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ABSTRACT... Objectives: To determine Vitamin B12 and Folic Acid Deficiency among Malnourished Children with Pancytopenia. Study Design: Cross-Sectional study. Setting: Department of Pediatric Sheikh Zayed Medical College / Hospital, Rahim Yar Khan. Period: 1st April 2017 to 25th February 2018. Material & Methodology: In this study 60 children having malnutrition and pancytopenia were included. The given performa was filled and record was maintained. Children visiting Paediatric OPD or admitted in the ward having severe malnutrition and pancytopenia in Complete Blood Count were included in the study. While the malnourished Children with normal blood count and children with malignancy e.g; Leukemia, lymphoma etc. were excluded from the study. Results: In this study, mean age of patients was 5 ± 4.2 years, mean weight 10.3± 7.6 kg, mean hemoglobin was 6 ±6.5 g/dl, mean folic acid was 7.7± 6.7 (median 5.6) and mean vitamin B12 563± 537 (median 367). Out of total 37 (61.7 %) were male. In this study, grade I malnutrition was 2 (3.3 %), grade II, 17 (28.3%) and grade III, 41(68.3%). Conclusion: Vitamin B 12 & Folic Acid deficiency is found to be a major factor of bone marrow suppression in malnourished children and our result showed that folic acid deficiency was significantly low in females and Vitamin B12 in males.

Key words: Folic Acid, Malnutrition, Pancytopenia, Vitamin B 12
There is often a pancytopenia with macrocytosis. The study we have conducted in malnourished children is to determine the relation of vitamin B12 and folic acid deficiency with pancytopenia.

Material & METHODOLOGY

Study Design
Cross Sectional Study

Sample Size
60 malnourished children with pancytopenia.

Study Subject
All the malnourished children presenting with pancytopenia was investigated for Vitamin B12 and Folic Acid level in their blood and find out the relation of Pancytopenia with these micronutrients.

Inclusion Criteria
Following Children were included in the study:
- Children visiting in Paediatric OPD or admitted in the Ward
- Children visiting in private clinics
- Severely Malnourished children (grade 3 Gomez Classification)
- Pancytopenia in Complete Blood Count

Exclusion Criteria
- Malnourished Children with normal blood count
- Children with malignancy e.g; Leukemia, lymphoma etc.

Data Collection Method
The data was collected on a predesigned questionnaire with variable including age, sex, vitamin B12 and folic acid levels in serum.

Data Analysis
SPSS version 23 was used for the analysis of collected data. Quantitative variables were age, weight of the child, degree of malnutrition, serum level of vitamin B12 and Folic acid. These variables were presented as mean and standard deviation. Qualitative variables were gender and socioeconomic status of the child. Post stratification Chi-Square was applied. P value ≤ 0.05 was taken as significant. Ethical approval was sought from Institutional Review Board.

RESULTS
In this study, the mean age of patients was 5 ± 4.2 years, mean weight 10.3± 7.6 kg, mean hemoglobin was 6 ±6.5 g/dl, mean folic acid was 7.7± 6.7 (median 5.6) and mean vitamin B12 563± 537(median 367). Out of total 37 (61.7 %) were male. In this study, grade I malnutrition was 2 (3.3 %), grade I I, 17(28.3%) and grade I I I, 41(68.3%).

Table-I shows that among malnourished children with pancytopenia 27 (45%) have normal serum Folic acid level, 7 (11.7 %) has excess and 26 (43.3%) has significant deficiency and it is more in female (P= 0.00). Regarding Vitamin B12 level37 (61.7%) has normal level, 12 (20%) has excess, and 11(18.3%) has deficiency and it is more in males (P = 0.05).

|                | Normal | Excess | Deficiency | Total | P-Value |
|----------------|--------|--------|------------|-------|---------|
| **Sex**        |        |        |            |       |         |
| Male           | 21 (56.8%) | 6 (16.2%) | 10 (27.0%) | 37 (100%) | 0.00    |
| Female         | 6 (26.1%)  | 1 (4.3%)  | 16 (69.6%) | 23 (100%) |         |
| **Total**      | 27 (45%)  | 7 (11.7%) | 26 (43.3%) | 60 (100%) |         |

|                | Normal | Excess | Deficiency | Total | P-Value |
|----------------|--------|--------|------------|-------|---------|
| **Sex**        |        |        |            |       |         |
| Male           | 19 (51.4%) | 8 (21.6%) | 10 (27.0%) | 37 (100%) | 0.05    |
| Female         | 18 (78.3%) | 4 (17.4%) | 1 (4.3%)  | 23 (100%) |         |
| **Total**      | 37(61.7%) | 12 (20%) | 11(18.3%)  | 60 (100%) |         |

