The Relationship Between Serum Visfatin, Blood Glucose, Lipid Metabolism and Nonalcoholic Fatty liver Disease in Simple Obese Children

mostafa Ahmed EL Foly

Minia University Faculty of Medicine

Iubna Anas Fawaz

Cairo University Kasr Alainy Faculty of Medicine

Ashraf Mohammed Osman

Minia University Faculty of Medicine

Salwa Hussien Swelam

Minia University Faculty of Medicine

Noura Elbakry (✉ nour_elbakry86@yahoo.com)

Minia University Faculty of Medicine

Research article

Keywords: Non-alcoholic fatty liver disease, metabolic syndrome, Visfatin

Posted Date: August 13th, 2019

DOI: <https://doi.org/10.21203/rs.2.12769/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Abstract Background Non-alcoholic fatty liver disease (NAFLD) ranges from simple steatosis to nonalcoholic steatohepatitis (NASH) leading to fibrosis and potentially cirrhosis, and it is one of the most common causes of liver disease worldwide. NAFLD is associated with other medical conditions such as metabolic syndrome, obesity, cardiovascular disease and diabetes. Visfatin is an adipocytokine hormone, which exerts an insulin-like effect by binding to the insulin receptor-1, we aim to investigate the correlation between serum Visfatin and both glucose, lipid metabolism and nonalcoholic fatty liver disease in Simple obese children. **Methods:** This prospective study included 62 children clinically evaluated as obese and 35 apparently healthy children, age and sex matched as controls. Patients were recruited from the emergency department, in-patient wards and out-patient clinics of the pediatric department of EL-Mina University, children's hospital. While controls were collected from healthy school children during day time between September, 2016 and October, 2017. Fasting Visfatin, glucose, hemoglobinA1c and lipid levels were assayed and abdominal ultrasonography was done for detection of NAFLD. **Results** There was a statistically significant correlation between serum Visfatin level and BMI ($p < 0.01$), cholesterol levels ($p < 0.01$), triglycerides levels ($p < 0.01$), LDL levels ($p < 0.01$), HDL levels ($p < 0.01$) in both overweight and obese groups. **Conclusions:** Visfatin plays an important role in regulation of glucose and lipid metabolism, also in inflammation and insulin resistance, suggesting a role in pathogenesis of Non-Alcoholic Fatty Liver Disease (NAFLD). **Key words:** Non-alcoholic fatty liver disease; metabolic syndrome; Visfatin

Background

Obesity (which is defined as either a body mass index (BMI) at or above the 95th percentile for children of the same age and sex specific BMI percentiles and overweight as a BMI at or above the 85th percentile but lower than the 95th percentile for children of the same age and sex) is concerned a major health problem in growing children with defined morbidity in different ages.[1] In Egypt, records of 2004 shown dramatic increase of obesity in Egyptian population with 2.4% among boys and 4.5% among girls of primary school children increased to 5.5% among boys and 5.6% among girls in 2007.[2,3] Among primary school children, 6% were obese and 10.5% were overweight with higher percentage in girls[4].

Metabolic syndrome is a major health problem not only in adult population but also in children. Patient is considered to have metabolic syndrome when having central obesity plus any two of the following four factors; raised triglyceride > 150 mg/dL, Reduced HDL < 40 mg/dL in men and < 50 mg/dL in women, raised systolic BP > 130 or diastolic BP > 85 mmHg, or treatment of previously diagnosed hypertension, raised fasting blood glucose (FBG) level 100 mg/dL, or previously diagnosed type 2 diabetes. [5]

Nonalcoholic Fatty liver disease (NAFLD) has a strong correlation with obesity, with a prevalence near 80% in obese patients while recorded only in 16% of populations with average BMI without metabolic risk factors.[6] NAFLD is considered as the hepatic presentation of metabolic syndrome and the severity of fatty liver in obese children runs in parallel with the degree of poor glycemic status.[7]

Adipose tissue is an active endocrine inflammatory organ in obese adults but its role in children still in debate. It is classified as white adipose tissue (WAT) and brown adipose tissue (BAT). [8–10]

Visfatin is a low molecular weight proteins secreted by WAT that exert many functions through several metabolic pathways. It has an endocrine, autocrine as well as paracrine regulatory roles in adipose tissue and cell proliferation, by exerting an Insulin mimicking effect. Visfatin binds and activates the insulin receptor, activating the downstream signaling molecules and allowing glucose transport to muscle and adipocyte tissue in addition to inhibiting hepatocyte glucose production, but not competing with insulin for its binding receptor.[11,12] also,Visfatin has a proinflammatory-atherosclerotic effect [7].

