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ORIGINAL ARTICLE

Role of Haematological Markers Predicting in Vitamin B_{12}, B_9 Status in Women

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ABSTRACT

Introduction and Aim: Both vitamin B_{12} (cobalamin) and vitamin B_9 (folate) are the essential micronutrients for the origin of red blood cells, DNA synthesis, and overall haematological health. Although disorders like megaloblastic anaemia can result from vitamin deficiencies, little is known about how these vitamins affect haematological parameters. This study was aimed to evaluate the role of haematological markers in predicting vitamin B_{12} and B_9 status among females aged 18-40 years. **Methods**: Using laboratory records from 150 female patients at Kasturba Hospital in Manipal from 2018 to 2022 a retrospective cross-sectional analysis was carried out. Serum levels of vitamin B_{12} and B_9, iron profile values, and complete blood count were examined. Reference ranges were used to classify the data into three groups: deficient, normal, and above-normal. Jamovi software was used to conduct statistical studies, including chi-square tests, with significance set $p < 0.05$. **Results**: Of the group, 37.7% had a folate insufficiency and 42.7% had a vitamin B_{12} deficiency. Thirty percent had low haemoglobin levels, and forty-four percent had a lower mean corpuscular volume (MCV). Haematological indicators such as haemoglobin, RBC count, WBC count, and MCV did not display a statistically significant correlation with vitamin B_{12} status, according to Chi-square analysis ($p>0.05$). **Conclusion:** It emphasizes the necessity of routine screening and early management by pointing out the significant frequency of vitamin B_{12} and B_9 deficiencies in the group under investigation. To better understand the relationship between haematological indicators and vitamin status, future studies should take into account co-morbid diseases, dietary practices, and genetic predispositions.

Keywords: Haematological markers; Vitamin B_{12} status; Folate (vitamin B_9) status; Nutritional deficiencies

INTRODUCTION

Vitamin B_{12} and vitamin B_9 are essential micronutrients, with shared functions and the deficiency can be associated with public health problems worldwide[1]. These two are water soluble vitamins; B_{12} is found largely in non-vegetarian sources, which is very important for normal neurological function, red cell production, and synthesis of DNA[2]. The main sources of vitamin B_{12}(cobalamin)are meat, dairy products, and that of folate (vit B_9) are leafy vegetables, fruits, and legumes as well as dairy products[3].

The human body retains a substantial reserve of vitamin B_{12}, ranging from 2 to 5 milligrams, compared to its daily needs. Consequently, even with severe malabsorption, it typically takes 2 to 5 years for a deficiency of vitamin B_{12} to manifest[4]. The Indian Council of Medical Research recommends daily dietary intakes of vitamin B_{12} 1μg/day for adults, 1.5 μg/day during pregnancy, and 1.2 μg/day during lactation. A vitamin B_{12} level of 200 pg/ml or lower is considered as deficient subclinical vitamin B_{12} insufficiency which is highly prevalent among the elderly and in impoverished countries, vegetarian populations and with excess alcohol.

Unlike vitamin B_{12}, in comparison to daily needs, the body's reserves of folate (5–10 mg) are quite tiny[5]. Therefore, folate must be ingested regularly. After many days of dietary folate limitation, serum folate levels fall. Folate deficiency is typically caused by dietary deficiencies and might affect the elderly and similar to people who are hyper-alimentating or haemolysing, population of alcoholics[6]. Assessments of folate in serum and red blood cells are used to make the diagnosis. Serum folate levels provide information about the patient's current folate levels, while red cell folate level provides information on folate levels for the six weeks' prior i.e. lifetime of RBC[7].

The synthetic form of folate is called folic acid. Folate is transformed into (tetra-hydrofolic acid) THF. This substance passes through a number of transfer/methylation processes that are critical for the synthesis of nitrogenous bases in RNA and DNA and are required for the development of red blood cells (RBCs)[8]. The inability to produce tetrahydrofolate due to a shortage in either vitamin B_{12} or folate inhibits cell proliferation in the marrow by causing a malfunction in DNA synthesis, but RNA synthesis and the synthesis of cytoplasmic components are unaffected which further results in megaloblastic anemia[5] with characteristic hyper-segmented polymorphic nuclear neutrophils[9].

