

Association of Vitamin B 12 and Folic acid with HOMA IR in urban middle aged women



Physiology

KEYWORDS: Metabolic syndrome; Micronutrients; Middle aged women

Ashok Pranita

Department of Physiology, Bharati Vidyapeeth Deemed University Medical College, Pune 411043, India

Balsubramanian B

Department of Physiology, Bharati Vidyapeeth Deemed University Medical College, Pune 411043, India

Joshi Sadhana

Department of Nutritional Medicine, Interactive Research School for Health Affairs, Bharati Vidyapeeth Deemed University, Pune, 411043, India

Wagh Girija

Department of Obstetrics and gynaecology, Bharati Vidyapeeth Deemed University Medical College, Pune 411043, India

Godbole Gayatri

Department of Physiology, Bharati Vidyapeeth Deemed University Medical College, Pune 411043, India

Vaidya S M

Department of Physiology, Bharati Vidyapeeth Deemed University Medical College, Pune 411043, India

ABSTRACT

Background: Middle aged women are reported to have high prevalence of metabolic syndrome which is also known as insulin resistance syndrome .HOMA IR is the best indicator of Insulin resistance. Micronutrient deficiencies are implicated in various metabolic disorders. The present study was aimed to examine the levels of micronutrients like vitamin B12, folic acid and homocysteine and their association with HOMA IR in middle aged women. **Methods:** This study was an observational cross-sectional study. Plasma levels of fasting glucose, vitamin B12, folic acid, fasting insulin and homocysteine were assessed in 300 women. Results were analyzed using Pearson's correlation. **Results :** Vitamin B12, folic acid concentrations were inversely associated and homocysteine was directly associated with HOMA IR. **Conclusion:** Low levels of vitamin B12, folic acid and high levels of homocysteine were major predictors of insulin resistance in middle aged women. Improving vitamin B12 and folic acid levels by dietary modifications and supplementation as well as decreasing homocysteine levels would be useful in improving insulin sensitivity and hence the health of middle aged urban women.

Introduction

The prevalence of metabolic syndrome is increasing in developing countries, especially in the South Asian countries. ¹ Recent data indicates that about one third of the Indian urban population has metabolic syndrome is also known as insulin resistance syndrome . Homeostasis model assessment ratio (HOMA IR) is the best indicator of Insulin resistance. ² Higher prevalence of Insulin resistance has been reported in middle aged women. ^{3,4}

Recent reports suggest that higher homocysteine is as an independent risk factor for development of metabolic syndrome. ^{5,6} Micronutrients like folic acid and vitamin B₁₂ play an important role in homocysteine metabolism via one carbon cycle. Folic acid acts as a methyl donor and vitamin B₁₂ acts as a co-factor in the metabolism of homocysteine. The deficiencies of both of these nutrients are implicated in hyperhomocysteinemia. ⁷

Obesity is more in urban middle aged women than in men due to socioeconomic transition causing significant shifts in dietary and physical activity patterns. Central obesity leads to abdominal adiposity, dyslipidemia and insulin resistance in middle aged menopausal women. ⁸

Hyperhomocysteinemia is more common among Indians due to deficiencies of folic acid and vitamin B₁₂, perhaps due to faulty cooking habits and inadequate consumption of animal origin foods. ⁹ It is also associated with insulin resistance. Very few studies have been done in India in this context. The present study was conducted to find out association of micronutrients like vitamin B₁₂, folic acid and homocysteine with HOMA IR in middle aged women.

Methods:

This study was an observational cross-sectional study. A written informed consent was taken and 300 women were recruited in this study. Patients with conditions like diabetes, hypertension, ischemic heart disease, thyroid disease, anaemia or any current infectious

condition, chronic liver and kidney disease, taking treatment of anemia and patients on anticancer drugs, glucocorticoids, thyroxine, oral anticoagulants or anticonvulsants, statins, thiazide diuretics, beta blockers or taking phytoestrogens, hormone replacement therapy, selective estrogen receptor modulator, vitamin supplements were excluded from the study.