The aim of this work is to estimate the relationship between serum Visfatin, blood glucose, lipid metabolism and nonalcoholic fatty liver disease in simple obese children.

Methods

Ninety seven children were enrolled in this study, sixty two were enrolled as patient while the other thirty five children were enrolled as controls (age and sex matched) (group I).The enrolled patients were 2–17years old fulfilled the following inclusion criteria:children with a BMI at or above the 85th percentile but lower than the 95th percentile were considered overweight and planned as group II, while children with a BMI exceeding the 95th were considered obese and planned as group III according to the Egyptian Growth Charts, (2002).[13]

Patients known diabetes, under treatment for chronic diseases (epilepsy, bronchial asthma, etc) and under steroids therapy all were excluded. The study conducted according to the principles of Helsinki and agreed by the faculty of medicine, Minia university, Ethical committee (No: 116–5–2016).Informed written consents from the patient's caregiver were obtained. Regarding obesity patients were asked about onset and course of obesity and medications, family history of obesity, diet habits including food composition, number of meals and snacks per day and complications of obesity.Regarding patient's lifestyle; full history of patient's activities, including exercise and type of exercise, watching TV, computers (hours/day),sleeping hours and pattern of sleep and eating in late hours also,clinical examination stress on acanthosisnigricans, goiter, special dysmorphic facial features, Pubertal stage, manifestations suggestive of Cushing syndrome or genetic obesity, also anthropometric measurement including measurement of body height,body weight, waist circumference and BMI.

Sample collection: 10 ml of venous blood samples were taken for, fasting serum glucose, ALT, AST, urea, creatinine levels total cholesterol, LDL, HDL and triglycerides levels using fully automated chemical auto-analyzer Dimension-ES, USA. Serum Visfatin levels by ELISA

Ultrasound sagittal view of liver right lobe for the evaluation of fatty liver was performed.

Statistical analysis: The numerical data were presented as means—standard deviations while non-numerical data were presented as percentage. Two tailed t-tests were used to analyze differences

between the control and patients groups. *P-values* less than 0.05 were considered statistically significant. The magnitude of correlations were determined by Pearson's correlation coefficient. All the data were analyzed by statistical package Prism 3.0 (GraphPad software, San Diego, CA, USA). Figures were done by Microsoft Office Excel 2007. Receiver-operating curve (ROC) was done for detection of Visfatin sensitivity and specificity in prediction of fatty liver disease in obese children.

Results

In the present study, significant difference between obese, overweight children and healthy ones regarding bodyweight Z-score centile (mean $\pm$ SD 0.5 $\pm$ 1.1, 0.05 $\pm$ 0.9, -0.35 $\pm$ 0.5 respectively) and ($p < 0.01$) and BMI Z-score centile (mean $\pm$ SD 0.9 $\pm$ 0.7, 0.1 $\pm$ 0.6, -0.97 $\pm$ 0.4 respectively) and ($p < 0.05$) (higher in obese compared to overweight children which were significantly higher than healthy ones) while no significant difference between the three groups of children regarding height Z-score centile. (mean $\pm$ SD 0.2 $\pm$ 1, 0.04 $\pm$ 1.1, -0.2 $\pm$ 0.9 respectively). (Table.1)

Mean diastolic blood pressure (DBP) values significantly higher in obese children compared to healthy ones ($p < 0.01$). (Table.1)

