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ORIGINAL ARTICLE

Evaluating Deficiency of Vitamin B12 and Risk Factors in Healthy Infants

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ABSTRACT

Background: The deficiency of vitamin b12 is highly extensive within the developed countries and is often found to remain undiagnosed within these populations. the main feature within infants suffering from vitamin b12 deficiency is altered neurological development and generalized growth. Effects of vitamin b12 deficiency on the brain can be prevented. To avoid these morbidities and mortality associated with vitamin b12 deficiency it is pivotal for clinicians to understand what other risk factors are associated with a deficiency within the infant population of developing countries.

Materials and methods: This cross-sectional study was conducted on 82 healthy infants for the assessment of Vitamin B12 at Pediatric Department of LGH, Lahore from March 2021 to August 2021. Participants were selected who were healthy. After recruitment, participants underwent hematological and biochemical indices analysis. Hemoglobin, serum vitamin b12, homocysteine and methylmalonic acid were different parameters measured. Maternal vitamin b12 deficiency was investigated along with risk factor vitamin b12 deficiency in healthy infants.

Results: A total of 82 recruited participants were selected after screening and meeting the recruitment criteria. After assessment of hematological data, anemia was diagnosed in 67.82% of infants (n=56). The breakdown of the anemic population showed that the male population was predominant with 58.2% affected males and 41.8% affected females. Decreased levels of plasma vitamin b12 concentration were documented in 22% of the population with a total number of 18 participants (male: 11, female: 7). Increased levels of homocysteinemia were documented in 49.1% of infants with n=40. Increased levels of methylmalonic acid were appreciated in all infants. As defined by previous criteria, the diagnosis of vitamin b12 deficiency was appreciated in 30 infants with a percentage of 38%. Furthermore, an assessment of folate deficiency showed that 8 out of 82 participants had concurrent folate deficiency in red cells with a percentile prevalence of 9.7%. maternal vitamin b12 deficiency was considered as risk factor for infant vitamin b12 deficiency

Conclusion: The prevalence of vitamin b12 deficiency in healthy infants is significantly high in developing and underdeveloped countries. Vitamin b12 deficiency cooccurs with anemia and other variation of biological markers. The study concluded that among the various risk factors that may predispose an infant to vitamin b12 deficiency, maternal b12 deficiency remains the highest appreciated risk factor.

Keywords: Vitamin B12, Risk Factors, Vitamin B12 deficiency, Maternal B12

INTRODUCTION

Cobalamine is the chemical name of vitamin b12 [1]. The deficiency of vitamin b12 is highly extensive within the developed countries and is often found to remain undiagnosed within these populations [2]. Vitamin b12 has an extensive range of functions in important processes within the body including those of erythroblast functions, formation, and maintenance of various components of the nervous system, and formation of various nucleic acids [3]. When deficient in individuals, its clinical symptoms present as poor development or function of the systems it is involved in. the main feature within infants suffering from vitamin b12 deficiency is altered neurological development and generalized growth [4]. Effects of vitamin b12 deficiency on the brain can be prevented. To avoid these morbidities and mortality associated with vitamin b12 deficiency it is pivotal for clinicians to understand what other risk factors are associated with a deficiency within the infant population of developing countries.

The most common cause of vitamin b12 deficiency in previous deficiency of vitamin b12 in mothers of infants [5], a diet deficient in the natural source of vitamin b12 such as a diet low in meat [6], and integral metabolic defects in the formation of vitamin 12. However, vitamin b12 deficiency due to maternal deficiency remains the highest causative factor. vitamin b12 deficiency is also highly prevalent in infants of Pakistan and there remains a literary gap to evaluate the causes and risk factors that predispose individuals to this condition. Therefore, the aim and objective of this literature piece are to evaluate the vitamin b12 deficiency among healthy infants and the causative risk factors that may predispose them to this deficiency.

MATERIAL AND METHODS

Inclusion and exclusion criteria: This clinical research was conducted in a tertiary care hospital setting in gynecology and pediatric department of LGH, Lahore from March 2021 to August 2021. Before recruitment of participants authors took written consent from the parents of infants included in the study. The participants were recruited on strict inclusion and exclusion criteria. The inclusion criteria included participants under one year of age, the participants must be of either sex and may fulfill the criteria of being healthy without any signs of any disease, the participants must be within the average range of growth and development as prescribed by Trivandrum Screening Developmental Test. The participants who met the inclusion criteria were recruited via different regular checkup visits at the pediatric department or sequential vaccination appointments. The exclusion criteria for the study included participants who are diagnosed to be vitamin b12 deficient or are receiving supplements of cobalamine, participants who do not fall into the average range of growth and development on the screening scale or participants whose parents wished not to take their children to study.