All women were asked to come to the hospital for blood sample collection in the morning (7:00–8:00 A.M.). Venous blood sample (10 ml) was taken from median cubital vein with aseptic precautions after an overnight fast. Fasting blood glucose was estimated using GOD-POD method. Fasting serum insulin, plasma levels of vitamin B₁₂ and folic acid were assessed by Chemiluminescence method. ¹⁰

Homeostasis Model Assessment Ratio (HOMA-IR) : Insulin resistance was calculated using homeostasis model assessment ratio (HOMA-IR) and HOMA-IR is calculated using following formula: ¹¹

$$\frac{\text{Fasting Glucose(mg/dl)} \times \text{Fasting Insulin}(\mu\text{U/mL})}{405}$$

405

Data is represented as mean (standard deviation). SPSS version 17.0 for Windows (SPSS Inc, Chicago) was used for the statistical analysis. Pearson's correlation was used to find out association of micronutrients like vitamin B₁₂, folic acid and homocysteine and their association with HOMA IR syndrome in middle aged women. P value of less than 0.05 was considered as significant difference.

Results:

Table 1:

Mean levels of Micronutrients (n=300)

	Mean (SD)
Vitamin B12	302.2 (113.8)
Folate	12.3 (5.2)
Homocysteine	20.1 (8.2)
HOMA	*3.48 (2.35, 5.29)

*Median and Interquartile for HOMA IR

Table 2

Associations of Micronutrients with HOMA IR .

	HOMA IR
Vitamin B12	-0.13*
Folate	-0.12*
Homocysteine	0.22 ***

* p < 0.05, ** p < 0.01, *** p < 0.001

Vitamin B12, folic acid concentrations were inversely associated and homocysteine was directly associated with HOMA.

Discussion : In our study vitamin B₁₂, folic acid concentrations were inversely associated and homocysteine was directly associated with HOMA IR. Some studies have not reported any difference between the folic acid levels of individuals with insulin resistance.^{12,13} But some studies have found correlation between vit B12 and IR.^{14,15,16} In addition to this, the relationship between folic acid, vitamin B₁₂ and IR is not clear but central obesity is associated with homocysteine level which is related to IR. In addition our study reported 61% of obese women and significantly increased Hcy levels like other studies.^{17,18} Obesity is considered a chronic inflammatory disease . Adipose tissue is an organ capable of synthesizing and segregating various hormones that have a systemic effects on energy homeostasis. Leptin and adiponectin and various pro-inflammatory cytokines like TNF- interleukin-1, which are produced mainly in visceral adipose tissue, are more involved in the origin and development of insulin resistance.^{19,20}

It is speculated that wrong feeding habits, common among the obese, causes low levels of vitamins and minerals.⁷ The results of our study show that obesity is a risk factor for vitamin B₁₂ and folic acid deficiency in females and suggest that obese individuals with IR should be evaluated in terms of vitamin B₁₂ deficiency. Thus Vitamin B₁₂ and folic acid supplementation and decreasing homocysteine levels can increase insulin sensitivity.

Our data suggest that lower vitamin B₁₂ and folic acid levels with higher homocysteine levels in Indian middle aged urban women increases the risk for insulin resistance. Improving vitamin B₁₂ and folic acid levels by dietary modifications and supplementation as well as decreasing homocysteine levels would be useful in improving insulin sensitivity and hence the health of middle aged urban women.

Funding

Bharati Vidyapeeth Deemed University, LBS Road,13 Sadashiv Peth, Pune, Maharashtra 411030, India. (BVDU/Research cell/2014-2015/5839)

Conflict of interest:

None.

Acknowledgement :

The authors acknowledge Dr.Banshi Saboo for academic guidance, all the subjects who volunteered in this study. The authors also acknowledge the Bharati Vidyapeeth Deemed University for partially funding this study (BVDU /Research cell/2014-2015/5839.)

References :

- Misra A, Bhardwaj S. Obesity and the metabolic syndrome in developing countries: focus on South Asians. Nestle Nutr Inst Workshop Ser. 2014;78:133-40. doi: 10.1159/000354952. Epub 2014 Jan 27.
- Yiqing Song, JoAnn E. Manson, Lesley Tinker, Barbara V. Howard, Lewis H. Kuller, Lauren Nathan, et al Insulin Sensitivity and Insulin Secretion Determined by Homeostasis Model Assessment (HOMA) and Risk of Diabetes in a Multiethnic Cohort of Women: The Women's Health Initiative Observational Study. Diabetes Care. 2007 July; 30(7):1747-1752
- Delavar MA, Lye MS, Khor GL, Hanachi P, Hassan ST. Prevalence of metabolic syndrome among middle aged women in Babol, Iran. Southeast Asian J Trop Med Public Health. 2009 May;40(3):612-28.
- Choi JH, Woo HD, Lee JH, Kim J. Dietary Patterns and Risk for Metabolic Syndrome in Korean Women: A Cross-Sectional Study. Medicine (Baltimore). 2015 Aug;94(34):e1424. doi: 10.1097/MD.0000000000001424.