Significant higher incidence of NAFLD in obese and overweight children compared to healthy ones ($p < 0.01$) for both. Seventy three percent of obese children 26.3% of overweight ones were having NAFLD. (Table.1)

Serum aminotransferase (ALT, AST) were two to five times the upper limits of normal in obese and overweight compared to healthy ones (mean $\pm$ SD for ALT 71.3 $\pm$ 21.4, 41.3 $\pm$ 19.1, 30.3 $\pm$ 4.4 respectively and (mean $\pm$ SD for AST 69.8 $\pm$ 24.5, 36.8 $\pm$ 5.5, 30.0 $\pm$ 4.4 respectively) ($p < 0.01$ and 0.05 respectively). (Table.2)

Regarding lipid profile in obese and overweight compared to healthy ones, mean total cholesterol (mean $\pm$ SD 238.1 $\pm$ 49.1, 160.7 $\pm$ 56.6, 147.1 $\pm$ 44.9, respectively),

LDL-cholesterol (mean $\pm$ SD 137.9 $\pm$ 18.8, 123.4 $\pm$ 14.2, 102.6 $\pm$ 17.4, respectively), HDL-cholesterol (mean $\pm$ SD 33.2 $\pm$ 13.4, 48.4 $\pm$ 19.2, 62.2 $\pm$ 16.3, respectively) and TG values (mean $\pm$ SD 143.1 $\pm$ 23.9, 35.2 $\pm$ 16.0, 88.4 $\pm$ 21.4, respectively) all were significantly higher in obese, overweight children compared to healthy children ($p < 0.01$ for all) except for HDL level which was higher in healthy children ($p < 0.01$). (Table.2)

Regarding glycemic control higher mean fasting blood glucose level (FBG) and Hb_{A1C}, were found in overweight (mean $\pm$ SD for FBS 99.5 $\pm$ 22.5 and Hb_{A1C} 6.19 $\pm$ 1.91) and obese (mean $\pm$ SD for FBS 148.5 $\pm$ 39.7 and Hb_{A1C} 7.49 $\pm$ 2.18) compared to healthy ones (mean $\pm$ SD 86.7 $\pm$ 14.9 and Hb_{A1C} 5.13 $\pm$ 0.64 respectively) ($p < 0.01$ for both). (Table.2)

Mean serum Visfatin level was higher in obese children (mean $\pm$ SD 301.3 $\pm$ 64.5) overweight children (mean $\pm$ SD 136.4 $\pm$ 24.1) compared to healthy children (mean $\pm$ SD 114.8 $\pm$ 23.7) ($p < 0.01$ for all). (Figure.2)

There were significant positive correlation between BMI, weight, cholesterol, TG and ALT and serum Visfatin levels. ($p < 0.01$ for all). (Table.3)

Significant ultrasonographic differences between obese, overweight and healthy children regarding the degree of hepatic steatosis ($p < 0.01$). (Figure.1)

ROC analysis of serum visfatin level showed an area under the curve (AUC) of 0.82 at cut off value for serum Visfatin of > 126.5 ng/ml. showing the sensitivity (78.1%) and specificity (61.4%) of serum Visfatin as a predictor of fatty liver disease in obese children. (Figure.3)

Discussion

Obesity exert a central role in the development of metabolic syndrome, NAFLD and a cardiovascular morbidity.[14]

Examining the diagnostic role of serum visfatin levels as a novel indicator in childhood obesity and evaluating the risk of fatty liver and poor glycemic condition showed that Visfatin promotes B cell maturation and inhibits [neutrophil apoptosis](#). The synthesis and secretion of Visfatin is regulated by Interleukin-6 (IL-6), growth factors, glucocorticoids, and TNF- α and up regulated in the course of pro-inflammatory cytokines release, under inflammatory conditions, by hyperglycemia and hypoxia [15,16] and down regulated by insulin, somatostatin and statins.[16]

In the present study, the BMI correlates closely with total body fat (TBF), which is in previous studies estimated using dual-energy x-ray absorptiometry (DEXA) scanning in children who are overweight and obese.[17]