Procedure: After the recruitment of participants, all the infants were examined clinically and underwent hematological assessment. Besides a complete blood picture focusing on hemoglobin certain special elements of biochemical nature were focused on by the authors. The biomechanical indices were folate and vitamin b12 for assessment of b12 deficiency anemia, homocysteine for hyperhomocysteinemia, and plasma methylmalonic acid. These biomarkers indices were evaluated by employing the ADVIA Centaur XP system. The hematologic samples taken from infants were subjected to pretreatment before the analysis of biomarkers. This pretreatment of blood resulted in the release of folate from blood, and this was followed by mixing blood folate with folate reagent. This mixture was allowed to mix and sit in place of shadow for about 90 minutes. This mixture was then ready to be analyzed in the ADIVA Centaur XP system. The outcomes of the analysis were subject to multiplication with a

dilution factor which was 21. The outcome achieved by this was considered as the concentration of folate within the body nanogram per milliliter (ng/ml). the concentration of folate within the blood was achieved by dividing the concentration of folate in the body by the hematocrit of each participant and then multiplied by a hundred.

The measured methylmalonic acid in plasma was assayed by allowing the use of chromatography via reverse-phase liquid chromatography. The armamentarium and steps followed for assaying of plasma methylmalonic acid were similar to that presented by Pederson et al. in the year 2011 [7].

The cutoff values for this study were derived from various recommendations from reputable authorities. The cutoff value for anemia was considered to be hemoglobin levels of less than 11 ng/ml and a hematocrit index of the same or less than 33 percent [8]. The cutoff values of homocysteine for diagnosis of hyperhomocysteinemia were considered to be more than or equal to 15 µmol/L [9]. Vitamin b12 deficiency was considered with a lower cutoff as less than or equal to 203 pg/ml [10]. the higher cutoff values for diagnosis of high methylmalonic acid are taken as 0.45 µmol/L [11]. deficiency of folate in red blood cells is taken as less than or equal to 151 ng/ml. to establish the diagnosis of vitamin b12 deficiency, lower levels of plasma vitamin b12 deficiency with at least one of the following parameters must be met by each participant.

- High levels of plasma methylmalonic acid
- Either hyperhomocysteinemia without folate deficiency, or normal values of vitamin b12 with an increased level of single or both methylmalonic acid and homocysteine which resolves after management.

RESULT

The total amount of recruited participants was 82 after screening and meeting the recruitment criteria. The mean age of participants was 8 months ± 1.5 months. Out of 82 participants, almost 58.53% (n=48) were male. The remaining 41.47% of participants were girls (n=34). 43 out of 82 recruited participants' mothers were on a low or no meat diet (53.6%). The characteristics of infants were as follows

Table 1: demographic and hematologic characteristics of infants

Demographic feature	value
Mean age	8 months ± 1.5 months
Gender	Male: 50 Female: 32
Social demographic classification	
Upper class	15
Middle class	29
Lower class	38
Hematologic indices of infants	10.4 ± 1.7
Biochemical indices of infants	
Mean plasma vitamin b12 levels	512 (420-785)
Mean levels of homocysteine	14.1 (13.1-15.1)
Mean levels of methylmalonic acid	2.8 (2.0-3.6)
Mean levels of folate in red cells	452 (405-525)

After assessment of hematological data suggests that anemia was diagnosed in 67.82% of infants (n=56). The breakdown of the anemic population showed that the male population was predominant with 58.2% affected males and 41.8% affected females. Decreased levels of plasma vitamin b12 concentration were documented in 22% of the population with a total number of 18 participants (male: 11, female: 7). Increased levels of homocysteinemia were documented in 49.1% of infants with n=40. Increased levels of methylmalonic acid were appreciated in all infants. As defined by previous criteria, the diagnosis of vitamin b12 deficiency was appreciated in 30 infants with a percentage of 38%. Furthermore, an assessment of folate deficiency showed that 8 out of 82 participants had concurrent folate deficiency in red cells with a percentile prevalence of 9.7%. Similar to the hematological assessment of infants, a hematological assessment of mothers was also made to measure the risk factor associated with maternal vitamin b12 deficiency. The results of the assessment showed that vitamin b12 deficiency in mothers is directly correlated to vitamin b12 deficiency in infants with a risk almost as high as 5 times.