- Esteghamati A, Hafezi-Nejad N, Zandieh A, Sheikhbahaee S, Ebadi M, Nakhjavani M. Homocysteine and metabolic syndrome: from clustering to additional utility in prediction of coronary heart disease. J Cardiol. 2014 Oct;64(4):290-6. doi: 10.1016/j.jcc.2014.02.001. Epub 2014 Mar 14.
- Kulkarni A, Dangat K, Kale A, Sable P, et al. (2011) Effects of Altered Maternal Folic Acid, Vitamin B12 and Docosahexaenoic Acid on Placental Global DNA Methylation Patterns in Wistar Rats. PLoS ONE 6(3):e17706. doi:10.1371/journal.pone.0017706.
- SN Pandey, ADB Vaidya, RA Vaidya, S Talwalkar. Hyperhomocysteinemia as a Cardiovascular Risk Factor in Indian Women : Determinants and Directionality. JAPI, 2006; VOL. 54:786-792.
- Freeman EW, Sammel MD, Lin H, Gracia CR. Obesity and reproductive hormone levels in the transition to menopause. Menopause. 2010 Jul;17(4):718-26.
- Setola E, Monti LD, Galluccio E, Palloschi A, Fragasso G, Paroni R, Magni F, Sandoli EP, Lucotti P, Costa S, Fermo I, Galli-Kienle M, Origgi A, Margonato A, Piatti P. Insulin resistance and endothelial function are improved after folate and vitamin B12 therapy in patients with metabolic syndrome: relationship between homocysteinemia levels and hyperinsulinemia. Eur J Endocrinol. 2004 Oct;151(4):483-9.
- Ibrahim A. Darwish Immunoassay Methods and their Applications in Pharmaceutical Analysis: Basi Methodology and Recent Advances Int J Biomed Sci. 2006 Sep; 2(3): 217-235.
- Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Turner. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28:412-419.
- Davut Baltaci, Ali Kutlucan, Serkan Öztürk, İsmail Karabulut, Hayriye Ak Yildirim, Ahmet Çeler, Gökhan Celbek, İsmail Hamdi Kara. Evaluation of vitamin B12 level in middle-aged obese women with metabolic and nonmetabolic syndrome: case-control study. Turk J Med Sci 2012; 42(5): 802-809
- Hak AE, Polderman KH, Westendorp IC, Jakobs C, Hofman A, Witteman JC, Stehouwer CD. Increased plasma homocysteine after menopause. Atherosclerosis 2000 Mar; 149(1):163-8.
- Seang-Mei Saw, Jian-Min Yuan, Choon-Nam Ong, Kazuko Arakawa, Hin-Peng Lee, Gerhard A Coetzee, and Mimi C Genetic, dietary, and other lifestyle determinants of plasma homocysteine concentrations in middle-aged and older Chinese men and women in Singapore 1-3. Am J Clin Nutr 2001; 73:232-9.
- Sjoholm A, Nystrom T. Endothelial inflammation in insulin resistance. Lancet 365(9459): 610-612, 2005
- Kaya C, Cengiz SD, Satiro lu H. Obesity and insulin resistance associated with lower plasma vitamin B12 in PCOS. Reprod Biomed Online 19: 721-726, 2009.
- Gargari BP, Aghamohammadi V, Aliasgharzadeh A. Effect of folic acid supplementation on biochemical indices in overweight and obese men with type 2 diabetes. Diabetes Res Clin Pract 94: 33-38, 2011.
- Tungtrongchitr R, Pongpaew P, Tongboonchoo C et al. Serum homocysteine, B12 and folic acid concentration in Thai overweight and obese subjects. Int J Vitam Nutr Res 73: 8-14, 2003.
- G. Hotamisligil, Inflammation and metabolic disorders, Nature 444 (2006), 860-867.
- C.M. Rondinone, Adipocyte-derived hormones, cytokines, and mediators, Endocrine 29 (2006), 81-90.