DBP it was significantly higher in obese children, obesity likely contribute to the increase levels of insulin and insulin-like growth factor I which may increase blood pressure [18], also Visfatin can promote vascular smooth muscle inflammation and play a potential role in vascular dysfunction and inflammation in some metabolic disorders.[19]

Nageswari *et al.*, (2007) found higher DBP values in the obese group children and hypothesized that higher DBP in obese children could be due to higher vasoconstrictor tone and/or increase in the cardiac output owing to increased circulatory load on heart. As a consequence of increase in BMI.[19] However, Divković. *et al.*, (2014) proved that overweight/obese children had significantly higher systolic blood pressure compared to eutrophic children, while DBP showed no difference in both groups.[20]

In the present study, NAFLD was significant higher in the obese children compared with overweight & healthy children. NAFLD is one of manifestations of metabolic syndrome. Risk factors associated with NAFLD include dyslipidemia, central obesity, type-2 diabetes mellitus, and insulin resistance (IR).[21]

NAFLD however, remains a diagnosis of exclusion, so other causes of chronic liver disease must be ruled out, especially HCV, alcoholic liver disease, and Wilson's disease (in young Patients).[22] In contrast to our study, *Ludwig et al., (1980)* proved that, rarely, physical examination reveals hepatomegaly.[23]

Our results showed mild to moderate elevations in transaminases two to five times the upper limits of normal in overweight and obese agreeing with the results of *Ekstedt et al., (2017)* & *Li Hui-ling et al., (2015)* who found The ALT and AST levels of the obese children were higher than the overweight group and explained that patients with NAFLD have insulin resistance (IR) which increases lipolysis from the adipose tissue. The resulting FFA will be taken up by the liver and can cause lipid peroxidation so increase production of inflammatory cytokines. Also accumulation of fat in the liver is a result of increased triglyceride synthesis, decreased triglyceride export through very-low density lipoprotein (VLDL), and reduced beta-oxidation. [24, 25]

Higher total cholesterol, LDL and TG were detected in obese and overweight children compared with control groups and also in the obese children was higher than overweight ones. While HDL was higher in healthy children who show normal levels of HDL which has a cardiovascular protective function confirming the higher risk of cardiovascular complication in other two groups, this is in agreement with *Holst-Schumacher et al., (2009)* who found higher mean serum concentrations of triglycerides but lower mean serum levels of HDL cholesterol in obese children compared to controls and demonstrated the alteration of lipoprotein levels and compositions are related to the greater risk of cardiovascular disease associated with obesity.[26]

Obesity-related hyperlipidemia is primarily characterized by increased levels of plasma free fatty acids and triglycerides, decreased levels of HDL with abnormal low-density lipoprotein (LDL) composition. [27]

Higher mean fasting blood glucose level (FBG) and Hb_{A1C} were found in overweight and obese compared to healthy ones and this confirming that obesity is a risk factor for impaired glucose tolerance, this is similar to that described by *Elghaffar et al., (2010)* who found that fasting blood sugar were significantly higher in obese children compared to non-obese controls and between the obese children and overweight children reflecting the relation between obesity & hyperglycemia as blood sugar concentrations increased with increasing adiposity.[28]

Insulin resistance is defined as the decreased ability of tissues to respond to insulin action and one of the insulin-responsive tissues is adipose tissue, insulin stimulates storage of triglycerides in adipose tissue through promoting the differentiation of

pre-adipocytes to adipocytes, increasing the uptake of glucose and fatty acids derived from circulating lipoproteins and lipogenesis in mature adipocytes, and inhibiting lipolysis. [29]

Insulin resistance is feature of metabolic syndrome and is a major predictor of the development of type 2 diabetes.[29] Visfatin is important to normal insulin secretion, but its relationship with diabetes risk and

progression is still a matter of debate. Thus, Visfatin may be a compensatory mechanism or part of the pathophysiology of diabetes. [30]

In adipokines, Visfatin is over expressed in the route of adipocyte differentiation and can significantly regulate insulin secretion, insulin receptor phosphorylation. [31, 32]

