fatty Liver Disease, Hepatitis C, Autoimmune Hepatitis, Wilson's Disease, Haemochromatosis, Hypothyroidism, Hypopituitarism, Starvation, inborn errors of metabolism.
- Subjects with daily alcohol consumption greater than 20 g for women & 30 g for men
- Patients with established diabetic neuropathy.
- Heavy weight body builders and professional athletes.

RESULTS

Data Analysis

- Primary endpoint –The primary endpoint is presented as proportion of patients with NAFLD who are Insulin Resistant as correlated by calf circumference. It will be summarized as a percentage with 95% confidence interval.
- Secondary endpoint – for correlation, chi square test was used

The SPSS Statistical Package (version 17.0; SPSS Inc., Chicago, IL) was used for all statistical analyses.

P value <0.05 will be considered as statistically significant

- The sex-wise distribution among the patients of the study showed majority males who were 90 (60%) and females were 60 (40%)
- There were majority patients who belong to the age group of 31–40 years, followed by 51–60 and 41–50 years. Least were from the age group >71 years. The mean age of patients was found to be 44.2 with a standard deviation of 12.09 years.
- The distribution of the patients based on co morbidities show majority didn't have any co morbidities. There were 6.7% with diabetes and 5.3% with hypertension and 4% with both diabetes and hypertension.
- In our study there were majority patients who had height between 171–180cm (46%). There were 29.3% with height 150–160cm and 24.7% with height 161–170cm.
- The study had weight majority between 71–80 kg followed by 34% between 61–70kg and least in 81–90 kg.
- Majority were with BMI more than 25 which is graded as over weight according to WHO for Asians and there were 49.3% with BMI <24.9.
- The waist hip ratio of patients showed that all males had waist hip ratio less than 1 and females there were 18 (12%) who had ratio >0.85.
- The fasting blood glucose showed 70.7% majority, with blood sugar <110 mg/dl. There were 22.6% with blood glucose level between 110–125 mg/dl. There were 6.7% with glucose level >126 mg/dl.
- The study showed that all the patients belong to HOMA-IR more than 2.9.
- The study showed that 53.4% belonged to 3rd and 4th quadrant and that 22.6% had calf circumference <36 cm.

The association between different factors and calf circumference (divided into quartiles) in our study was done using ANOVA it showed association and significant difference in age, sex, height, weight, waist hip ratio and serum insulin.

The study further subjected the variables into post hoc testing (Turkey HSD), this showed in age group difference in the 3rd and 4th quartiles.

- In case of waist hip ratio significance was seen between first and third quartile which ascertain the probability of diabetes with increasing waist and hip circumference.
- In case of serum insulin significance was seen in the group of people >42 cm calf circumference meaning to imply that in this study patients with increased calf circumference showed insulin resistance.
- The study saw correlation of different variables with respect to calf circumference, it showed positive correlation with sex, height, weight, BMI, waist hip ratio and serum insulin.

There was negative correlation which was significant with age.

- The study was able to establish a correlation between calf circumference and weight, increasing calf circumference was observed as the weight of the patients increased.
- The study observed that calf circumference decreased with extremes of age.
- All the patients in our study had greater probability for cirrhosis.
- All the patients in our study had insulin resistance

DISCUSSION

BMI

- In a study done by Vanjiappan S et al⁶, had 21.6% patients who were over weight and 54.3% who were obese. In our study there were 51% were over weight, which was much higher than the above study.
- Studies have shown that NAFLD is increased among obese patients. similar findings are seen in our study with 51% who had BMI>25

The waist hip ratio of patients showed that all males had waist hip ratio less than 1 and females there were 18 (12%) who had ratio >0.85.

The fasting blood glucose showed 70.7% majority, with blood sugar <110 mg/dl. There were 22.6% with blood glucose level between 110-125 mg/dl. There were 6.7% with glucose level >126 mg/dl.

- Targher G et al⁷, patients with type 2 Diabetes Mellitus have approximately 80% more intrahepatic fat content than age, sex, and body weight-matched non-diabetic controls, and their serum liver enzymes are less representative of the severity of intrahepatic fat accumulation.

