**ORIGINAL RESEARCH PAPER**

**EFFECT OF VITAMIN B12 AND FOLIC ACID ON CHOLESTEROL**

**ABSTRACT**

**Introduction** - Atherosclerotic disease is most important cause of premature death1. Over past few decades it has been noted that moderate elevation of homocysteine contributes atherosclerotic vascular disease. The vitamin B12 and folic acid play a key role in homocysteine metabolism. Homocysteine is sulphur containing amino acid, produced in small amount in body. It is metabolized by remethylation requires vitamin B12 and Folic acid for transsulfuration2. Boushey et al suggested that an increase in plasma homocysteine results in cardiovascular risk. Out of these two, folic acid is most important determinant as it lowers homocysteine level in both normal and hyperhomocysteinemia subjects3. Lutteri et al4 had suggested that vitamin B12 and folic acid significantly reduced the homocysteine level by 30%.

Cholesterol is a vital component of all mammalian cells, and it is essential for normal functioning of the body. Lipids and lipid derivatives serve as biologically active molecules affecting a wide range of functions. They serve as structural components of biological membranes and energy reserves. However high levels of cholesterol in the blood circulation, depending on how they are transported with lipoproteins, and are strongly associated with increased risk of cardiovascular diseases (CVD)5.

Kumar et al6 demonstrate that in rats offspring from vitamin B12 (B12) deficient mothers had higher adiposity and altered lipid metabolism. They hypothesized that this may be due to dysfunctional adipocyte. These rats had higher total cholesterol, triglycerides, IL-6, and TNF-a and had lower adiponectin and leptin compared with control offspring. This reported association was mediated through adiposity highlighting the potential role of low vitamin B12-induced adipocytes dysfunction7.

The vitamens folic acid and B12 participate in one carbon metabolism as coenzymes. One carbon metabolism is biochemical pathways that donates and regenerate one-carbon units methyl group8. Vitamin B12 functions as a coenzyme for 5-methyltetrahydrofolate (MTHF)-dependent methionine synthase (MS) which catalyses the synthesis of methionine from homocysteine91011. Methionine is then converted to s-adenosylmethionine (AdoMet), a universal methyl group donor for methylation of DNA and RNA. Both vitamin B12 and folic acid play important roles in regulating the levels of AdoMet and homocysteine12.

Folic acid first isolated from Spinach. Folic acid composed of a heterocycle, p-aminobenzoic acid and glutamic acid. Folic acid is present in a wide variety of plants and animal tissues; the richest sources are yeast, liver, kidney and green vegetables. Folic acid undergoes reduction catalyzed by the dihydrofolate reductase to give dihydrofolic acid. It is required for the synthesis of purine and the methylation of RNA13. It is required for metabolism of the essential amino acid, Methionine14. Folic acid is a synthetic, oxidized form of folate with high bioavailability15. Oral supplementation of folate is necessary as it is not synthesized in humans16. Folate is essential for the regulation of Homocysteine, DNA and RNA metabolism, and methylation of multiple proteins. The liver is the main organ for folate storage and metabolism, and bile flow plays an important role in the folate hepatobiliary circulation17. Liver disease causes defects in the formation of 5-methyltetrahydrofolate (5-MTHF)18. Folate deficiency is a common occurrence in many liver diseases19. Folate deficiency causes structural changes in the DNA, neurological diseases, membrane defects due to hypomethylation of phospholipids, increased oxidative stress in the liver tissue and increased homocysteine level1920. Therefore, current study was designed to understand the mechanisms of how vitamin B12 and folic acid reduce the cholesterol level.

**Material & Method** - Hospital based cross sectional study was conducted in central clinical biochemistry laboratory June 2016 to Nov. 2017. The study comprised of 60 cases of those having serum cholesterol above 190 mg/dL. & 60 controls having normal serum cholesterol.

Results - In the present study, in cases serum cholesterol were found to be 366.6 ± 13.99 mg/dL & while in control group it was 147.6 ± 2.943 mg/dL. The mean level of vitamin B12 in cases was 366.6 ± 13.9 pg/mL and in the controls was 427.3 ± 19.50 pg/dL. The mean level of folic acid in cases was 10.17 ± 0.43 ng/mL and in the controls was 12.93 ± 0.25 ng/mL. Serum vitamin B12 & Folic acid level correlated with serum cholesterol and r value was -0.7040 and -0.3598.