Serum Visfatin was higher in obese & overweight patients compared with controls. Also it was higher in patients who develop metabolic syndrome (dyslipidemia, NAFLD and IR). The accumulation of body fat, particularly in a visceral distribution reduces the sensitivity to insulin in skeletal muscle, liver tissue, and adipose tissue; this “insulin resistance” predisposes to glucose intolerance, hypertriglyceridemia and low levels of HDL.[18] The presence of NAFLD itself is a significant predictor of serum Visfatin levels as reported by *Dahl et al.,(2010)*. [33] In insulin resistance a direct relationship between plasma Visfatin level and type 2 diabetes mellitus. Visfatin binds to the insulin receptor at a site differ from that of insulin and causes hypoglycemia by stimulating glucose utilization in adipocytes and myocytes and reducing glucose release from liver. [34]

However, *Fukuhaara et al.,(2005)* and *Li Hui-ling et al.,(2015)* found that Type 1 diabetic children and adolescents had a significantly lower Visfatin level compared to controls and no difference of serum Visfatin levels between the healthy and overweight children and the difference only was between the healthy and obese children [35,25], also *Ihsan et al.,(2017)* published that overweight/obese individuals there was negative relation between Visfatin level and anthropometric and lipid profile parameters, which can be explained by functional healthy fat tissue in this early life time even in a group of patients with increased body fat.[36]

In our study there was a significant difference between the obese children and healthy ones in the ultrasonographic findings of NAFLD and between the obese children and overweight ones with the frequency of 65.6% and 26.7%, respectively. Lipid accumulation in the liver leads to hepatic inflammation and cytokine production. [40]

Both *Jarrar et al.,(2008)* and *Younossi et al.,(2011)* showed significantly lower serum visfatin levels in NAFLD obese patients compared with patients with simple steatosis obese ones, overall, three studies suggested a protective role of visfatin in NAFLD progression.[7, 37]

Our results showed the receiver-operating characteristic curve for serum Visfatin as a predictor of fatty liver in obesity, it shows an area under the curve (AUC) of 0.82 at cut off value for serum Visfatin of > 126.5 ng/ml, this mean sensitivity of 78.1% and specificity of 61.4% of serum Visfatin as a predictor of fatty liver disease in obese children.

Limitations Of The Study

The smaller sample size which due to refusal of many patients to share in this study. Also, liver biopsy which is the most diagnostic tool for NAFLD could not be done due financial issue.

List Of Abbreviations

BMI: Body mass index, LDL: Low density lipoprotein, HDL: High density lipoprotein, Bp: Blood pressure, FBG: Fasting blood glucose, WAT: White adipose tissue, BAT: Brown adipose tissue, TNF- α :Tumor necrosis factor- α , ALT: Alanin aminotransferase, AST: Aspartate aminotransferase, DBP: Diastolic blood pressure, CHD: Coronary heart disease,IL-7:Interleukin-7,IL-6:Interleukin-6,TBF:Total body fat, DEXA: Dual-energy x-ray absorptiometry, IR: Insulin resistance, VLDL: Very-low density lipoprotein, FFA: Free fatty acid.

Declarations

Acknowledgments: None

Funding: Personally funded by the authors.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' Contributions:

MA, LA, AM and SH participated in the study design, data collection an interpretation and wrote the manuscript. AM and NA analyzed the immunological data and SH, LA and MA participated to discuss the results and to write the manuscript. MA supervised the research group. All authors listed in a manuscript have contributed substantially to the work and seen revise and approved the submitted version.

Authors' information: Available

Ethics approval and consent to participate: The study was conducted According to the declarations of Helsinki and approved from the faculty of medicine scientific committee in Minia University (No: 116-5-2016).Written consents were obtained from patients' caregivers.

Consent for publication: Not applicable

Competing interests: The authors declare that they have no competing interests.