Calf Circumference

- The study by Zhang W. et al²⁷. had mean calf circumference in males 35.7cm which is similar to the current study.
- The mean calf circumference in females was 34.6cm which is less than our study we had mean of 41.4cm.
- The study done by Choe EY et al., at Seoul, South Korea found a mean of calf circumference of 34.7± 3.3cm. In our study it was bit higher, it was found to be 39.08
- Erkan G et al., study saw significant difference and association of Waist hip ratio, BMI and sex among the NAFLD patients similar to the current study.
- The study by Vanjiappan S et al⁶, saw association of BMI which was significant and similar to the current study.

All the patients in our study had greater probability for cirrhosis and all had insulin resistance.

Association

The association between different factors and calf circumference (divided into quartiles) in our study was done using ANOVA it showed association and significant difference in age, sex, height, weight , waist hip ratio and serum insulin.

Post Hoc

The study further subjected the variables into post hoc testing(Turkey HSD), this showed in age group difference in the 3rd and 4th quartiles. In sex, height and weight difference was significant in all quartiles. In the case of waist hip ratio significance was seen between first and third quartile. In case of serum insulin significance was seen in the group of people >42 cm calf circumference.

- The study by Zhang W. et al⁹, showed that higher quadrants of calf circumference were in males and similar findings were seen in this current study. The risk elevated progressed from the lowest to the highest quartiles of calf circumference sex and age. Similar findings were seen in our study.
- The study by Zhang W. et al⁹, saw association with HOMA-IR score which was not seen in our study.

This study demonstrated a correlation of lean body mass with plasma glucose, fat and insulin levels.

- We studied the correlation of different variables with respect to calf circumference.
- It showed positive correlation with sex, height, weight, BMI, waist hip ratio and serum insulin.
- There was significant negative correlation with age. As age increases calf circumference was observed to decrease.
- Calf circumference reflects body muscle mass and peripheral subcutaneous fat.

The peripheral adiposity in the lower body was found to be associated with insulin resistance and glucose metabolism.

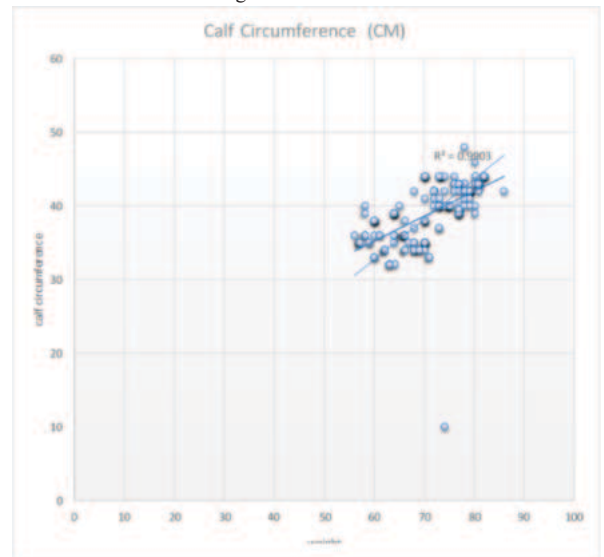


Figure 1 : Correlation Between Calf Circumference And Weight.

