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VITAMIN B12 AND OBESITY: REVIEW

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Abstract:

The primary reason behind the increasing increase in overweight is increased consumption of calories, while several other variables such as inheritance as well as exercise certainly contribute. Numerous studies have connected the amount of vitamin B12 to overweight. The present investigation aimed at determining that predict vitamin B12 pathology in persons who are obese at the beginning of their lives. They additionally provide recommendations about the potential uses of B12 in therapy contexts, specifically in the area of obesity prediction. B12 (vitamin may be used to forecast the possibility of disease and to spot indicators associated with anxiety and overweight. Furthermore, a number of studies investigated into a connection between MS and the vitamin B complex, including the presence of folic acid and vitamin B12.

Keyword: Obesity, B12, metabolic syndrome, cardiovascular disease, insulin resistance.

Introduction

Of being overweight, there is an increase in abdominal mass. (1) A different approach to define obesity is as an abnormal build-up of fat causing a person to put on more weight than is healthy. Essentially, the sole kind of energy store that can lead to adipose tissue growing larger than is required is triacylglycerol, a form human obesity. (2) Adipose tissue is unable to expand over whatever is required due to additional power archiving, such as liver and skeletal muscle proteins or glucose glycogen. (3) While it is currently demonstrated that steroids that are anabolic enhance lean muscle mass, which in turn increases body mass, these findings are currently only noted in underweight persons. (4) Adipose tissue, like any additional connective tissue, may vary greatly between people as a result of hyperplasia and hypertrophic. (5)

Review

Although people with short statures often measure lower than tall individuals, it is impossible to describe obese solely in the context of body mass index. Thus, we need to normalize human body mass and height. The most straightforward way to put it (m2) is the person's

body mass index (BMI), that can be expressed as the amount of weight in kilograms multiplied with length multiplied. The fact that it came from death benefit charts emphasizes how important this amount of weight is for adjusting length. (6) A BMI of 27.8 (kg/m2), approximately twenty percent above the typical weight for that structure, is regarded as a clear sign of life danger (7). The World Health Organization, best known as the WHO, established the definition of being obese in the year 1985, with an abdominal mass index (BMI) of more than thirty percent adult males and more then 28.6 for women.

Etiology of obesity

- **Acquired Causes of Obesity**

Although the incidence of obesity and overweight varies by country, it is becoming more likely for occidental nations like Australia may be affected by this condition for a greater percentage of their population (10). The illness is growing in prevalence among youngsters. (11) The variation across countries occasionally indicates that outside influences have the main impact for the incidence of illnesses. a report from the latest research, obese is expected to be substantially more costly for healthcare then cigarette use, while representing the next most preventable cause of mortality after cigarettes. (12)

The primary contributory factor for being overweight is a physiological discrepancy in the amount of power required versus calories consumed. Lack of exercise among kids in addition to greater intake of calories through the consumption either carbohydrates or fats are believed to be linked to obesity among kids (13) and 14). But this is not a simple problem, especially for children, since a low childhood weight is one sign that can potentially predict overweight at some point in life. (16)

A possible outcome of the condition Cushing's syndrome is fat. It was additionally connected to abdominal or truncal being overweight, and it's difficult to differentiate from conventional obese. To tell the difference among Cushing's syndrome versus being overweight, among the primary objectives for testing such as moderate-dose glucocorticoid suppressed testing will be to accomplish this division. Psychotherapy without thyroid medication can reverse the majority of the body mass gained caused by water retention, which is the uncommon explanation for overweight in cases of hyperthyroidism. Nonetheless, obesity can also be caused by slight reductions in metabolism in cases of severe or subtle hypothyroidism. Because insulinoma is a fairly uncommon condition, it is an extremely rare reason for overweight. Since more calories are consumed to avoid a condition known as insulinomas can result in significant increases in weight. (17)

- **Genetic Causes of Obesity**

The majority of the results of genome-wide searching for genes associated with the risk of obesity have been verified in corresponding studies from a diverse group that includes people from differing cultural backgrounds. (18) Several regions have high logged average chances ratings, but some of the particularly interesting ones include 2q14 (a protein encoding elevated triglycerides D2S410), 1p36 (a genetic for the TNF receptor D1S468), and 6q27 (a

locus connected to transient newborn diabetic mellitus). Conversely, prospective gene methods investigate variations in genomes which have been deemed significant.