References

- Kuczmarski Robert J. 2000 CDC growth charts for the United States; methods and development. Vital and health statistics. Series 11, Data from the national health survey. 2002; 246: 1-190.
- Talat Mohamed A.; EL Shahat Eman. Prevalence of overweight and obesity among preparatory school adolescents in Urban Sharkia Governorate, Egypt. Egyptian Pediatric Association Gazette. 2016; 64.1: 20-25.

- Sharaf Mesbah Fathy, Mansour Elhussien Ibrahim, Rashad Ahmed Shoukry. Child nutritional status in Egypt: a comprehensive analysis of socioeconomic determinants using a quantile regression approach. *Journal of biosocial science*.2019; 51(1): 1–17.
- Hassan N. E., El-Ashry H. H., Awad A. H., El-Masry S. A., Yusuf M. M., Sallam M. M., & Anwar M. Adiponectin in obese children and its association with blood pressure and anthropometric markers. *Medical Research Journal*.2011; 10.1: 1–4.
- De onis, Lobstein T. Defining obesity risk status in the general childhood population: which cut-offs should we use?. *International Journal of Pediatric Obesity*.2010; 5.6: 458–460.
- Käräjämäki A. J., Bloigu R., Kauma H., Kesäniemi Y. A., Koivurova O. P., Perkiömäki J.& Ukkola O. Non-alcoholic fatty liver disease with and without metabolic syndrome: different long-term outcomes. *Metabolism*. 2017;66: 55–63.
- Younossi Z. M., Page S., Rafiq N., Binerdinc A., Stepanova M., Hossain N. & Baranova A. A biomarker panel for non-alcoholic steatohepatitis (NASH) and NASH-related fibrosis. *Obesity surgery*.2011;21(4): 431–439.
- Tilg Herbert, Moschen Alexander R. Evolution of inflammation in nonalcoholic fatty liver disease: the multiple parallel hits hypothesis. *Hepatology*. 2010; 52.5: 1836–1846.
- Polyzos Stergios A., Kountouras J., Zavos C., & Deretzi, G. Nonalcoholic fatty liver disease: multimodal treatment options for a pathogenetically multiple-hit disease. *Journal of clinical gastroenterology*. 2012; 46.4: 272–284.
- Mohamed A. A., Sabry S., Abdallah A.M., Elazeem N. A. A., Refaey D., Algebaly & Omar H.. Circulating adipokines in children with nonalcoholic fatty liver disease: possible noninvasive diagnostic markers. *Annals of gastroenterology*.2017; 30:457.
- Jamali R. Non-alcoholic fatty liver disease: diagnosis and evaluation of disease severity. *Thrita*.2013;2(4): 43–51.
- Yilmaz Y. Circulating vaspin and its relationship with insulin sensitivity, adiponectin and liver histology in subjects with non-alcoholic steatohepatitis. *Scandinavian journal of gastroenterology*.2012;47(4): 489–490.
- Hassan N. E. Waist circumference and central fatness of Egyptian primary-school children. *Eastern Mediterranean Health Journal*.2008;14(4).
- Sen Y., Kandemir N., Alikasifoglu A., Gonc N., & Ozon A. Prevalence and risk factors of metabolic syndrome in obese children and adolescents: the role of the severity of obesity. *European journal of pediatrics*.2008; 167(10):1183–1189.
- ZhongM., Tan H. W., Gong H. P., Wang S. F., Zhang Y. & Zhang W. Increased serum visfatin in patients with metabolic syndrome and carotid atherosclerosis. *Clinical endocrinology*.2008; 69(6): 878–884.
- PandzićJ. V. Adipocytokines as mediators of metabolic role of adipose tissue. *Acta medica Croatica: casopis Hrvatske akademije medicinskih znanosti*.2010; 64(4):253–262.

