Prevalence and risk determinants of metabolic syndrome in obese worksite workers in hill city of Himachal Pradesh, India

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Abstract

Objective: We report prevalence and risk factors of metabolic syndrome (MS) in the obese workforce of organized sector in hill city of Himachal Pradesh (HP), India.

Methods: The cross-sectional survey study of employees of organized sectors in Shimla city of HP, India, was conducted to collect data of demographics, health behavior, psychosocial factors, anthropometry, blood pressure, and blood chemistry to measure blood glucose and lipid profile in fasting state in 3004 employees using validated tools. Out of 3004 subjects screened, data of 418 subjects with body mass index of $\geq 30$ are analyzed to estimate the prevalence of MS and its risk determinants. The association of demographics, health behavior, and psychosocial factors as the risk determinants were analyzed using multivariable logistic regression modeling.

Results: MS was prevalent in 57.6% [95% confidence interval (CI): 52.8%–62.3%]. The central obesity (odds ratio: 10.6, 95% CI: 2.32–48.4) and consumption of frequent or daily alcohol (odds ratio: 1.94, 95% CI: 1.05–3.59), and extra salt (odds ratio: 3.34, 95% CI: 1.09–10.2) were independent risk factors for MS. The consumption of tobacco, vegetables, sugar-sweetened drinks, physical inactivity, and psychosocial factors had no significant association with MS in obese population.

Conclusions: MS is highly prevalent among obese employees of organized sector. The consumption of alcohol and extra salt were major behavioral risk factors for MS and therefore have important implications in behavioral modifications for prevention of MS among obese employees in organized sectors.

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1. Introduction

Metabolic syndrome (MS) is an emerging risk factor for diabetes and cardiovascular disease (CVD).1,2 The CVD and diabetes are the leading causes of disease burden globally. There is a trend of increasing incidence of obesity with rapid urbanization and economic transition.3 Prevalence of MS is higher in the obese population. The obesity refers to increased body fat mass. The majority of the patients of obesity have metabolic abnormalities of MS. However, about 25% of the obese patients may not have metabolic abnormalities and are referred to as metabolically healthy obese.4–8 Understanding of risk factors for MS in the obese population is of great importance in formulating evidence-based interventions for its prevention. Health risk behavior and psychosocial factors could influence the risk of MS in the obese population.

There are number of observational and a few interventional studies determining the risk factors of MS.9–12 However, studies on risk determinants of MS among obese populations are limited. We aimed to estimate the prevalence and health behavior, depression, anxiety, and stress as the risk determinants of MS in the obese population of employees working in different organized sectors of Shimla city in the hill state of Himachal Pradesh (HP).

2. Methods

2.1. Study design, population, and sampling method

In this cross-sectional survey study of employees working in different government and public sector units in Shimla city, individuals selected by convenient sampling method formed the study population. The Shimla city is situated at about 800 feet height above sea level at coordinates of $31.1048^\circ$ north and $77.1734^\circ$ east. An attempt was made to select organized sectors from different departments involved in varied areas of services, e.g.
education, health, police, transportation, business houses, and public sector units. Employees with body mass index (BMI) of ≥30 formed the study sample of present reporting.

2.2. Survey instruments

World Health Organization steps (WHO STEPs) approach survey instrument was used to record the data on sociodemographic, health behavior. The psychosocial factors such as depression, anxiety, and stress were measured using the scale-21 (DASS-21). The anthropometry data were measured using validated tools. Weight was recorded using hard surface spring balance weighing machine calibrated against standard weight, height using Secca stadiometer and waist circumference with 1 cm width non-stretchable measuring tape. The blood pressure (BP) was measured using a digital BP recorder, Omron model HEM 7201. The measurement of blood glucose and lipid profile was done using fully autoanalyzer Arba Panacea using standard kits in fasting state.

2.3. Survey team and training

Four contractual research staff of multidisciplinary research unit (MRU) of the Department of Health Research, Government of India, under MRU scheme, consisting of lab assistant, two lab technicians, and one research associate (post Ph.D.) constituted the research team. The research team was trained by investigators to administer survey instruments. Pretesting of administration of survey instruments was evaluated for each member on 10 subjects, and reliability of the responses and data collected were cross-checked by investigators. The discrepancies observed with the data recorded with any member were addressed through retraining. Once members were well-versed with the use of survey instruments, the survey study was initiated.