- **Physical Pathology of Obesity**

Rheumatology is a major expense associated with overweight. Osteoporosis in the joints of the ankle and knee can be directly caused by injury associated with amount of extra weight one carries. (20) Non-weight-bearing knees can nevertheless be affected by altered cartilage, bone, and muscle breakdown.

Obstructive asleep apnea is a physiologically different condition that results in a deficit of ventilation during thoracoabdominal movements. Overweight could be caused by fat deposits in the neck and throat and impact seventy percent of individuals with obstructive sleep apnea (21). A reduction in remaining capacity of the lungs is associated with higher pressures across the lower abdomen (22) The level of oxygen in the air throughout the night changes and is usually low, thus the oxygen concentration measurement is not very useful for diagnosing (23) The only circumstances that affect the respiratory system in the absence of fundamental lung diseases are serious overweight levels.

Although thirty-three percent of obese people feel extremely tired throughout daylight hours while almost fifty percent sleep noisily, only five percent of obese people suffer sleep apnea that is obstructive. Obstructive snoring has been related to every obesity-related issue, including pressure and heart failure. Hypertension of the lung is also possible as a result of lung artery bed a decrease in blood during apnoea that persists during prolonged waking period. Although it has been linked to the emergence of pulmonary hypertension in some individuals, the condition has yet to be shown to serve as an indicator on its own themselves. (24)

Obesity and Insulin Resistance

The probability for getting diabetic increases every self-reported weight gained by nine percent per kg (25), usually starts to increase at a BMI of 22 (26), and increases by forty times beginning at a body mass index (B of 35 or above. (27, 28) resistant to insulin is widely recognized as a basic defect associated with type 2 diabetes with being overweight. Type 2 diabetes is significantly associated with obesity and overweight in every ethnic and racial background and among men and women alike. More than ninety percent of diabetes are obese or overweight people. (29) Usually, obesity and insulin resistance tend to happen prior to the onset of hyperglycemia. Present arguments state that higher levels of insulin put pressures on pancreas beta cell results, which is why diabetes of the second type occurs. (30

Vitamin B12

The vitamin B12 is essential to the health of humans. Vitamins B12, B6, and especially folate (vitamin B9) lower blood homocysteine amounts; mild elevations in methionine levels in blood are associated with coronary cardiovascular disease with neurological injury. (31-34) Furthermore, shortages of these nutrients are connected to a variety of malignant tumor forms

(35) , anemia, neuropathy, anomalies of the neural tube's development, including (36,37) developmental malformations. (38)

The use of vitamin B12 supplementation had no effect on medically sound fully developed or premature babies, but it may be helpful for malnourished youngsters. Serum or plasma vitamin concentrations indicate tissue stores. (39)

Severe deficiencies of vitamin B12 in the body are a sign of conditions like pernicious anemia that are associated with a lack of vitamin B12, as well as situations in which there is insufficient dietary intake or inadequate absorption ability. (40) Nevertheless, elevated blood levels of the B12 vitamin may stay elevated despite typical tissue retention in certain situations, especially leukaemia and diabetic with retinal degeneration, where the cells and tissues that normally store vitamins B12 are destroyed. It appears form the data that a lack of vitamin B12 happens more often than one might think. (41) Vitamin B12 deficiency can occur in herbivores along with individuals who cannot absorb the vitamin from diet. Along with devout vegetarians and vegans, there are some who limit their intake of meat or similar animal-based foods (42)

Vitamin B12 level was associated with obesity

Low levels of vitamin B12 were associated with obesity and overweight, but not with the presence of insulin resistance, a condition called metabolic syndrome, or sexuality. The sole association between B12 supplement and the index of body mass had an adverse correlation. (43) The biological process of an individual carbon requires B12. It contributes to the generation of ATP in cells and to epigenetic regulation activities such as DNA formation, restoration, and modification (44). The B12 molecule is concentrated in animal tissues, hence foods produced from animals are the only source of this vitamin.

Meals high in vitamin B12 include milk and other dairy products cattle, lamb, poultry, eggs, and liver (45). The two main causes of vitamin B12 insufficiency are inadequate consumption of animal products and vitamin B12 malabsorption (46). A lack of vitamin B12 is particularly prevalent in obese individuals, including obese kids and adolescents (47), obese women with polycystic ovarian syndrome (48), especially obese pregnant women (49–51), as reported by numerous investigations. However, conflicting findings have been found in earlier studies on the connection between serum vitamin B12 concentrations and obesity (49–56).

