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Haematological Profile in Children with Protein Energy Malnutrition in North Central Nigeria

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Abstract - Background : Protein Energy Malnutrition (**PEM**) is associated with various changes in the body systems including changes in the haematologic system. These changes affect all the blood cells.. Observations about haematological changes in this group of children have been inconsistent due to frequent and constant changes in haemopoiesis resulting from this condition. This has limited the usefulness of these parameters in the anticipatory care of these patients thus the need to describe and validate the changes and possible haematological disturbance among children with **PEM** informed this study in Ilorin, North-central Nigeria.

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Haematological Profile in Children with Protein Energy Malnutrition in North Central Nigeria

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Abstract - Background : Protein Energy Malnutrition (PEM) is associated with various changes in the body systems including changes in the haematologic system. These changes affect all the blood cells. Observations about haematological changes in this group of children have been inconsistent due to frequent and constant changes in haemopoiesis resulting from this condition. This has limited the usefulness of these parameters in the anticipatory care of these patients thus the need to describe and validate the changes and possible haematological disturbance among children with PEM informed this study in Ilorin, North-central Nigeria.

Methodology : All children admitted into the Emergency Paediatric Unit (EPU) with a diagnosis of PEM were enrolled over a period of one year (January – December 2009). Controls were well children attending the routine clinic without haematologic or infectious condition. Haematological profiles were determined using auto-analyzer SMX 60. Data entry and analysis were carried out with a micro-computer using the Epi info version 3.5 (2008) software packages and p value of < 0.05 was regarded as significant.

Results : Ninety children with PEM and 90 age and sex matched controls were studied. Children with PEM had lower mean values for haemoglobin, haematocrit and mean corpuscular haemoglobin (p<0.05) when compared with controls. The mean value of WBC in the children with PEM was $12.8 \pm 11.6 \times 10^3$ cell/mm³ while it was $5.9 \pm 8.7 \times 10^3$ cell/mm³ among the controls (p= 0.001). The mean value of platelet counts were $291.8 \pm 131.7 \times 10^9 / L$ and $326.4 \pm 133.9 \times 10^9 / L$ for the subjects and controls respectively (p=0.0001). A statistical significant difference was observed in the lymphocyte count of the various classes of PEM with the edematous forms having higher counts (p= 0.0001).

Conclusion / Recommendation : In conclusion, Children with Protein Energy Malnutrition had lower red cell indices and platelet count, and a higher white cell count than the controls. Also the edematous forms of PEM had higher granulocyte and lymphocyte counts when compared to the non edematous forms.

The study hereby recommends that more frequent studies be carried out to describe in more details the trend of

such changes in these conditions. This would enhance the anticipatory care and outcome of the children affected.

Keywords : Children, Protein Energy Malnutrition, Haematologic profiles.

I. INTRODUCTION

Protein Energy Malnutrition (PEM), is defined as a spectrum of diseases arising as a result of an absolute, or relative deficiency of calories and or protein in the diet^{1,2}. It is globally the most important risk factor for illness and death, with hundreds of millions of young children affected³.

According to UNICEF in 2005, malnutrition was associated with approximately 50% of child deaths worldwide⁴. It has been estimated that PEM affect every fourth child in the developing world⁴, with the regional prevalence for the severe forms ranging from 1-7%⁵. It is associated with 49% of the 10 million deaths occurring in children in the developing world and 52% of all under five deaths in Nigeria⁶, with 24% and 16% of the total under-5 Nigerian population estimated to have suffered from mild-moderate and severe malnutrition respectively from 1973 to 1983^{7,8}. The hospital based incidence of severe PEM in Nigeria varies from 3.18% in Ilorin⁹. 4.39% in Ibadan⁸ and 4.5% in Ife¹⁰.

Protein Energy Malnutrition results in various changes in the body including changes in haematologic profile of the body. Low red cell count resulting in anaemia has always been a constant feature of protein energy malnutrition and may be normochromic normocytic, microcytic hypochromic, or, macrocytic^{11,12}. The anaemia of malnutrition may be attributable to various factors such as iron deficiency, and /or reduced red cell production in adaptation to a smaller lean body mass^{2,12}. Erythropoietin deficiency, deficiencies of vitamins (folic acid, B12,) or trace elements (copper, zinc), infections and chronic diseases have also been implicated^{2,12,13}.

White cell changes seen in protein energy malnutrition varies and such changes have been attributed to various factors. These include the synergist relationship which PEM has with infections and thymic atrophy seen in children with PEM¹⁶.

