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Vitamin B_{12} and Folic Acid: Significance in Human Health

Nutritionist's Perspective

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Vitamin B_{12} and folic acid are essential for formation of red blood cells, and are also believed to prevent disorders of central nervous system, mood disorders, and dementia [1]. Nutritional anemia due to vitamin B_{12} and/or folate deficiency is generally associated with hyperhomocysteinemia, which has been linked with pregnancy complications like pre-eclampsia, recurrent pregnancy loss and intra-uterine growth restriction [2]. A common cause of vitamin B_{12} deficiency is poor intake or absorption mediated by three transport proteins *viz* haptocorrin (HC), intrinsic factor (IF) and transcobalamin II (TCII). The deficiency is more common among vegetarians because they lack vitamin B_{12} in their diets [3]. Some of gastrointestinal diseases, such as Celiac disease or Crohn's disease which interfere with food absorption, may also lead to vitamin B_{12} deficiency [4]. Several studies from many parts of India (Bengaluru, Chennai, Delhi, Hyderabad, Pune, Varanasi) suggest that a large proportion of individuals (20-40%) are deficient in vitamin B_{12} and folic acid, presumably due to adherence to a strict vegetarian diet. Reports also suggest that polymor-phisms in genes involved in vitamin B_{12} absorption also contribute to the large pool of vitamin B_{12} deficiency. The National Health and Nutrition Examination Survey also estimated that 3.2% of adults over age 50 have a seriously low vitamin B_{12} level, and up to 20% may have a borderline deficiency. Large amounts of folic acid can mask the damaging effects of vitamin B_{12} deficiency by correcting the megaloblastic anemia caused by vitamin B_{12} deficiency [5].

Vitamin B_{12} deficiency has also been associated with dysfunctional immune response leading to increased susceptibility to infections. The study published in this issue of *Indian Pediatrics* [6] has observed the effect of nutritional parameters, serum albumin, folate and vitamin B_{12} levels in children with acute lymphoblastic leukemia (ALL) on recovery of bone marrow and peripheral blood counts as well as mortality during induction phase. The authors observed that a significant decline in folate levels on serial assays during chemotherapy, and folate-deficient children had higher risk for delayed marrow recovery and counts on day 14. Hypo-albuminemia, and vitamin B_{12} and folate deficiencies were associated with toxic deaths during induction phase of ALL. A consistent and significant decline in serial folate levels during initial two months of chemotherapy revealed that there could be an increased demand for folic acid and vitamin B_{12} in the presence of ALL, or it may be due to drug and nutrient interaction, which needs to be further explored. In multivariate analysis, folate deficiency continued to be a significant risk factor for incomplete bone marrow recovery and delayed recovery of counts. As the sample size is small, no convincing pathophysiology was established to support these findings. Further, there are two areas where vitamin B_{12} nutrition needs physiological research in India – first, in terms of its absorption, and second, in terms of functional indices of its deficiency.

The road to curing most children with acute lymphoblastic leukemia (ALL), the most common childhood cancer, may be the greatest success story in the history of cancer. The modern therapy for childhood ALL began in Boston when Dr. Sidney Farber, a pathologist at the Children's Hospital, developed an interest in childhood leukemia. Farber wondered whether folic acid would also cure ALL because it too featured immature blood cells and anemia. He tried it in some children, but it failed. He then reasoned that folic acid may have stimulated the growth of leukemia cells as well as normal cells and instead tried to block that stimulation with an antagonist of folic acid, aminopterin. Methotrexate (MTX) is an anti-cancer and antifolate drug that inhibits cell division by reducing intracellular amounts of reduced tetrahydrofolates. Experimental data have shown that increased folate concentrations intracellularly inhibit MTX metabolism and toxicity. It was concluded that folic acid supplements of 75-200 µg/day affect the proliferative capacity of the bone marrow. Sadananda, *et al*. [7] reported that folate levels were significantly high among ALL patients as compared to normal children. Although individually vitamin B_{12} and homocysteine were not significantly different between ALL and normals, the combined effect of all three parameters was significantly different. Thus, in the given context of public health significance; a comprehensive epidemiological and genetic study is necessary to understand the burden of vitamin B_{12} deficiency across the diverse geographical regions of the country. The authors also reported that the effect of undernutrition was not seen on the prognosis with ALL chemotherapy, which could be due to high prevalence of undernutrition (66%) among the studied population. Generally, high micronutrient deficiencies are a common phenomenon in all the children with high undernutrition [8]. Furthermore, the quality of the evidence is weak overall because most studies to date were cross-sectional, and established temporal relationship between vitamin B12 and folic acid, and ALL. Therefore, early detection and treatment is important. The studies should aim to assess the burden of vitamin B_{12} deficiency throughout the country *vis-à-vis* deficiency of the two other micronutrients, folate and iron.

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