# Case Series of Megaloblastic Anemia due to Vitamin B12 Deficiency in Exclusively Breastfed Infants Born to Vegan Mothers in a Rural Area

Singh V*, Nigwekar P**, Dhyabar A*, Garg A*, Vaidya S*, Lonare N*

**Abstract**

*Background: Megaloblastic Anemia is due to Vitamin B12 and /orfolic acid deficiency. Vitamin B12 deficiency can be caused by decreased absorption, decreased intake or impaired utilization. In recent years nutritional deficiency has been seen to be far more common in vegan families. In infants, it is related to maternal deficiency with resultant inadequate body stores and prolonged exclusive breast feeding. Folate deficiency can be caused by impaired absorption, utilization and infants who consume only goat's milk.*

**Key words:** *Vitamin B12 deficiency, Anemia, Vegan Mother*

## Introduction

Megaloblastic Anemia is not frequent during infancy. Vitamin B12 deficiency anemia, considered rare was observed in infants fed exclusively on the breast milk by anemic or malnourished mother who were suffering from vitamin B12 deficiency. A study has put the incidence of folate deficiency as 6.8%, Vitamin B12 as 32% and combined deficiency as 20% in North Indian children.[1] Vitamin B12 is a water soluble vitamin and plays a major role in human metabolic reactions. Humans are totally dependent on dietary vitamin B12. Strictly vegetarian diets do not provideadequate amounts of this essential nutrient. Dietary sources of vitamin B12 are almost exclusively from animal foods. Vitamin B12 deficiency in infancy may be due to an inborn error of absorption and metabolismbut most reported cases are breast fed infants of mothers, who themselves are deficientin vitamin B12 as a result of strict vegetarian diet.[2,3]

**Criteria adopted for study :**

1. Each child was assigned a socioeconomic status according to Modified Kuppuswami Classification.
2. Mother was considered vegan if vegetarian with non-consumption of dairy products & eggs.
3. Hyperpigmentation of nail beds and knuckles, glossitis, angular stomatitis and bald tonguewere considered as a feature of vitamin B12 deficiency.
4. Microcytosis wasdefined as MCV < 80 femtolitre, Macrocytosis as MCV> 95 femtolitre & Microcytic anemia as MCV between 80-95 femtolitre.
5. Serum vitamin B12 normal value: 200–800 pg/ml.
6. No history of any medication intake & other major medical disorder.

**Case Presentations:**

**Case 1:** A 7 month's old male infant was born full term (40 weeks) by cesarean delivery with birth weight of 2.9 kg. He was exclusively breast fed till 7 months of age. Infant presented with noisy breathing and fever since 1 week andwas hospitalized as a case of pneumonia. On admission, he was found to be pale. Weight was 6500 gm (3rd–50thpercentile) and other anthropometric measures were within normal limits. Blackish knuckle pigmentation of fingers and toes were seen. There was no lymphadenopathy and no organomegaly.

**Case 2:** A 8 month old male infant was born full term (40 weeks) by cesarean delivery with birth weight 2.5 kg and exclusively breast fed till 8 months of age. Infant presented with complaint of progressive pallorsince 2 months. Hewas hospitalized as a case of severe anemia. Weight was 7200 g (3rd–50thpercentile) and other anthropometric measures were within normal limits.

*Resident, **Associate Professor, Dept. of Paediatrics, Rural Medical College, Pravara Institute of Medical Sciences, Loni, Maharashtra

**Corresponding author-**
Dr. Vivek Singh
Resident, Dept. of Paediatrics, Rural Medical College,
Pravara Institute of Medical Sciences, Loni, Maharashtra
email: vivekhims@gmail.com

Blackish knuckle pigmentation of ?ngers and toes with glossitis were seen.

**Case 3:** A 6 month old female infant, born full term with birth weight 2.5 kg. She was exclusively breast fed till 6 months of age. Infant presented with complain of excessive irritabilitysince 6 days. On admission, she was found to have moderate pallor. Her weight was 6000 gm (3rd–50th percentile) and other anthropometric measures were within normal limits. Blackish knuckle pigmentation of fingers and toes were seen (Fig. 1,2 & 3).

**Case 4:** A 6 month old female infant, born full term with birth weight 2.7 kg. She was exclusively breast fed till 6 months of age, came for vaccination. She was found to be pale, with a weight of 5900 gm (3rd–50th percentile) and other anthropometric measures were within normal limits.

**Case 5:** A 7 month old male infant, born full term with birth weight 3 kg and was exclusively breast fed till 7 months of age, presented with complaint of blackish knuckle pigmentation of fingers and toes. He was found to be pale, with a weight of 6520 gm (3rd–50th percentile) and other anthropometric measures are within normal limits.

In all cases no organomegaly was there. Neurodevelopmental assessment was appropriate for age. Mothers were strictly vegan. All infants were belonging to very low socioeconomic state as per modified Kuppuswamy's classification.