Conclusion - vitamin B12 and folic acid has been found to lower serum cholesterol level and ultimately reduce the incidence of cardiovascular diseases. The present study shows that vitamin B12 and folic acid can also reduce one of the risk factors of cardiovascular diseases through its action on serum cholesterol.

**Biochemistry**

**KEY WORDS:** Metastasis, Bone, Breast, Prostate, Lung
Discussion

Cholesterol is a vital component of all mammalian cells, and it is essential for normal functioning of the body. Lipids and lipid derivatives serve as biologically active molecules exerting a wide range of functions. Lipid serves as structural components of biological membranes, provide energy reserves however, high levels of cholesterol in the blood circulation, depending on how they are transported within lipoproteins, and are strongly associated with increased risk of cardiovascular diseases (CVD)\(^7\).

The dietary supply of the methyl donor’s vitamin B12 & Folic acid is essential for normal growth, development, and physiological functions through the life course. Both human\(^11,12,18\) and animal6 studies have shown that deficiency of vitamin B12 is associated with altered lipid profile and metabolic disorder, and it has been hypothesized that this may be due DNA methylation changes. Tetrahydrofolate is active form of the folic acid. The Tetrahydrofolate is the carrier of one-carbon units. One carbon compound is an organic molecule that contains only a single carbon atom. This one carbon group is transferred to cobalamin to form methylcobalamin. Methylcobalamin is transferred methyl group to homocysteine for formed Methionine. So in folic acid and vitamin B12 deficiency no conversion of homocysteine to Methionine leads to accumulation of homocysteine. Homocysteine level in blood is positively correlated with atherosclerosis.

The close relationship of vitamin B12, folic acid, and homocysteine in the one-carbon cycle plays an important role in regulating the levels of S-adenosylmethionine and S-adenosyl homocysteine. S-adenosylmethionine is used in the methylation of DNA, RNA, proteins, phospholipids, and a number of other small molecules and it also altered ratio between S-adenosylmethionine and S-adenosylhomocysteine. Fernandez-Roig et al. have shown that vitamin B12 deficiency and Folate deficiency led to DNA hypomethylation in the brain.

Low vitamin B12 is associated with higher total cholesterol, induced cholesterol biosynthesis and homocysteine in adipocytes; increased expression of SREBP1 and SREBP2; and genes responsible for cholesterol biosynthesis; reduced S-adenosylmethionine to S-adenosylhomocysteine ratio and caused hypomethylation of SREBF1 and LDLR genes in their regulatory regions leading to increased mRNA expression; and increased expression of SREBP1c, LDLR, and HMGR in human adipose tissue\(^20\).

Folic acid (vitamin B9) is a synthetic, oxidized form of folate its high bioavailability\(^7\). It is not synthesized in humans body, so oral supplementation of folate is necessary. Folate is not only a structural component of cells but is also essential for the regulation of homocysteine, methylation of DNA and RNA\(^14\).

Folic acid acts as a potent antioxidant by scavenging free radicals and reducing oxidative stress. Folic acid prevents the oxidation of lipid. Folic acid has a hepatoprotective function and significantly prevents liver damage by oxidative stress fibrosis. By limiting oxidative damage, folic acid reduces the severity of the inflammatory response and prevents fibrogenesis\(^21\).

Folic acid stimulates reduced glutathione through the transsulfuration pathway from homocysteine\(^14\) and protects the liver by reducing serum homocysteine. Several studies have shown that folate deficiency or mutations in enzymes involved in homocysteine catabolism can result in increased homocysteine levels\(^19\).

Conclusion

Although, vitamin B12 and folic acid has been found to lower serum cholesterol level and ultimately reduce the incidence of cardiovascular diseases. The present study shows that vitamin B12 and folic acid can also reduce one of the risk factors of cardiovascular diseases through its action on serum cholesterol.

This supplementation had varying effects on the serum cholesterol, which depended on both the vitamin concentrations and the interaction between the two vitamins. The combination of these two vitamins intensified the effects on the serum cholesterol.

References