2.4. Implementation strategy of a survey study

The head of the management was approached by the team with the request letter explaining the objectives of the study, and their permission was sought on a voluntary basis. When permission for survey study was granted, the list of all employees was prepared with the help of management. The appointment for employees volunteering to participate in the study was fixed day prior for the study in batches. A separate room was provided by the management for the survey team to conduct the study.

2.5. Ethical approval

The study protocol was approved by the IGMC ethical committee.

2.6. Data collection

The data collection started from March 2017 to March 2018. The self-reported data of socioeconomic, demographic, and health risk behavior were recorded. The dietary intake was recorded using food frequency questionnaire to capture intake of sugar-sweetened drinks, butter and/or ghee (liquefied butter) and use of extra salt at the table, vegetables, and fruits. The frequency of consumption was reported as never/occasional, frequent or daily and based on consumption, less than once a week, more than 4 times in a week, or all days in a week, respectively. The consumption of alcohol was recorded as never or occasional (once a month or so), frequent (two to three times a week), or daily. The current consumption of tobacco in smoke and/or smokeless form was recorded as tobacco consumer. The frequent or daily consumers of sugar-sweetened drinks, vegetables, fruits, extra salt, butter, and alcohol were labeled as consumers, while daily consumers of tobacco were labeled as tobacco consumers. The stress, anxiety, and depression were recorded using validated questionnaire on depression, anxiety, and stress (DASS-21) scale. This was followed by physical examination to measure weight in kilograms (Kg) in light clothes using validated flat surface spring balance weighing machine. The waist circumference was measured in centimeters using 1 cm width non-stretchable flexible measuring tape in erect posture at the end of expiration during normal breathing at a midpoint between the anterior superior iliac crest and last rib holding measuring tape parallel to the ground. Three readings were measured, and an average was used for analysis. Height was measured using Secca stadiometer without shoes or hat, if any, subject standing erect and looking straight ahead with tragus of the ear and inferior margin of eye orbit parallel to the ground. The height was measured in meters. Three readings of BP at an interval of 2–3 min were measured after 5 min of rest using appropriate size BP cuff in sitting position, back resting, and uncrossed feet supported on the ground with validated digital BP recorder OMERON model HEM 7201, and an average value was taken for analysis.

The 5 ml of venous blood sample was drawn after 8–10 h of fasting and collected in appropriate vials to measure blood glucose and lipid profile next morning. The blood sample was transported to MRU lab of IGMC hospital in cold chain container for processing and estimation. Blood glucose and lipid profile were measured using standard kits and standardized solution in fully autoanalyzer model EM360 Transasia. The socioeconomic state was calculated based on education, employment status, and per capita income using Kuppuswamy method.

3. Definitions

Metabolic syndrome: The MS was diagnosed using modified 3rd adult treatment panel (ATP III) criteria based on presence of any of the following three out of five criteria:

➢ Fasting blood glucose ≥100 mg/dl and/or diabetic on sugar lowering drugs;
➢ BP ≥130/85 mmHg and/or hypertensive patients on drugs;
➢ Triglyceride level ≥150 mg/dl or on lipid lowering drugs;
➢ High density lipoprotein cholesterol (HDL-C) ≤40 mg/dl in men and ≤50 mg/dl in women;
➢ Waist circumference ≥90 cm in men and ≥80 cm in women.

Dyslipidemia: It was diagnosed if any of the following criteria was met:

➢ Total cholesterol more than 240 mg/dl;
➢ Low density lipoprotein cholesterol (LDL-C) more than 130 mg/dl;
➢ Triglyceride levels more than 150 mg/dl;
➢ HDL-C less than 40 mg/dl in males and less than 50 mg/dl in females.

Mixed dyslipidemia: It was diagnosed when combination of elevated total cholesterol (≥240 mg/dl) and/or elevated levels of LDL-C (≥130 mg/dl) with elevated triglyceride (≥150 mg/dl) was found.

Physical inactivity: The subjects were labeled physically inactive if, cumulative moderate intensity exercise was of less than 150 min in a week.

Stress: It was diagnosed with DASS-21 score of ≥15.

Anxiety: DASS-21 score of ≥8.