- DeurenbergP, Deurenberg-Yap M., Foo L. F., Schmidt G. & Wang J..Differences in body composition between Singapore Chinese, Beijing Chinese and Dutch children. *European journalof clinical nutrition*.2003; 57(3):405.
- Abbasi A., Corpeleijn E., Postmus D., Gansevoort R. T., De Jong P. E., Gans R. O.& Bakker S. J.Plasma procalcitonin is associated with obesity, insulin resistance, and the metabolic syndrome. *The Journal of Clinical Endocrinology & Metabolism*.2010; 95(9):E26-E31.
- Nageswari K. S., Sharma R., & Kohli D. R. Assessment of respiratory and sympathetic cardiovascular parameters in obese school children. *Indian journal of physiology and pharmacology*.2007; 51(3); 235.
- Divković D., Selthofer-Relatić K., Ćosić A., Drenjančević I., Kristek J. & Radić R.Serum visfatin concentration in eutrophic and overweight/obese male children in early childhood. *Periodicum biologorum*.2014 ;116(2):191–196.
- Setji T. L., Holland N. D., Sanders L. L., Pereira K. C.,Diehl A.M., & Brown A. J.Nonalcoholic steatohepatitis and nonalcoholic fatty liver disease in young women with polycystic ovary syndrome. *The Journal of Clinical Endocrinology & Metabolism*.2006;91(5):1741–1747.
- Sahebkar A., Sancho E., Abelló D., Camps J., & Joven J. Novel circulating biomarkers for non-alcoholic fatty liver disease: A systematic review. *Journal of cellular physiology*.2018; 233(2):849–855.
- Ludwig J, Viggiano TR, McGill DB, Oh BJ. Nonalcoholic steatohepatitis: Mayo Clinic experience with a hitherto unnamed disease. *Mayo Clin Proc*. 1980; 55: 434–8.
- Ekstedt M.,Hagström H., Nasr P.,Hammar U., Stål P., Hultcrantz R.& Kechagias S. Fibrosis stage but not NASH predicts mortality and time to development of severe liver disease in biopsy-proven NAFLD. *Journal of hepatology*.2017;67(6):1265–1273.
- Li Hui-ling Lu,Li R. Z., Ma X. Y. & Kang S. X. Study of serum visfatin and blood glucose and lipid metabolism, NAFLD in simple obese children. *International journal of pediatric endocrinology*.2015; 1: 74.
- Holst-Schumacher I., Nuñez-Rivas H., Monge-Rojas R. & Barrantes-Santamaría M. Components of the metabolic syndrome among a sample of overweight and obese. Costa Rican schoolchildren. *Food and nutrition bulletin*.2009;30(2):161–170.
- Clemente-Postig M.,Tinahones F. J.,Cardon F. 162 adipose tissue gene expression of factors related to lipid processing in obesity. *Atherosclerosis Supplements*.2011; 129(1):36–37.
- Elghaffar A., Hafez M. H., Shaaban F. A., Abu Ismail L. A. & Rashed R. G. Resistin and obesity-associated insulin resistance in children. *Journal of Genetic Engineering and Biotechnology*.2010;8(2): 17–25.
- Lillioja S., Mott D. M., Spraul M., Ferraro R., Foley J. E., Ravussin E.& Bogardus C. Insulin resistance and insulin secretory dysfunction as precursors of non-insulin-dependent diabetes mellitus: prospective studies of Pima Indians. *New England Journal of Medicine*.1993; 329(27):1988–1992.