Anaemia is a major problem worldwide and the most frequent hematologic disorder found in newborns and young children. Haemoglobin (Hb), haematocrit, or red blood cell counts that are below the typical age- and sex-adjusted values are considered to be anaemic in clinical practice[10].

Serum and plasma concentrations of these vitamins are the most helpful indicators for determining the status of the population with regard to folate and vitamin B_{12}. Additionally, variations in haematological indices in folate and vitamin B_{12} deficiency may aid in the diagnosis. These indices include mean corpuscular volume (MCV), red cell distribution width (RDW), mean platelet volume (MPV), platelet distribution width (PDW), RBC, haemoglobin (Hb), and haematocrit (HCT). But there is not much information available regarding these factors[11]. The aim of this study was to illustrate the role of these haematological markers in predicting the vitamin B_{12} and folate status in the body of women thereby preventing the occurrence of anaemia to some extent.

MATERIALS AND METHODS

- **Study design:** Retrospective cross-sectional study.
- **Study population:** Laboratory records of young and middle-aged females with serum vitamin B_{12} and B_9 reports from Kasturba Hospital, Manipal, were included.
- **Study setting:** Conducted over one year at the Department of Biochemistry, Kasturba Medical College (KMC), and the Department of Medical Laboratory Technology, MCHP, Manipal.
- **Sample size:** Data from 150 females aged 18-40 years were analysed. Records from January 2018 to December 2022 were included complete blood counts, serum vitamin B_{12}, B_9, ferritin, total iron binding capacity (TIBC), and serum iron levels.
- **Ethical approval:** Approved by the Institutional Research Committee (IRC) and Institutional Ethics Committee (IEC 533/2023) of Manipal Academy of Higher Education.
- **Eligibility criteria:**

1. Inclusion: Females aged 18-40 years with recorded vitamin B_{12} levels.
2. Exclusion: Individuals without vitamin B_{12} data.

- **Procedure:** Data from medical records were collected. Vitamin B_{12} levels were categorized as deficient (<197 pg/ml), suboptimal, normal, and above normal. Haematological parameters were compared across groups. The analysis explored patterns and associations within the dataset, emphasizing the role of haematological markers in diagnosing vitamin deficiencies.
- **Statistical analysis:** Data were analysed using Jamovi (version 2.3.26). Results were expressed as mean $\pm$ standard deviation. Associations between vitamins and haematological parameters were assessed using the with $p < 0.05$ considered significant.

RESULTS

The laboratory reports of total 150 female subjects with vitamin B_{12} level of age group between 18- 40 years were analysed in this study. Out of this vitamin B_9 was available in 79 cases. Available data related to iron profile, haematological parameters such as haemoglobin and red cell indices were collected.

All data were transferred to Jamovi for analysis. The analysed data was summarised in tables as follows:

The analysis of the dataset reveals a comprehensive array of haematological and nutritional parameters among the participants. Haematological measures include platelet count, white blood cell count, and haemoglobin averages and standard deviations indicative of diverse profiles among the subjects. These findings collectively underscore the complexity of individuals' haematological and nutritional statuses, highlighting the need for further investigation into potential deficiencies and their implications for overall health and well-being. Understanding these parameters provides valuable insights for implementing targeted interventions aimed at optimizing haematological health and mitigating potential health risks within the population (Table 1).

In Table 2, categorised laboratory information is provided as per the normal range.

A Chi-square test was performed to assess the relationship between vitamin B_{12} and hematological parameters. From Table 3, it is evident that there was no statistically significant association between vitamin B_{12} and hematological parameters (p-values of p> 0.05 stating their association to be statistically insignificant).