During this research, a sizable, nationally representative sample of mature Americans was examined for connections among serum levels of B12 and overweight. To the greatest extent of the information we have, this is the largest study that has been conducted to investigate the connection between universal overweight and circulating vitamin B12 levels. The results of earlier studies investigating the connection among overweight adults and plasma levels of vitamin B12 have been unclear (49–56).

Our outcomes correspond to line with earlier studies (47, 49–51, 53, 54, 57, 58) that discovered a negative correlation between serum vitamin B12 levels and overweight. nevertheless, most of this earlier research was restricted to a particular population—pregnant

women, for example—its conclusions were unable to be generalized to other communities (49–51, 57). Additionally, the results we obtained aligned well the outcomes of previous research endeavors involving juveniles and teenagers (54, 58).

There are several possible explanations for these correlations. A plausible rationale could be that insufficient levels of serum vitamin B12 bind folic as 5-the amino acid methyl, hindering the production of aminotransferase from methylene and consequently decreasing muscle accumulation and the creation of proteins (48). Another possibility is adipocyte malfunction, that is believed to be connected through inflammatory processes with decreased levels of vitamin B12 (51, 59). By reduced intake from food or digestion, heightened breakdown and retention in the fat cells (50), or modifications to intestinal microbiota identities, that could affect the availability of vitamin B12 metabolism (60, 61), overweight can additionally lower blood levels of vitamin B12 in the body. It's important to note how recent Danish research discovered a substantial correlation between higher BMI and lower plasma vitamin B12 levels although these was brought about by an inherited predisposition.

Role of Vitamin B12 and Folate in Metabolic Syndrome

Among the most devastating and crippling conditions affecting a big number individuals globally is mitochondrial dysfunction, but the incidence is rising alarmingly. A collection of pathogenic metabolic problems together referred to as MS includes elevated blood pressure, resistant to insulin, atherogenic dyslipidemia, also known as central or abdominal fat accumulation, chronic hypertensive (62).

In addition to increasing obesity thus acid manufacturing, deficiencies in folate that cobalamin amounts may interfere with the production of DNA and induce inflammation inside the cells (63). Another non-proteinogenic amino acids called methionine is created when protein from food like homocysteine are broken down (64) Because hyperhomocysteinemia causes atherosclerosis vascular-endothelial damage (66), it can also lead to insulin resistance (65), which can cause cardiac and neurological disorders. Investigations demonstrate the efficacy of vitamins B12, folic acid, and various other B complex vitamins supplementation to decrease the concentrations of homocysteine inside the human system. The connection among MS as well as the B-12 complicated, notably the amino acids folic acid and the B12 vitamin, has become the subject of numerous investigations undertaken internationally. Supplementing with folic acid as well as vitamin B12 has been linked in various trials to a reduction in res stant to insulin (69) and heart disease (68).

Conclusion

The results of the present research indicate that biochemical indicators are critical when it comes to overweight identification and for lowering the likelihood of consequences from the condition. According to this research, B12 (vitamin can be utilized to forecast the likelihood of inflammatory when serve as an indicator for pressure or overweight.