- Haider D. G., Mittermayer F., Schaller G., Artwohl M., Baumgartner-Parzer S. M., Prager G. & Wolzt M. Free fatty acids normalize a rosiglitazone-induced visfatin release. *American Journal of Physiology-Endocrinology and Metabolism*.2006; 291(5):E88-E890.
- Grunfeld C. Leptin and the immunosuppression of malnutrition. *The Journal of Clinical Endocrinology & Metabolism*.2002; 87(7):3038–3039
- Hammarstedt A., Pihlajamäki J., Rotter Sopasakis V., Gogg S., Jansson P. A., Laakso M., & Smith U. Visfatin is an adipokine, but it is not regulated by thiazolidinediones. *The Journal of Clinical Endocrinology & Metabolism*. 2006; 91(3):1181–1184.
- Dahl T. B., Haukeland J. W., Yndestad A., Ranheim T., Gladhaug I. P., Damås J. K. & Bjørø K. Intracellular nicotinamide phosphoribosyl transferase protects against hepatocyte apoptosis and is down-regulated in nonalcoholic fatty liver disease. *The Journal of Clinical Endocrinology & Metabolism*.2010; 95(6):3039–3047.
- Deepa S. S. and L. Q. Dong. APPL1: role in adiponectin signaling and beyond. *American Journal of Physiology-Endocrinology and Metabolism*.2009; 296(1):E22-E36.
- Fukuhara A., Matsuda M., Nishizawa M., Segawa K., Tanaka M., Kishimoto K., Matsuki Y., Murakami M., Ichisaka T., Murakami H. Visfatin: a protein secreted by visceral fat that mimics the effects of insulin. *Science*. 2005; 307:426–430.
- Ihsan I., Rini E. A., & Yaswir R. Visfatin levels in non-obese, obese, and insulin resistant adolescents. *Paediatrica Indonesiana*.2017; 56(5):291–6.
- Jarrar M. H., Baranova A., Collantes R., Ranard B., Stepanova M., Bennett C. & Younossi Z. M. Adipokines and cytokines in non-alcoholic fatty liver disease. *Alimentary pharmacology & therapeutics*.2008; 27(5): 412–421

Tables

Table 1. Some important clinical data of the patients and controls

Variable		Groups			P. value
		Group (I) (n=35)	Group (II) (n=30)	Group (III) (n=32)	
Weight (kg) (Z score)		-0.35 ±0.5	0.05 ± 0.9	0.5 ± 1.1	0.01**
Height (cm) (Z score)		-0.2± 0.9	0.04 ± 1.1	0.2± 1	0.31 ^{NS}
Body mass index(Z score)		-0.97 ± 0.4	0.1 ± 0.6	0.9 ± 0.7	0.01**
Age (year)		8.3 ± 4.6	8.6 ± 5.1	9.1 ± 4.7	0.77 ^{NS}
Sex	Male	16 (45.7%)	15 50.0%)	14 (43.8%)	0.88 ^{NS}
	Female	19 (54.3%)	15 50.0%)	18 (56.3%)	
Diastolic blood pressure	Normal	35 (100.0%)	22 73.3%)	11 (34.4%)	0.01**
	High	-----	8 (26.7%)	21 (65.6%)	
Hepatomegaly	No	35 (100.0%)	22 (73.3%)	11 (34.4%)	0.01**
	Yes	-----	8 (26.7%)	21 (65.6%)	

Table 2. Some important laboratory findings among studied groups

	Groups			<i>p. value</i>
	Group (I) (n=35)	Group (II) (n=30)	Group (III) (n=32)	
ALT (U/L)	30.3 ± 4.4	41.3 ± 19.1	71.3 ± 21.4	0.01*
AST (U/L)	30.0 ± 4.4	36.8 ± 5.5	69.8 ± 24.5	0.01*
Cholesterol (mg/dl)	147.1 ± 44.9	160.7 ± 56.6	238.1 ± 49.1	0.01*
Triglycerides (mg/dl)	88.4 ± 21.4	135.2 ± 16.0	143.1 ± 23.9	0.01*
LDL (mg/dl)	102.6 ± 17.4	123.4 ± 14.2	137.9 ± 18.8	0.01*
HDL (mg/dl)	62.2 ± 16.3	48.4 ± 19.2	33.2 ± 13.4	0.01*
FBS (mg/dl)	86.7 ± 14.9	99.5 ± 22.5	148.5 ± 39.7	0.01*
Hb _{A1C}	5.13 ± 0.64	6.19 ± 1.91	7.49 ± 2.18	0.01*
Serum visfatin (ng/ml)	114.8 ± 23.7	136.4 ± 24.1	301.3 ± 64.5	0.01*

Due to technical limitations, table 3 is only available as a download in the supplemental files section

Figures

Figure 1

Figure 1: Abdominal sonar findings among studied groups

Figure 2

Figure 2: Serum visfatin among studied groups

Figure 3

Figure 3: Serum visfatin among studied groups

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table3.pdf](#)