Depression: DASS-21 score ≥10.
4. Data analysis

The data of 418 employees with BMI ≥30 out of the total of 3004 employees screened with complete data were analyzed to estimate the prevalence and the risk factors of MS among obese employees. The characteristics of the study population were reported in absolute counts, and percentages for categorical variables and mean ± standard deviation for continuous variable were distributed normally. The significance of the difference in the distribution of sociodemographic, occupation, type of organized sector, health behavior, stress, anxiety, depression, and cardiometabolic risk factors was compared between group with and without MS using the $\chi^2$ test. The association of MS with sociodemographic characteristics, psychosocial factors, and health risk behavior were analyzed with univariate logistic regression model, by estimating crude odds ratios. The number of behavioral risk factors has been found to be in univariate logistic regression model entered in multivariable logistic regression modeling to determine the independent association with MS and adjusted odds ratio with 95% confidence interval (CI), respectively. The variables having significant association in univariate logistic regression model entered in multivariable logistic regression modeling are reported in Table 1. The study sample is reported in Table 2. The statistical analysis was done using STATA, version 13.

5. Results

5.1. Characteristics of the study population and prevalence of MS

Detailed description of sociodemographics, health behavior, occupation status, and organized sectors-wise representation of the study sample is reported in Table 1. The study sample consisted of middle age (48.0 ± 9.4) population, 56.1% male, predominantly married, about 3/4th from upper class (ULC), upper middle class (UMC), and upper class (UC) socioeconomic state with the education level of graduation and above in about 40%, mostly engaged in skilled and professional occupation in diverse organized sectors. There was a significant gender-based difference in the distribution of marital status, socioeconomic state, nature of occupation, and types of organized sectors employment. The consumption of extra salt and sugar-sweetened drinks was significantly higher in males though the consumption of vegetable and fruit were similar. The tobacco and alcohol consumption was recorded only in men. Physical inactivity was equally prevalent among men and women and of whom two-third were leading a sedentary life. The cardiometabolic risk factors were highly prevalent among the obese population; about 84% had dyslipidemia, 52% were hypertensive, and about 18% were diabetic. The mixed dyslipidemia was the common most form of dyslipidemia. The MS was prevalent in 57.6%, had 95% CI of 52.8%–63.2%, and was significantly more in men as compared with women. Hypertension and central obesity were more prevalent in men. Overall, less than 10% of obese employees had symptoms of depression, anxiety, and/or stress and were equally prevalent among men and women.

5.2. Distribution characteristics of MS

The detailed description of distribution characteristics of MS in the study sample is reported in Table 2. MS was more frequent among men, and the frequency distribution varied significantly across organized sectors, the nature of jobs employees were engaged in, and employees consuming tobacco, alcohol, and extra salt. MS was equally prevalent among employees with different levels of education and socioeconomic state, consumption status of vegetables, fruits, and sugar-sweetened drinks, and status of psychosocial factors.

5.3. Risk determinants of MS

The demographic, health behavior, and central obesity were analyzed as the potential independent risk factors for MS (Table 3). The consumption of alcohol and extra salt and central obesity were significantly associated with MS in the obese population. There was a trend of association with physical inactivity, consumption of sugar-sweetened drinks, and consumption of vegetables but was statistically not significant. The odds of MS was low in those consuming butter and/or ghee with central obesity, while consumption of sugar-sweetened drinks had a positive association with central obesity. The psychosocial factors had no significant association.

5.4. Risk determinants of cardiometabolic risk factors

The detailed description of the association of demographic, behavioral, and psychosocial factors with components of MS is reported in Table 4. In brief, age, gender, consumption of tobacco, and consumption of alcohol had a significant association with components of MS. There was a trend of inverse association of consumption of butter and/or ghee with central obesity, while consumption of sugar-sweetened drinks had a positive association with central obesity. The psychosocial factors had no significant association.

6. Discussion

The prevalence of MS is increasing with the emerging epidemic of obesity. In a cross-sectional study of obese employees of organized sector in hill city of HP, India, MS was prevalent in 57.6%, having 95% CI of 52.8%–63.2%. The central obesity and consumption of alcohol and extra salt were the independent risk factors associated with MS. Although, the physical inactivity and consumption of sugar-sweetened drinks demonstrated trends of association, it was statistically not significant. The psychosocial factors such as depression, anxiety, and stress were not significantly associated with MS.