References

1. Gray DS. Diagnosis and prevalence of obesity. Med Clin North Am. 1989;73:1– 13.
2. Ferreira IM, Verreschi IT, Nery LE, et al. The influence of 6 months of oral anabolic steroids on body mass and respiratory muscles in undernourished COPD patients. Chest. 1998;114:19–28. .
3. Bjorntorp P. Metabolic implications of body fat distribution. Diabetes Care. 1991;14:1132–43. .
4. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab. 2004;89:2548–56. .
5. Prins JB. Adipose tissue as an endocrine organ. Best Pract Res Clin Endocrinol Metab. 2002;16:639–51. .
6. Metropolitan Life Insurance Company. New weight standards for men and women. Stat Bull Metrop Insur Co. 1959;40:1. [Google Scholar]
7. Burton BT, Foster WR. Health implications of obesity: an NIH Consensus Development Conference. J Am Diet Assoc. 1985;85:1117–21. .
8. World Health Organisation. Energy and protein requirements. Report of a joint FAO/WHO/UNU expert consultation. Geneva, Switzerland: World Health Organisation; 1985. WHO Technical Report Series 724. [PubMed]
9. World Health Organisation. The global epidemic of obesity. Geneva, Switzerland: World Health Organisation 1997.
10. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004;363:157–63. [PubMed]
11. Cameron AJ, Welborn TA, Zimmet PZ, et al. Overweight and obesity in Australia: the 1999–2000 Australian Diabetes, Obesity and Lifestyle Study (AusDiab) Med J Aust. 2003;178:427–32. .
12. Booth ML, Chey T, Wake M, et al. Change in the prevalence of overweight and obesity among young Australians, 1969–1997. Am J Clin Nutr. 2003;77:29– 36. .
13. Sturm R. The effects of obesity, smoking, and drinking on medical problems and costs. Obesity outranks both smoking and drinking in its deleterious effects on health and health costs. Health Aff (Millwood) 2002;21:245–53. .
14. Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective, observational analysis. Lancet. 2001;357:505–8. .
15. Butte NF. Fat intake of children in relation to energy requirements. Am J Clin Nutr. 2000;72(Suppl):1246S–1252S. .
16. Robinson TN. Television viewing and childhood obesity. Pediatr Clin North Am. 2001;48:1017–25. .
17. Bhargava SK, Sachdev HS, Fall CH, et al. Relation of serial changes in childhood body-mass index to impaired glucose tolerance in young adulthood. N Engl J Med. 2004;350:865–75. [PMC free article] .

18. Al-Adsani H, Hoffer LJ, Silva JE. Resting energy expenditure is sensitive to small dose changes in patients on chronic thyroid hormone replacement. J Clin Endocrinol Metab. 1997;82:1118–25.
19. Snyder EE, Walts B, Perusse L, et al. The human obesity gene map: the 2003 update. Obes Res. 2004;12:369–439. .
20. Liu YJ, Xu FH, Shen H, et al. A follow-up linkage study for quantitative trait loci contributing to obesity-related phenotypes. J Clin Endocrinol Metab. 2004;89:875–82. .
21. Felson DT, Anderson JJ, Naimark A, et al. Obesity and knee osteoarthritis. The Framingham study. Ann Int Med. 1988;109:18–24. .
22. Malhotra A, White DP. Obstructive sleep apnoea. Lancet. 2002;360:237–45. .
23. Fleetham JA. Upper airway imaging in relation to obstructive sleep apnea. Clin Chest Med. 1992;13:399–416. .
24. Strohl KP, Strobel RJ, Parisi RA. Obesity and pulmonary function. In: Bray GA, Bouchard C, James WP, editors. Handbook of Obesity. New York: Marcel Dekker; 1997. pp. 725–39.
25. Series F, Marc I, Cormier Y, La Forge J. Utility of nocturnal home oximetry for case finding in patients with suspected sleep apnea hypopnea syndrome. Ann Intern Med. 1993;119:449–53. .
26. Ford ES, Williamson DF, Liu S. Weight change and diabetes incidence: findings from a national cohort of U.S. adults. Am J Epidemiol. 1997;146:214–22. .
27. Colditz GA, Colditz GA, Willett WC, et al. Weight as a risk factor for clinical diabetes in women. Am J Epidemiol. 1990;132:501–13. .
28. Hu FB, Manson JE, Stampfer MJ, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med. 2001;345:790–7. [PubMed] [Google Scholar
29. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. JAMA. 1999;282:1523–9. .
30. Albu J, Pi-Sunyer FX. Obesity and diabetes. In: Bray GA, Bouchard C, James WPT, editors. Handbook of Obesity. New York: Marcel Dekker; 1998. pp. 697–707.
31. 37. DeFronzo RA. Lilly lecture 1987. The triumvirate: beta-cell, muscle, liver. A collusion responsible for NIDDM. Diabetes. 1988;37:667–87. .
32. 38. Stampfer MJ Malinow MR Willett WC et al. . A prospective study of plasma homocyst(e)ine and risk of myocardial infarction in US physicians. JAMA 1992;268:877-881
33. Selhub JMiller JW. The pathogenesis of homocysteinemia: Interruption of the coordinate regulation by S-adenosylmethionine of the remethylation and transsulfuration of homocysteine. Am J Clin Nutr. 1992;55:131-138.
34. Voutilainen S Lakka T Porkkala-Sarataho E Rissanen T Kaplan GA Salonen JT. Low serum folate concentrations are associated with an excess incidence of acute coronary events: The Kuopio Ischaemic Heart Disease Risk Factor Study Eur J Clin Nutr. 2000;54:424-428.
35. Allen L. How common is vitamin B-12 deficiency?Am J Clin Nutr. 2009;89: 693S-696S.