Table-I. Sex distribution versus Folic Acid and vitamin B 12 in malnourished children with pancytopenia.
DISCUSSION
In malnourished children, there are different factors leading to bone marrow suppression. Iron deficiency anemia leads to microcytic, hypochromic anemia. Other vitamins and minerals can also cause anemia. Folic acid and Vitamin B\textsubscript{12} are essential components in DNA synthesis. Folic acid is directly involved while Vitamin B\textsubscript{12} participates as a co-factor. A deficiency of Vitamin B\textsubscript{12} causes the same symptoms as folic acid deficiency. Deficiency of either factor disrupts the maturation process of cells which leads to megaloblastic change in precursors. Ifra Sameen, Yasmin Chana described that Pancytopenia due to Folic Acid and Vitamin B 12 deficiency is more common in malnourished children.\textsuperscript{7} Sarode R, Garewal G et al found that during progression (in terms of duration) of megaloblastosis, anemia is followed by thrombocytopenia and then neutropenia.\textsuperscript{8} Gomber S, Kumar S et al found that isolated deficiency of Vitamin B12 or in combination with iron deficiency, is an important cause of anemia. Same is with Folic acid deficiency.\textsuperscript{9}

Talarmin F, Hugard L et al recognized that vitamin B12 and Folic acid deficiencies are common in underdeveloped countries and are responsible of megaloblastic anemia and pancytopenia.\textsuperscript{10} Sarode R1, Garewal G et al found that out of 139 patients of pancytopenia, 102 cases in whom the biochemical parameters were available, vitamin B12 deficiency was detected in 76%, folate deficiency in 6.8%, combined B12 and folate deficiency in 8.8%; the remaining 7.8% had normal vitamin levels at presentation.\textsuperscript{11} Palaniyandi Anitha, Rajendra Prasad Sasitharan et al reported Helicobacter pylori (H. pylori) related B12 deficiency presenting as pancytopenia in pediatric age groups.\textsuperscript{12}

Hansen PB, Jorgensen LM found that the patients suffering from pancytopenia of folic acid deficiency were improved after the administration of folic acid.\textsuperscript{13} Osman Yokus, Ozlem Sahin Balci\textsuperscript{k} described a patient who admitted with walking difficulties for 15 days the investigations showed pancytopenia and elevated LDH. His condition was improved after treatment with folic acid and vit B12.\textsuperscript{14} Ozlem Pelin Sim\textsuperscript{c}ek, Nazli Gönç et al described a 16-month-old infant who presented with developmental regression, pancytopenia, skin pigmentation and tremor resulting from vitamin B12 deficiency.\textsuperscript{15} 109 pediatric patients with pancytopenia were analyzed by Shishir Kumar Bhatnagar, Jagdish Chandra et al retrospectively and megaloblastic anemia was found to be the most common etiological factor (28.4 per cent).\textsuperscript{16} Sushant Mane, Sonali singh et al intramuscular methylcobalamin for 2 weeks followed by oral methylcobalamin and folic acid.\textsuperscript{17} Enver Atay, Mehmet Akin found decreased count in different cell lines in some patients out of 212.\textsuperscript{18} During finding the frequency of the different causes of Pancytopenia, Tariq Aziz, Liaquat Ali et al observed pancytopenia in a large number (40.90%) of patients who were diagnosed as Megaloblastic Anemia. Out of them, 77.77 % had vitamin B12 deficiency.\textsuperscript{19}

Ravindra Sarode, G Garewal et al concluded that during progression (in terms of duration) of megaloblastosis, anemia is followed by thrombocytopenia and then neutropenia.\textsuperscript{20} Salma Haq, Nasir Iqbal et al found that Folic acid deficiency (62.5%) was the commonest cause of megaloblastic anemia.\textsuperscript{21} This study revealed that almost half of children having malnutrition and pancytopenia has folic acid deficiency and it was more in female (P = 0.00), whereas one fifth of these children has vitamin B12 deficiency and more in male (P = 0.05). In contrast to our study, some of the previous studies have described that deficiency of Vitamin B12 was more common than folic acid deficiency in patients with severe acute malnutrition.\textsuperscript{22,23}

CONCLUSION
Vitamin B 12 and Folic Acid deficiency may be a major factor of bone marrow suppression in malnourished children and our result showed that folic acid deficiency was significantly low in females and Vitamin B12 in males.

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| 2     | Ghulam Mustafa          | Data analysis.                                           |                     |
| 3     | Sajida Khalid           | Data collection, Literature review.                      |                     |
| 4     | Shoaib Younis           | Data collection.                                         |                     |
| 5     | Riaz ul Haq             | Literature review.                                       |                     |
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