The association of central obesity with MS suggests the truncal distribution of adipose tissue and identifies an obese population at a risk of metabolic abnormalities. Although increased BMI is a good indicator of increased adiposity, however, it does not provide information about the distribution and functionality of adipose tissue. The obesity is a pathophysiological condition reflecting the state of dysregulated energy homeostasis as a result of the resistance of central neural centers to leptin, regulating appetite and satiety. The resultant imbalance between intake and expenditure increases the adiposity. The increased adiposity is associated with a state of inflammation resulting in insulin resistance and associated metabolic abnormalities. What transforms metabolically healthy adiposity to adiposity with a metabolic abnormality is unclear. Is it the insulin resistance that determines the distribution of fat in event of excess caloric intake? Or is it a type of fuel substrate that determines the site of fat deposition? Analysis of association between types of fuel substrate consumed with central obesity in the present study revealed trends of association with consumption of sugar-sweetened drinks [odds ratio: 2.85 (0.66–12.3)], and an inverse association with consumption of butter and/or ghee [odds ratio: 0.27 (0.07–1.01)]. The refined carbohydrate-based diet is an important determinant of dyslipidemia than saturated fat diet observed in the latest reviews of observational studies. The observational and interventional studies suggests that sugar-sweetened beverages increases the risk of obesity and diabetes.

The number of behavioral risk factors has been found to be in association with MS in cross-sectional and longitudinal
observational studies. Meta-analysis of cohort studies reported 84% rise in risk of MS among heavy alcohol drinkers, while light drinkers have 14% lower risk compared with non-drinkers. In the present study, frequent or daily alcohol drinkers had significant association with MS compared with never or occasional drinkers with odds ratio of 1.71 and 95% CI of 0.97–1.71. The animal experimental studies have demonstrated improvement in insulin sensitivity and hypertension with salt reduction diet. The salt-sensitive individuals with excessive salt intake predispose to hypertension and diabetes and have the common basis of cell membrane defect where increased sodium is exchanged with calcium leading to increased cytosolic calcium levels. High cytosolic calcium in pancreatic beta cells in turn hikes the secretion of insulin resulting in hyperinsulinemia and in a smooth muscle cell of the arteries, advances the vascular tone leading to hypertension and microvascular dysfunction of skeletal muscles and reduced glucose uptake and its insulin resistance. In the present study, the association of use of extra salt with MS was found to be statistically significant even after adjustment of alcohol intake, central obesity, and physical inactivity [odds ratio (95% CI): 3.34 (1.09–10.2)]. The active and passive smoking has been reported to be associated with MS in observational studies. The meta-analysis of cohort studies reported significant raise in the risk of MS in a population exposed to tobacco smoke and had a dose–response relationship. Risk of MS was significantly higher in heavy smokers compared with light and non-smokers.
there was no significant association with MS [odd ratio (95% CI): 0.96 (0.46–2.01)]. In the present study among obese population, whether obesity modifies the effect of tobacco consumption on the risk of MS needs to be studied.

The physical inactivity and consumption of sugar-sweetened drinks have been reported to be associated with MS in number of observational studies. However, we did not find any significant association. There was a trend of higher risk of MS among obese employees leading to sedentary life [odds ratio (95% CI): 1.22 (0.81–1.85)] and those consuming sugar-sweetened drinks [odds ratio (95% CI): 1.15 (0.58–2.27)].

The consumption of saturated fat (butter/ghee) had trends of an inverse association with MS adjusted for age, gender, physical inactivity, consumption of extra salt, alcohol, and sugar-sweetened drinks [odds ratio (95% CI): 0.76 (0.50–1.17)]. The type of fuel substrate; a carbohydrate or saturated fat determines the site of fat deposition: viscera or subcutaneous depot. The analysis of the association between the consumption of butter/ghee with central obesity revealed the odds of central obesity was significantly low among obese population consuming butter and/or ghee [odd ratio (95% CI): 0.27 (0.07–1.01)], while odds of central obesity was 2.85 (0.66–12.3) in those consuming sugar-sweetened drinks. Prospective population-based follow-up observational studies and meta-analysis of cohort studies reported lower risk of developing central obesity in people consuming dairy fats significantly.