**Lab Investigations:**

| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 |
|---|---|---|---|---|---|
| Hb% | 7.8 | 6.0 | 8.2 | 7.9 | 8 |
| TLC | 3800 | 2700 | 4200 | 5600 | 5200 |
| MCV | 105 | 118 | 110 | 105 | 100 |
| MCH | 21.9 | 22 | 21.2 | 22 | 20.8 |
| MCHC | 33.7 | 32.4 | 33.1 | 34 | 32 |
| Platelet counts | 98,000 | 82,000 | 100,000 | 90,000 | 79,000 |
| Reticulocyte count | 0.3% | 0.6% | 0.4% | 0.5% | 0.5% |
| PBS | Dimorphic anemia | Macrocytic Hypochromic | Macrocytic Hypochromic | Macrocytic Hypochromic | Macrocytic Hypochromic |
| Serum Vit. B12* | 118 | 105 | 110 | 106 | 104 |

*Normal Vit. B12 Level: 200- 800 pg/ml

On the basis of above data four patients were diagnosed as Megaloblastic Anemia due to vitamin B12 deficiency & one patient was diagnosed as dimorphic anemia. Vitamin B12 was supplemented in doses of 1mg/day for 2 weeks with folic acid 0.5mg/day followed by vitamin B12 0.1mg/dose every month till correction of anemia. Few weeks after the start of therapy Hb% level starts improving. Proper diet with complimentary feeding was advised for all infants. Mothers were also counseled about the diet modification.

**Cases showing pallor and blackish knuckle pigmentation in fingers**

Fig. 1

Fig. 2

Fig. 3

**Peripheral smear showing Macrocytosis, ovalocytes, Anisocytosis, Poikilocytosis and Hypersegmented neutrophils**

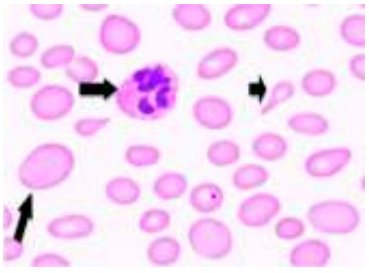

Fig. 4

## Discussion

Vitamin B12 deficiency usually occurs in infants born to vegan mothers and this is an important cause of anemia & developmental delay. The average daily requirement for an infant is 0.5-0.6 µg/day. Vitamin B12 is freed from binding proteins in food through the action of pepsin in the stomach and binds to salivary proteins called cobalophilins, or R-binders. In the duodenum, bound vitamin B12 is released by the action of pancreatic proteases. The released vitamin B12 binds to intrinsic factor produced by gastric parietal cells and is transported to the distal ileum. Within ileal cells, vitamin B12 associates with a major carrier protein, transcobalamin II, and is secreted into the plasma. Transcobalamin II delivers vitamin B12 to the liver and other cells of the body, including rapidly proliferating cells in the bone marrow and the gastrointestinal tract. In the absence of intrinsic factor, cobalamin is absorbed ineffciently by passive diffusion.[4] Megaloblastic anemia due to cobalamin or folate deficiency is due to ineffective erythropoiesis. Vitamin B12 is necessary for DNA synthesis and its deficiency prevents cell division in the marrow. Due to deficiency of folate or vitamin B12, red blood cells become large with nuclear or cytoplasmic asynchrony, a characteristic of all megaloblastic anemias. Non specific manifestations of megaloblastic anemia include weakness, fatigue, failure to thrive and irritability. Other features seen are pallor, glossitis, vomiting and diarrhea. Neurologic symptoms include hypotonia, developmental delay, seizures, psychiatric changes, ITS (Infantile Tremor Syndrome) and subacute combined degeneration of spinal cord.[3] In peripheral smear, macrocytic red cells, hypersegmented neutrophils, anisocytosis and poikilocytosis are seen. Reticulocyte count is low, elevated homocysteine and LDH levels in blood are seen. Serum vitamin B12 levels were low with normal folate and ferritin levels.

In India, especially in rural areas where people tend to be vegetarians (not even dairy products), vitamin B12 deficiency during pregnancy is common.[5] Vitamin B12 supplementation in pregnant and lactating women, and the use of complementary vitamin B12-rich foods in infants aged >6 months are useful in preventing megaloblastic anemia but in a developing country like India, economic problems may profoundly impact the consumption of meat and other animal products. Unlike infants, even if the serum levels of vitamin B12 are low, pregnant women generally show no related signs or symptoms because they usually consume large amounts of leafy vegetables containing high folate content that masks the hematological effects of vitamin B12 deficiency.[6] If vitamin B12 deficiency in infants is not treated early, it leads to anemia & developmental delay, developmental regression and convulsions. Cognitive and developmental delay may persist despite of adequate therapy even though the hematological problems may disappear completely.[7] In our case series, infants clinically had pallor and blackish knuckle pigmentation of fingers and toes. Smear showed macrocytosis, severe anisocytosis, poikilocytosis and hypersegmented neutrophils with occasional fragmented cells and tear drop cells (Fig. 4). Reticulocyte count was low with significant low levels of Vitamin B12 were found in all subjects.

## Conclusion

This shows that Megaloblastic Anemia is very common in exclusively breast feed infants whose mothers are strict vegans. It also highlights the importance of vitamin B12 supplementation during pregnancy and lactation especially in case of vegans, whose infants are more likely to be affected than other babies. In infants diagnosed with anemia, it is important to rule out megaloblastic anemia, as it is a preventable cause of developmental delay.

## Recommendation

Vitamin B12 supplementation should be given to all pregnant and lactating mothers along with iron & folic acid tablets, especially vegan mothers of rural areas.

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