36. Cravo LMason BDayal Yet al. . Folate deficiency enhances the development of colonic neoplasia in dimethylhydrazine-treated rats Cancer Res. 1992;52:5002-5006.
37. Selhub J Rosenberg I. Folic acid. In: Ziegler EE Filer LJ, eds. Present Knowledge in Nutrition 7th edn. Washington, DC: ILSI Press; 1996:206-219.
38. ThompsonMD Cole DEC Ray JG . Vitamin B-12 and neural tube defects: the Canadian experience. Am J Clin Nutr. 2009;89:697S-701S.
39. HerbertV. The 1986 Herman Award Lecture. Nutrition science as a continually unfolding story: the folate and vitamin B12 paradigm. Am J Clin Nutr. 1987;46:387-402.
40. Vogiatzoglou AOulhajASmith AD. Determinants of plasma methylmalonic acid in a large population: implications for assessment of Vitamin B12 status. Clin Chem. 2009;55:2198-2206.
41. Baltaci, D., Kutlucan, A., Turker, Y., Yilmaz, A., Karacam, S., Deler, H., ... & Kara, I. H. (2013). Association of vitamin B12 with obesity, overweight, insulin resistance and metabolic syndrome, and body fat composition; primary care-based study. *Medicinski Glasnik*, *10*(2).
42. Choi SW, Friso S. Epigenetics: a new bridge between nutrition and health. *Adv Nutr.* (2010) 1:8–16. 10.3945/an.110.1004
43. Heyssel RM, Bozian RC, Darby WJ, Bell MC. Vitamin B12 turnover in man. The assimilation of vitamin B12 from natural foodstuff by man and estimates of minimal daily dietary requirements. *Am J Clin Nutr.* (1966) 18:176–84. 10.1093/ajcn/18.3.176
44. O'Leary F, Samman S. Vitamin B12 in health and disease. *Nutrients.* (2010) 2:299–316. 10.3390/nu2030299
45. Pinhas-Hamiel O, Doron-Panush N, Reichman B, Nitzan-Kaluski D, Shalitin S, Geva-Lerner L. Obese children and adolescents: a risk group for low vitamin B12 concentration. *Arch Pediatr Adolesc Med.* (2006) 160:933–6. 10.1001/archpedi.160.9.933
46. Kaya C, Cengiz SD, Satiroglu H. Obesity and insulin resistance associated with lower plasma vitamin B12 in PCOS. *Reprod Biomed Online.* (2009) 19:721–6. 10.1016/j.rbmo.2009.06.005
47. Knight BA, Shields BM, Brook A, Hill A, Bhat DS, Hattersley AT, et al.. Lower circulating B12 is associated with higher obesity and insulin resistance during pregnancy in a non-diabetic white british population. *PLoS ONE.* (2015) 10:e0135268. 10.1371/journal.pone.0135268
48. Krishnaveni GV, Hill JC, Veena SR, Bhat DS, Wills AK, Karat CL, et al.. Low plasma vitamin B12 in pregnancy is associated with gestational 'diabesity' and later diabetes. *Diabetologia.* (2009) 52:2350–8. 10.1007/s00125-009-1499-0
49. Sukumar N, Venkataraman H, Wilson S, Goljan I, Selvamoni S, Patel V, et al.. Vitamin B12 status among pregnant women in the UK and its association with obesity and gestational diabetes. *Nutrients.* (2016) 8:E768. 10.3390/nu8120768
50. Baltaci D, Kutlucan A, Turker Y, Yilmaz A, Karacam S, Deler H, et al.. Association of vitamin B12 with obesity, overweight, insulin resistance and metabolic syndrome, and body fat composition; primary care-based study. *Med Glas.* (2013) 10:203–10.