Psychosocial factors such as depression, anxiety, and stress operates through activation of hypothalamic, pituitary, and adrenal axis resulting in enlarged levels of cortisol, affecting the immune system and metabolic pathways. The association of depression, anxiety, and stress with MS and diabetes is found variable in observational studies. We assessed depression, anxiety, and stress as per the criteria established for diagnosis of depression [26–31,40–42].

| Characteristics | Obese with MS | Obese without MS | Odds ratio (95% CI) | p value |
|-----------------|---------------|------------------|---------------------|---------|
| Age | 241 (57.6%) | 177 (42.3%) | 1.00 (0.99–1.03) | 0.36 |
| Gender (male) | 149 (61.8%) | 90 (50.8%) | 1.56 (1.05–2.31) | 0.02 |
| Marital status | Married | 237 (98.3%) | 170 (96%) | 2.43 (0.70–8.46) | 0.14 |
| Socioeconomic state | LMC | 63 (26.1%) | 40 (22.6%) | Reference | 0.27 |
| | UMC | 87 (36.1%) | 55 (31%) | 1.00 (0.59–1.69) | |
| | ULC | 30 (12.4%) | 22 (12.4%) | 0.86 (0.43–1.70) | |
| | UC | 61 (25.3%) | 60 (33.9%) | 0.64 (0.37–1.09) | |
| Education status | Primary | 23 (9.5%) | 17 (9.6%) | Reference | 0.62 |
| | Middle | 116 (48.1%) | 77 (43.5%) | 1.11 (0.55–2.21) | |
| | Higher | 102 (42.3%) | 83 (46.8%) | 0.90 (0.45–1.81) | |
| Occupation | Unskilled | 5 (2%) | 6 (3.3%) | Reference | 0.04 |
| | Semi-skilled | 10 (4.1%) | 9 (5%) | 1.33 (0.30–5.91) | |
| | Skilled | 153 (63.4%) | 88 (49.7%) | 2.11 (0.62–7.17) | |
| | Professional | 73 (30.2%) | 74 (41.8%) | 1.18 (0.34–4.05) | |
| Health risk behavior | Police | 8 (3.3%) | 10 (5.6%) | 1.56 (0.30–5.91) | |
| | Business house | 114 (47.3%) | 56 (31.6%) | 1.11 (0.55–2.21) | |
| | HRTC | 11 (4.5%) | 9 (5%) | 1.47 (0.31–7.17) | |
| | Education | 9 (3.7%) | 13 (7.3%) | 0.86 (0.24–3.0) | |
| | PSU | 99 (41%) | 89 (50.2%) | 1.39 (0.52–4.5) | |
| Characteristics | Adjusted odd ratio (95% CI) | Two-sided p value |
|-----------------|-------------------------------|-----------------|
| Age | 1.00 (0.98–1.02) | 0.77 |
| Gender (male) | 1.17 (0.73–1.86) | 0.55 |
| Socioeconomic state | 0.87 (0.73–1.05) | 0.46 |
| Tobacco consumption | 0.96 (0.46–2.01) | 0.92 |
| Alcohol consumption | 1.94 (1.05–3.59) | 0.03 |
| Sugar-sweetened drinks | 1.15 (0.58–2.27) | 0.67 |
| Consumption of butter/ghee | 0.76 (0.50–1.17) | 0.22 |
| Consumption of vegetables | 2.68 (0.40–17.9) | 0.30 |
| Consumption of extra salt | 3.34 (1.09–10.2) | 0.03 |
| Central obesity | 10.6 (2.32–48.4) | 0.001 |
| Physical inactivity | 1.22 (0.81–1.85) | 0.34 |

CI, confidence interval; MS, metabolic syndrome; BMI, body mass index; SD, standard deviation; HRTC, Himachal roadways transport corporation; PSU, public sector unit; LMC, low middle class.
among obese subjects to gain insight into possible association with MS but did not find any significant association with obese population.

6.1. Limitation of study

The estimation of consumption of butter/ghee, extra salt, sugar-sweetened drinks, and alcohol was not quantified. Although, the frequency of consumption is a surrogate marker for quantity consumed, internal and external validation of the data captured by the survey team was not done to ensure the quality of data. Thus, the present data should be interpreted in this context. Future intervention studies are required to evaluate the role of dietary and psychosocial factors as the risk factors for MS in the obese population.