REFERENCES

- 1) Cernea S, Cahn A, Raz I. Pharmacological management of nonalcoholic fatty liver disease in type 2 diabetes. Expert review of clinical pharmacology. 2017 May 4;10(5):535-47.
- 2) Lonardo A, Nascimbeni F, Maurantonio M, Marrazzo A, Rinaldi L, Adinolfi LE. Nonalcoholic fatty liver disease: Evolving paradigms. World journal of gastroenterology. 2017 Sep 28;23(36):6571-92.
- 3) Dietrich P, Hellerbrand C. Non-alcoholic fatty liver disease, obesity and the metabolic syndrome. Best practice & research Clinical gastroenterology. 2014 Aug 1;28(4):637-53.
- 4) Manal F. Abdelmalek, Anna Mae Diehl. Harrison's Principles of Internal medicine. Nonalcoholic Fatty Liver Diseases and Nonalcoholic Steatohepatitis. 364. 19th edition. Mc Graw Hill publications. 2015.
- 5) Patel V, Sanyal AJ, Sterling R. Clinical presentation and patient evaluation in nonalcoholic fatty liver disease. Clinics in liver disease. 2016 May 1;20(2):277-92.
- 6) Vanjiappan S, Hamide A, Ananthakrishnan R, Periyasamy SG, Mehalingam V. Nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus and its association with cardiovascular disease. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2018 Jul 1;12(4):479-82.
- 7) Targher G, Byrne CD. Nonalcoholic fatty liver disease: a novel cardiometabolic risk factor for type 2 diabetes and its complications. The Journal of Clinical Endocrinology & Metabolism. 2013 Feb 1;98(2):483-95.
- 8) Yki-Järvinen H. Non-alcoholic fatty liver disease as a cause and a consequence of metabolic syndrome. The lancet Diabetes & endocrinology. 2014 Nov 1;2(11):901-10.
- 9) Zhang et al. Association of calf circumference with insulin resistance and non-alcohol fatty liver disease: the REACTION study BMC Endocrine Disorders (2017) 17:28
- 10) Takamura T, Kita Y, Nakagen M, Sakurai M, Isoe Y, Takeshita Y, Kawai K, Urabe T, Kaneko S. Weight-adjusted lean body mass and calf circumference are protective against obesity-associated insulin resistance and metabolic abnormalities. Heliyon. 2017 Jul 1;3(7):e00347.
- 11) Choe EY, Lee YH, Choi YJ, Huh BW, Lee BW, Kim SK, Kang ES, Cha BS, Lee EJ, Huh KB, Younossi ZM. Waist-to-calf circumference ratio is an independent predictor of hepatic steatosis and fibrosis in patients with type 2 diabetes. Journal of gastroenterology and hepatology. 2018 May;33(5):1082-91.
- 12) Erkan G, Sayın I, Polat FB, Çorakçı A, Ataç GK, Değertekin H. The relationship between insulin resistance, metabolic syndrome and nonalcoholic fatty liver disease in non-obese non-diabetic Turkish individuals a pilot study. Turk J Gastroenterol 2014; 25 (1): 63-8.
- 13) Yang KC, Hung HF, Lu CW, Chang HH, Lee LT, Huang KC. Association of non-alcoholic fatty liver disease with metabolic syndrome independently of central obesity and insulin resistance. Scientific reports. 2016 Jun 1;6: 27034.
- 14) Díez-Rodríguez R, Ballesteros-Pomar MD, Calleja-Fernández A, González-De-Francisco T, González-Herráez L, Calleja-Antolín S, Cano-Rodríguez I, Olcoz-Goñi JL. Insulin resistance and metabolic syndrome are related to non-alcoholic fatty liver disease, but not visceral adiposity index, in severely obese patients. Rev Esp Enferm Dig. 2014 Dec;106(8):522-8.
- 15) Kasturiratne A, Weerasinghe S, Dassanayake AS, et al. Influence of non-alcoholic fatty liver disease on the development of diabetes mellitus. J Gastroenterol Hepatol 2013; 28: 142-7.
- 16) Fan JG, Li F, Cai XB, et al. Effects of nonalcoholic fatty liver disease on the development of metabolic disorders. J Gastroenterol Hepatol 2007; 22: 1086-91.
- 17) Okamoto M, Takeda Y, Yoda Y, et al. The association of fatty liver and diabetes risk. J Epidemiol 2003; 13: 15-21.
- 18) Lallukka S, Yki-Järvinen H. Non-alcoholic fatty liver disease and risk of type 2 diabetes. Best Practice & Research Clinical Endocrinology & Metabolism. 2016 Jun 1;30(3):385-95.
- 19) Park JS, Cho MH, Ahn CW, Kim KR, Huh KB. The association of insulin resistance and carotid atherosclerosis with thigh and calf circumference in patients with type 2 diabetes. Cardiovascular diabetology. 2012 Dec;11(1):62.
- 20) Boemeke L, raimundo FV, Bopp M, Leonhardt LR, Fernandes SA, Marroni CA. The correlation of neck circumference and insulin resistance in NAFLD patients. Arquivos de gastroenterologia. 1 jan/march 2019
- 21) Saad MA, Rosa ML, Lima GB, Antunes da Cruz Filho R. Can neck circumference predict insulin resistance in older people? A cross-sectional study at primary care in Brazil. Cadernos de saude publica. 2017 Aug 21;33:e00060916
- 22) Alkassabany YM, Farghaly AG, El-Ghitany EM. Prevalence, risk factors, and predictors of nonalcoholic fatty liver disease among schoolchildren: a hospital-based study in