Table 1: Summary of age, haematological and biochemical profile

Variables	Mean	S.D.	Subjects (n)
Age	28.19	6.70	150
Vitamin B_{12} (pg /ml)	433.53	511.19	150
Folate (ng/mL)	7.74	5.49	79
Serum iron (ug/dL)	66.78	65.99	79
Ferritin (ng/mL)	162.76	271.50	65
TIBC (ug/mL)	341.42	92.66	67
Hb (g/dL)	10.86	2.621	148
WBC (cells/mL)	7567.12	2738.64	146
RDW %	16.20	4.57	146
RBC	4.22	2.39	147
Neutrophils (%)	58.27	12.18	146
Platelets (cells/mL)	276746.58	118902.79	146
MCV (fL)	84.09	12.66	146
MCH (pg)	27.67	1.96	146
MCHC (g/dL)	32.57	2.55	146

Table 2: Categorised laboratory information according to normal range

Parameter	Range	Category	Count	% of total
Vitamin B_{12} (pg/ml)	197-771	Deficient	64	42.7%
		Normal	67	44.7%
		More than normal	19	12.7%
Folate (ng/ml)	4.8-37.3	Deficient	29	37.7
		Normal	48	62.3%
Haemoglobin (g/dL)	12-15	Normal	105	70%
		Low	45	30%
Mean corpuscular volume (MCV)	83-101	Low	59	40.4%
		Normal	73	50%
		High	14	9.6%

Table 3: Chi square test- association between vitamin B_{12} and hematological parameters

Hematological Parameter / range	Reference	Vitamin B12		Total	Degrees of freedom	Chi-square Value	p-value
		Deficient	Normal				
Hemoglobin (12-15 g/dL)	Normal	22	18	40	1	0.778	0.378
	Low	41	47	88			
	Total (n)	63	65	n=128			
White blood cell count (4000-10000 cells /cu mm)	Normal	49	40	89	1	0.058	0.810
	Low	3	3	6			
	Total (n)	52	43	n=95			
Red blood cell count (3.8-4.8 million)	Normal	38	31	69	1	0.995	0.318
	Low	11	5	16			
	Total (n)	49	36	n=85			
Mean cell volume (83-101 femto liter)	Normal	34	30	64	1	0.295	0.587
	Low	24	26	50			
	Total (n)	58	56	n=114			
Neutrophils (42-74 percentage)	Normal	47	42	89	1	0.632	0.427
	Low	6	3	9			
	Total (n)	53	45	n=98			

Data from 150 female subjects revealed an average age of 28.19 years (±6.70). Mean vitamin B_{12} levels were 433.53 pg/ml (±511.19), and mean folate levels were 7.74 ng/ml (±5.49). Substantial variability was observed in iron-related markers and haematological parameters, including haemoglobin, WBC count, and platelet count.

Statistical analysis revealed no significant associations between vitamin B_{12} and haematological parameters ($p > 0.05$).

DISCUSSION

Vitamin B_{12} or B_9 deficiency is one of the reasons for megaloblastic anaemia which includes hematologic picture such as macrocytic erythrocytes, decreased platelets, decreased leucocytes, increased mean corpuscular volume. In our retrospective study we have studied these hematologic pictures in females by comparing them in two groups normal vitamin B_{12} level and decreased vitamin B_{12} level.

In this retrospective study, levels of serum vitamin B_{12} was available in 150 female subjects between the age group 18 to 40 years during the period Jan 2018 to Dec 2022. Significant percentage of studied population i.e., 42.7% out of 150 were having vitamin B_{12} deficiency. Serum folate levels were available in 77 subjects, 37.7% out of this had folate deficiency. In an azar cohort study by Azimi et al.[12], 61% of the study population had vitamin B_{12} deficiency and 16.8% of population had folate deficiency. A study conducted using several Brazilian demographic subgroups found that vitamin B_{12} deficiency was prevalent in 4.9% of the group under observation, folate deficiency was virtually non-existent (0.3%). Other research have revealed similar findings[13–19]. Low levels of vitamin B_{12} and folate were found in a significant proportion of participants (98.2% and 27.1%, respectively) in a published study by Fakhrizadeh et al.[20], that examined serum folate and vitamin B_{12} in healthy Iranian adults. According to Golbahar et al.[21], there is no fortification of grain products with folic acid in their nation, incorrect vegetable preparation, and a high incidence of low folate and vitamin B_{12} levels in their study. These factors could be the cause of these deficiencies. A study from India conducted by Sivaprasad et al.[22], found that prevalence of B_{12} deficiency is more among 20 to 60 years aged urban population compared to vitamin B_9 deficiency which is similar to our study. A study conducted by Mishra et al.[23], among children with megaloblastic anaemia found that increased number of children are having vitamin B_{12} and B_9 deficiency among which girls are more than boys.