6.2. Conclusion

The cross-sectional study of obese employees of organized sectors in Shimla city of hill state of HP revealed that more than 50% had MS. Central obesity and consumption of alcohol and extra salt were found to be independently associated with MS. The consumption of sugar-sweetened drinks and physical inactivity had trends of association but were statistically not significant. Consumption of butter and/or ghee had trends of inverse association with MS.

Funding source

The study was funded under the scheme of multi disciplinary research unit (MRU) of Ministry of health division of department of health research government of India.

Conflict of interest

All authors have none to declare.

References

1. Choi SH, Kim Sm, Kim YE, et al. Prevalence and cardiovascular disease risk of metabolic syndrome using National Cholesterol Education Program and International Diabetes Federation definition in Korean population. Metabolism. 2007;56:552–558.
2. Malik S, Wong ND. Metabolic syndrome, cardiovascular risk and screening for subclinical atherosclerosis. Expert Rev Cardiovasc Ther. 2009 Mar;7(3):273–280.
3. Flegel KM, Carroll MD, Ogden CL, et al. Prevalence and trends in obesity among US adults, 1999–2008. JAMA. 2010;303:235–241.
4. Mensah GA, Moldad AH, Ford E, et al. Obesity, metabolic syndrome, and type 2 diabetes: emerging epidemics and their cardiovascular implications. Cardiol Clin. 2004;22:485–504.
5. Chan JM, Rimm EB, Colditz GA, et al. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care. 1994;17:961–969.
6. Wildman RP, Muntner P, Reynolds K, et al. The obese without cardiometabolic risk factor clustering and the normal weight with cardiometabolic risk factor clustering: prevalence and correlates of 2 phenotypes among the US population (NHANES 1999–2004). Arch Intern Med. 2008;168:1617–1624.
7. Karalis AO, Brochu M, Rabasa-Lhoret R. Can we identify metabolically healthy but obese individuals (MHO)? Diabetes Metab. 2004;30:569–572.
8. Ruderman NB, Schneider SH, Berchtold P. The “metabolically-obese,” normal-weight individual. Am J Clin Nutr. 1981;34:1617–1621.
9. Sun K, Ren M, Liu D, et al. Alcohol consumption and risk of metabolic syndrome: a meta-analysis of prospective studies. Clin Nutr. 2014 Aug;33(4):596–602.
10. Sun K, Liu J, Ning G. Active smoking and risk of metabolic syndrome: a meta-analysis of prospective studies. PLoS One. 2012;7(10):e47791.
11. Sun K, Liu D, Wang C, Ren M, Yang C, Yan L. Passive smoke exposure and risk of diabetes: a meta-analysis of prospective studies. Endocrine. 2014 Nov;47(2):421–427.
12. Lin KP, Liang TL, Liao IC, Tsay SL. Associations among depression, obesity, and metabolic syndrome in young adult females. Biol Res Nurs. 2014 Jul;16(3):327–334.
13. Lovibond SH, Lovibond PF. Manual for the Depression Anxiety and Stress Scale. 2nd ed. Sydney: Psychology Foundation; 1995.
14. Patro BK, Jayashree K, Gupta PK. Kuppuswamy’s socioeconomic status scale 2010 the need for periodic revision. Indian J Pediatr. 2012;79:395–396.
15. Barzilai N, Wang J, Massilon D, et al. Leptin selectively decreases visceral adiposity and enhances insulin action. J Clin Invest. 1997;100:3105–3110.
16. Morton GJ, Gelling RW, Niswender KD, et al. Leptin regulates insulin sensitivity via phosphatidylinositol-3-OH kinase signaling in mediodiasal hypothalamic neurons. Cell Metab. 2005;2:411–420.
17. Friedman JM, Halaas JL. Leptin and the regulation of body weight in mammals. Nature. 1998;395:763–770.
18. Shi H, Kokoeva MV, Inouye K, Tzameli I, Yin H, Flier JS. TLRI links innate immunity and fatty acid-induced insulin resistance. J Clin Invest. 2006;116:3015–3025.
19. Quan J, Liu J, Gao X, et al. Palmitate induces interleukin-8 expression in human aortic vascular smooth muscle cells via Toll-like receptor 4/nuclear factor-kB pathway (TLR4/NF-kB-E). J Diabetes. 2014;6:33–41.
20. Li Y, Cheng M, Yang S, et al. Involvement of ER stress and IKKα in lipotoxicity induced by palmitate. PLoS One. 2014;9(2):e89728.
21. Li B, Yang S, Wang D, Qiu Q, et al. Adipose tissue inflammation and insulin resistance of high-fat diet mice. Am J Physiol Endocrinol Metab. 2006;291:E275–E281.
22. Gillman MW, Cupples LA, Millen BE, Ellison RC, Wolf PA. Inverse association of dietary fat with development of ischemic stroke in men. JAMA. 1997;278:770–777.
decreases insulin sensitivity in overweight/obese humans. J Clin Invest. 2009;119:1322–1334 [PMC free article] [PubMed].