DISCUSSION

As previously mentioned in the study vitamin b12 deficiency within undeveloped and developed countries is significantly alarming as the majority of these cases remain subclinical and go undiagnosed. This academic literary piece aimed to fill the gap in the literature and provide a valuable source of information on vitamin b12 deficiency in infants. This study shows that the prevalence of vitamin b12 deficiency in seemingly healthy infants was as high as 38%. This study showed that vitamin b12 deficiency was accompanied by hyperhomocysteinemia, increased methylmalonic acid, and decreased level of folate in red cells. This section of discussion will discuss the prevalence of vitamin b12 deficiency in Pakistan and around the world and associated risk factors such as maternal vitamin b12 deficiency.

To assess the deficiency of vitamin B12 in Pakistani children a study was conducted by Hassan et al. 2019 in the city of Peshawar. The study was conducted from January 2019 to June 2019 and was cross-sectional. The total sample size of the study was 228 participants. A total of 60 participants in the sample size word diagnosed to be deficient in vitamin B12 deficiency which made a prevalence percentage of 34.6% wait a maximum number of affected participants being female [12]. These findings are different from the outcomes of this clinical experiment in that this study reported a higher prevalence of vitamin B12 deficiency with a predominance in the male population however the study included in the discussion shows an increased predominance in the female population. The variation in results could be accounted for due to the difference in the age of recruited participants.

Due to limited studies conducted on vitamin B12 deficiency in infants in Pakistan, studies conducted in other developing or underdeveloped countries were also reviewed to compare and contrast the outcomes of this clinical research. A study was conducted by Goraya in 2020 and assessed vitamin B12 deficiency among infants. The study publication included 25 infants who belonged to lower socioeconomic status with mothers being on a low meat diet. All the participants of this study were anemic and showed signs of malnutrition. the participants have then subjected to vitamin B12 supplements and were assessed for improvement. the results showed improvement in the anemic state as early as the 4th day and vitamin B12 deficiency was marked as the cause of anemia in all infants [13]. This study showed the prevalence of vitamin B12 deficiency causing anemia to be as high as 100% in all infants. this increased prevalence of anemic state and vitamin B12 deficiency could be accounted for due to lower social-economic demographic status. Another study conducted by Umansankar et al. In the year 2020 studied the prevalence of vitamin b12 deficiency among children. The nature of this study was perspective and was conducted in a tertiary care hospital. The study sample included 111 participants. prevalence of vitamin B12 deficiency was seen in 64.8% of the participants with 72 out of 111 participants suffering from vitamin B12 deficiency [14]. Above mentioned studies show a very high prevalence of vitamin b12 deficiency and show that an extensive amount of vitamin B12 deficiency children may go undiagnosed, and prevalence is so high that a large number of morbidity and mortality may be associated with this condition if remain unacknowledged.

Risk factors for vitamin B12 as appreciated in this study were also reviewed in literature and maternal deficiency of vitamin b12 was appreciated as a major risk factor for vitamin B12 deficiency among the infants. A study was conducted by Finkelstein in 2021. The authors evaluated the correlation between maternal vitamin b12 deficiency resulting in vitamin B12 deficiency in their infants. This study population included perinatal females

who were recruited for the cohort study. The complete sample size included 419 participants. the results of the study showed that63.2% of the participants had vitamin b12 deficiency. Furthermore, when assessing newly born children, 40.8% of the infants have been diagnosed with vitamin b12 deficiency [15]. The outcomes of this study are similar to those suggested by the authors of this study. vitamin B12 deficiency in mothers has directly correlated to vitamin b12 deficiency in neonates and poses a risk factor for new generations.

The discussion of study outcomes suggests that the prevalence of vitamin b12 deficiency is significantly high in developing and underdeveloped countries. Vitamin b12 deficiency cooccurs with anemia and other variation of biological markers. The study concluded that among the various risk factors that may predispose an infant to vitamin b12 deficiency, maternal b12 deficiency remains the highest appreciated risk factor.

CONCLUSION

This study aimed to fill the literature gap on the prevalence of anemia, vitamin b12 deficiency, and other alterations in biochemical indices in infants who were seemingly healthy and associated risk factors such as maternal vitamin b12 deficiency. This study is proposed to fill the literature gap and provide a prototype for further research and increase the knowledge of disease and its prevalence among practitioners and the general population.

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