- Alexandria, Egypt. Arab Journal of Gastroenterology. 2014 Jun 1;15(2):76-81.
- 23) A, Pereira SE, Saboya CJ, Ramalho A. Nonalcoholic fatty liver disease relationship with metabolic syndrome Cordeiro in class III obesity individuals. BioMed research international. 2015.
 - 24) Bruno AD, Rodrigues MH, Alvares MC, Nahas-Neto J, Nahas EP. Non-alcoholic fatty liver disease and its associated risk factors in Brazilian postmenopausal women. Climacteric. 2014 Aug 1;17(4):465-71.
 - 25) Bugianesi E, Gastaldelli A, Vanni E, Gambino R, Cassader M, Baldi S, Ponti V, Pagano G, Ferrannini E, Rizzetto M. Insulin resistance in non-diabetic patients with non-alcoholic fatty liver disease: sites and mechanisms. Diabetologia. 2005 Apr 1;48(4):634-42.
 - 26) El-Karakasy HM, El-Raziky MS, Fouad HM, Anwar GM, El-Mougy FM, El-Koofy NM, El-Hennawy AM. The value of different insulin resistance indices in assessment of non-alcoholic fatty liver disease in overweight/obese children. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2015 Apr 1;9(2):114-9.
 - 27) Wang X, Zhang N, Yu C, Ji Z. Evaluation of neck circumference as a predictor of central obesity and insulin resistance in Chinese adults. International journal of clinical and experimental medicine. 2015;8(10):19107.
 - 28) Hatipoğlu N, Doğan S, Mazicioğlu MM, Kurtoglu S. Relationship between neck circumference and non-alcoholic fatty liver disease in childhood obesity. Journal of clinical research in pediatric endocrinology. 2016 March;
 - 29) Li L, Liu DW, Yan HY, Wang ZY, Zhao SH, Wang B. Obesity is an independent risk factor for non-alcoholic fatty liver disease: evidence from a meta-analysis of 21 cohort studies. Obesity Reviews. 2016 Jun;17(6):510-9.
 - 30) Mager DR, Yap J, Rodriguez-Dimitrescu C, Mazurak V, Ball G, Gilmour S. Anthropometric measures of visceral and subcutaneous fat are important in the determination of metabolic dysregulation in boys and girls at risk for nonalcoholic fatty liver disease. Nutrition in Clinical Practice. 2013 Feb;28(1):101-11.
 - 31) Hu Y, Chen J, Yang L, Chen P, Li J, Chen L, Chen J, Huang X, Zhang Y, Bu S, Huang Q. The value of neck circumference (NC) as a predictor of non-alcoholic fatty liver disease (NAFLD). Journal of clinical & translational endocrinology. 2014 Dec 1;1(4):133-9.
 - 32) Marchesini G, Brizi M, Morselli-Labate AM, Bianchi G, Bugianesi E, McCullough AJ, Forlani G, Melchionda N. Association of nonalcoholic fatty liver disease with insulin resistance. The American journal of medicine. 1999 Nov 1;107(5):450-5.
 - 33) Sesti G, Fiorentino TV, Hribal ML, Sciacqua A, Perticone F. Association of hepatic insulin resistance indexes to nonalcoholic fatty liver disease and related biomarkers. Nutrition, Metabolism and Cardiovascular Diseases. 2013 Dec 1;23(12):1182-7.
 - 34) Stabe C, Vasques AC, Lima MM, Tambascia MA, Pareja JC, Yamanaka A, Geloneze B. Neck circumference as a simple tool for identifying the metabolic syndrome and insulin resistance: results from the Brazilian Metabolic Syndrome Study. Clinical endocrinology. 2013 Jun;78(6):.
 - 35) Pang Q, Zhang JY, Song SD, Qu K, Xu XS, Liu SS, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World Journal of Gastroenterology: WJG. 2015 Feb 7;21(5):1650.
 - 36) Motamed N, Sohrabi M, Ajdarkosh H, Hemmasi G, Maadi M, Sayeedian FS, Pirzad R, Abedi K, Aghapour S, Fallahnezhad M, Zamani F. Fatty liver index vs waist circumference for predicting non-alcoholic fatty liver disease. World journal of gastroenterology. 2016 March 14.
 - 37) Boemeke L, raimundo FV, Bopp M, Leonhardt LR, Fernandes SA, Marroni CA. The correlation of neck circumference and insulin resistance in NAFLD patients. Arquivos de gastroenterologia. 1 jan/march 2019.
 - 38) EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. JHepatology(2016).