51. Allin KH, Friedrich N, Pietzner M, Grarup N, Thuesen BH, Linneberg A, et al.. Genetic determinants of serum vitamin B12 and their relation to body mass index. *Eur J Epidemiol.* (2017) 32:125–34. 10.1007/s10654-016-0215-x
52. Abu-Samak M, Khuzaie R, Abu-Hasheesh M, Jaradeh M, Fawzi M. Relationship of vitamin B12 deficiency with overweight in Male Jordanian Youth. *J Appl Sci.* (2008) 8:3060–3. 10.3923/jas.2008.3060.3063
53. Reitman A, Friedrich I, Ben-Amotz A, Levy Y. Low plasma antioxidants and normal plasma B vitamins and homocysteine in patients with severe obesity. *Isr Med Assoc J.* (2002) 4:590–3.
54. Tungtrongchitr R, Pongpaew P, Tongboonchoo C, Vudhivai N, Changbumrung S, Tungtrongchitr A, et al.. Serum homocysteine, B12 and folic acid concentration in Thai overweight and obese subjects. *Int J Vitam Nutr Res.* (2003) 73:8–14. 10.1024/0300-9831.73.1.8
55. Baltaci D, Kutlucan A, Ozturk S, Karabulut I, Yildirim HA, Celer A, et al. Evaluation of vitamin B12 level in middle-aged obese women with metabolic and nonmetabolic syndrome: case-control study. *Turk J Med Sci.* (2012) 42:802–9.
56. Gunanti IR, Marks GC, Al-Mamun A, Long KZ. Low serum vitamin B-12 and folate concentrations and low thiamin and riboflavin intakes are inversely associated with greater adiposity in Mexican American children. *J Nutr.* (2014) 144:2027–33. 10.3945/jn.114.201202
57. Kumar KA, Lalitha A, Pavithra D, Padmavathi IJ, Ganeshan M, Rao KR, et al.. Maternal dietary folate and/or vitamin B12 restrictions alter body composition (adiposity) and lipid metabolism in Wistar rat offspring. *J Nutr Biochem.* (2013) 24:25–31. 10.1016/j.jnutbio.2012.01.004
58. Castaner O, Goday A, Park YM, Lee SH, Magkos F, Shiow STE, et al. The gut microbiome profile in obesity: a systematic review. *Int J Endocrinol.* (2018) 2018:4095789 10.1155/2018/4095789
59. Woodard GA, Encarnacion B, Downey JR, Peraza J, Chong K, Hernandez-Boussard T, et al.. Probiotics improve outcomes after Roux-en-Y gastric bypass surgery: a prospective randomized trial. *J Gastrointest Surg.* (2009) 13:1198–204. 10.1007/s11605-009-0891-x
60. Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, Lung, and Blood Institute/American Diabetes Association conference on scientific issues related to management. Grundy SM, Hansen B, Smith SC Jr, Cleeman JI, Kahn RA. *Arterioscler Thromb Vasc Biol.* 2004;24:0–24.
61. Implication of homocysteine in diabetes and impact of folate and vitamin B12 in diabetic population. Mursleen MT, Riaz S. *Diabetes Metab Syndr.* 2017;11 Suppl 1:0–6.
62. The molecular and cellular effect of homocysteine metabolism imbalance on human health. Škovierová H, Vidomanová E, Mahmood S, et al. *Int J Mol Sci.* 2016;17:1733.
63. [Association between metabolic syndrome and hyperhomocysteinemia in an Algerian population] Zendjabil M, Abbou O, Chellouai Z. *Ann Pharm Fr.* 2017;75:54–58.

64. Association of homocysteine with type 2 diabetes: a meta-analysis implementing Mendelian randomization approach. Huang T, Ren J, Huang J, Li D. *BMC Genomics.* 2013;14:867
65. Effects of B-vitamins on plasma homocysteine concentrations and on risk of cardiovascular disease and dementia. Clarke R, Lewington S, Sherliker P, Armitage J. *Curr Opin Clin Nutr Metab Care.* 2007;10:32–39.
66. Effect of vitamin B6, B9, and B12 supplementation on homocysteine level and cardiovascular outcomes in stroke patients: a meta-analysis of randomized controlled trials. Kataria N, Yadav P, Kumar R, Kumar N, Singh M, Kant R, Kalyani V. *Cureus.* 2021;13:0.
67. Folic acid and vitamin B12 supplementation in subjects with type 2 diabetes mellitus: a multi-arm randomized controlled clinical trial. Satapathy S, Bandyopadhyay D, Patro BK, Khan S, Naik S. *Complement Ther Med.* 2020;53:102526.