28. Wolf A, Bray GA, Popkin BM. A short history of beverages and how our body treats them. Obes Rev. 2008;9:151–164 [PubMed].

29. Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective, observational analysis. Lancet. 2001;357:505–508.

30. Schulze MB, Manson JE, Ludwig DS, et al. Sugar-sweetened beverages, weight gain, and incidence of type 2 diabetes in young and middle-aged women. Jama. 2004;292:927–934.

31. Chen L, Appel LJ, Loria C, et al. Reduction in consumption of sugar-sweetened beverages is associated with weight loss: the PREMIER trial. Am J Clin Nutr. 2009;89:1299–1306.

32. Hoffmann IS, Cubeddu LX. Salt and the metabolic syndrome. Nutr Metabol Cardiovasc Dis : Nutr Metabol Cardiovasc Dis. 2009;19(2):123–128. ISSN: 1590-3729.

33. Eun NG, Mee KS, Mi-Kyeong C. Association between 24-h urinary sodium excretion and obesity in Korean adults: a multicenter study. Nutrition. 2017;41:111–119. ISSN: 1873-1244.

34. Oh SW, Han KH, Han SY, Koo HS, Kim S, Chin HJ. Association of sodium excretion with metabolic syndrome, insulin resistance, and body fat. In: Vilela-João Martin J, ed. Medicine. vol. 94(39). 2015:e1650. 

35. Fonseca-Alaniz MH, Brito LC, Borges-Silva CN, Takada J, Andreotti S, Lima FB. High dietary sodium intake increases white adipose tissue mass and plasma leptin in rats. Obesity (Silver Spring). 2007;15:2200–2208 [PubMed].

36. Lopes KL, Furutawawa LN, de Oliveira IB, Dolinkoff MS, Heinmann JC. Perinatal salt restriction: a new pathway to programming adiposity indices in adult female Wistar rats. Life Sci. 2008;82:728–732 [PubMed].

37. Garg R, Sun B, Williams J. Effect of low salt diet on insulin resistance in salt sensitive versus salt resistant hypertension. Hypertension. 2014;64(6):1384–1387. https://doi.org/10.1161/HYPERTENSIONAHA.114.03880.

38. Houston TK, Person SD, Fletcher MJ, Liu K, Irribarren C, Kiefe CI. Active and passive smoking and development of glucose intolerance among young adults in a prospective cohort: CARDIA study. BMJ. 2006;332:1064–1069. https://doi.org/10.1136/bmj.38779.s94028.55.

39. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. JAMA. 2007;298:2654–2664. https://doi.org/10.1001/jama.298.22.2654.

40. Tuomilehto J, Lindstrom J, Eriksson Jc, et al. Prevention of type 2 diabetes mellitus by changes in lifestyles among subjects with impaired glucose tolerance. N Engl J Med. 2001;344:1343–1350 [PubMed].

41. Hahn V, Halle M, Schmidt-Trucksass A, et al. Physical activity and the metabolic syndrome in elderly German men and women. Results from the population-based KORA-survey. Diabetes Care. 2009;32:511–513 [PMC free article] [PubMed].

42. Dube JJ, Allison KL, Rousson V, et al. Exercise dose and insulin sensitivity: relevance for diabetes prevention. Med Sci Sports Exerc. 2012;44:793–799.

43. Holmberg S, Thelin A. High dairy fat intake related to less central obesity: a male cohort study with 12 years’ follow-up. Scand J Prim Health Care. 2013 Jun;31(2):89–94.

44. Schwingshackl L, Hoffmann G, Schwedhelm C, et al. Consumption of dairy products in relation to changes in anthropometric variables in adult populations: a systematic review and meta-analysis of cohort studies. PLoS One. 2016 Jun 16;11(6):e0157461.