In our study there is no association between serum B_{12} level and haematological markers such as haemoglobin, red cell indices, total leucocyte count. A study conducted by Azimi et al.[12], studied similar association between WBC, MCV, MCH, MCHC, RDW with folate levels found p value >0.05 indicating no statistically significant correlation. While other parameters like RBC, Hb, platelets had p-values <0.05, indicating statistical significance, which goes contrary to our study. In the study, the author also demonstrated no statistically significant association of vitamin B_{12} values with WBC, MCV, having p-values>0.05 which aligns with our study. While the association of vitamin B_{12} with Hb and RBC had a p-value <0.05 proving to be statistically significant which is opposite to our study.

The correlation between vitamin B_{12} concentration and Hb, MCV, MCH, and Hct has been supported by a number of research[24–26]. But most research[27–30] and the most recent meta-analysis did not establish such a link. The investigation regarding the relationship between haematological markers and the status of vitamin B_{12} and folate among female patients aged 18-40 years has yielded nuanced insights. Folate and vitamin B_{12} deficiencies are recognized as global health concerns, with substantial implications for haematological health and overall well-being. While the study revealed a notable prevalence of deficiencies in both vitamins alongside lower-than-normal haemoglobin levels, the direct associations between these deficiencies and haematological parameters appeared complex.

Despite the widespread prevalence of vitamin B_{12} and folate deficiencies, the study demonstrated limited significant association between haematological parameters and the levels of these vitamins. Notably, haemoglobin levels exhibited no significant associations with either vitamin B_{12} or folate levels, suggesting that anaemia in this cohort may not be solely attributable to these deficiencies. Similarly, other parameters such as red blood cell count, white blood cell count, and platelet count did not exhibit significant relationships with vitamin B_{12} or folate levels. However, certain findings hinted at potential connections. For instance, while mean corpuscular volume (MCV) showed a borderline significant association with folate levels, it did not show with vitamin B_{12} levels. This suggests a nuanced influence of folate status on red blood cell size and haematopoiesis, warranting further investigation.

Despite the study's insightful findings, several limitations need acknowledgment. The retrospective nature of the study and the specific demographic focus on females aged 18-40 years may limit the generalizability of the results. Additionally, demographic details and clinical symptoms and other factors such as dietary habits, genetic predispositions, and comorbidities were not explored but could significantly impact the observed associations. Furthermore, this lack of significant association prompts further investigation into potential underlying reasons. One possibility is that the levels of vitamin B_{12} and folate within the studied population might not be sufficiently varied to elicit observable effects on haematological parameters. Alternatively, factors such as genetic predispositions, dietary habits, absorption issues, or interactions with other nutrients could influence the relationship between vitamin B_{12}/folate levels and haematological parameters. Furthermore, it is essential to consider the complex interplay between these nutrients and other physiological processes that may indirectly impact haematological parameters. Therefore, additional comprehensive studies with larger and more diverse populations, along with detailed dietary and health assessments, are warranted to better elucidate the intricate relationships between vitamin B_{12}, folate, and haematological parameters. Such investigations are crucial for informing clinical practices and interventions aimed at optimizing haematological health and addressing potential deficiencies in vitamin B_{12} and folate.

More study is required to determine the impact of other factors, such as homocysteine levels and methyl malonic acid (MMA) on blood folate and vitamin B_{12} concentrations in order to obtain better and more reliable results.

CONCLUSION

This study highlights the prevalence of vitamin B_{12} and folate deficiencies among females aged 18-40 years. Comprehensive screening and management strategies are essential for addressing these deficiencies and optimizing haematological health. Further research is needed to explore interactions between haematological markers and vitamin status, considering dietary, genetic, and health factors.

Conflict of Interest

The authors declare no conflicts of interest.

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