This paper set to validate existing literature on these changes especially in a condition where possible

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adaptational changes development can occur frequently. It will also evaluate further, possible haematologic changes in the sub classes of protein energy malnutrition.

II. METHODOLOGY

The study was a case control study carried out at the University of Ilorin Teaching Hospital among children (6 -59 months old) with PEM and controls were children with normal nutritional status without haematological or infectious conditions. All consecutive admissions into the Emergency Paediatric Unit with a diagnosis of PEM based on the Wellcome classification that fulfilled the inclusion criteria were enrolled. Controls were well children attending the routine clinic without haematologic or infectious condition. Children with history suggesting ongoing haemolysis and haemoglobinopathies were excluded.

The minimum calculated sample size with 10% attrition rate was 90, thus 90 subjects each were selected for the study and control groups with a total of 180 participants for the study.

A semi-structured questionnaire (proforma) was used to obtain information from the subjects using interview method. Relevant information on the child's socio-demographic characteristics, nutritional indices and laboratory findings were documented.

Study participants were grouped into upper, middle and lower socioeconomic classes based on the Oyediji socio-economic classification scheme¹³.

Under aseptic conditions, after cleaning the venepuncture site with 70% alcohol, 5ml of venous blood was collected by venepuncture using a fixed hypodermic needle. The blood specimen was decanted into a sample bottle containing ethylene diamine tetra acetate (EDTA) and gently mixed to prevent clotting. The sample was analysed using an automated blood analyzer model/Symax KX 21®.

Data entry and analysis were carried out with a micro-computer using the Epi info version 3.5 (2008) software packages. Chi-square test and student t-test were used to test for statistical significance of the difference for discrete and continuous variable respectively. A p value of < 0.05 was regarded as significant. Analysis of variance (ANOVA) was used for some comparisons.

The study was approved by the Ethics and Research Committee of the University of Ilorin Teaching Hospital. Informed consent was obtained from the parents/caregivers of participants.

III. RESULTS

A total of 180 children - 90 with Protein Energy Malnutrition and 90 controls- were studied. Among the PEM group, 59 (65%) were males and 31 (34.4%) were females with a male to female ratio of 1.9:1. The mean age of the children with PEM was 22.7 + 14.4 months compared to 29.3 + 16.9 months for the controls and the difference was not significant (p=0.08)(Table 1).

Table 1 : The socio-demographic characteristics of the subject and controls.

Variable	PEM (n=90)	Controls (n=90)	χ^2	P
Age (month)				
Range	9.0-59.0	6.0-59.0		
Mean± S.D	22.7±14.4	29.3±16.9	t=7.95	0.08
Gender				
Male	59(65.6%)	53(58.9%)		
Female	31(34.4%)	37(41.1%)	0.85	0.356
Social Economic Class				
I	2(2.2)	4(4.4)		
II	6(6.8)	27(30.0)		
III	26(28.8)	35(38.9)	28.17	0.000012
IV	38(42.2)	16(17.8)		
V	18(20.0)	8(8.9)		
Maternal Educational Status				
None	25(27.8)	9(10)		
Primary	29(32.2)	20(22.2)	19.025	0.0002
Secondary	21(23.3)	23(25.6)		
Post secondary	15(16.7)	38(42.2)		

Thirty eight (42%) of the children with PEM were in socio-economic class (SEC) IV, 26 (28.8%) in SEC III, 18(20%) in SEC V and only 2(2.2%) in SEC I. The subjects were of a lower socioeconomic class compared to the controls ($p=0.00001$)(Table 1).

Of the 90 mothers interviewed, 29 (32.2%) had primary education, 25 (27.8%) had no form of education, while 21(23.3%) and 15(16.7%) had secondary and tertiary education respectively. The educational status of mothers of children with PEM were lower compared to that of controls ($p=0.0002$) (Table 1).

The mean haematocrit values for the subjects and controls were $30.4 \pm 6.3\%$ and $32.0 \pm 6.1\%$ respectively while their mean haemoglobin values were $10.1 \pm 2.1\text{g/dl}$ and $10.9 \pm 15.0\text{g/dl}$ respectively and the difference was statistically significant ($p=0.019$ and

0.003 respectively) with the subject having a lower value (Table 3) The mean values of the mean corpuscular volume were $72.4 \pm 10.9\text{fl}$ and $72.6 \pm 13.6\text{fl}$ in the subjects and controls respectively and the values were similar ($p = 0.913$,while the mean values for mean corpuscular haemoglobin concentration and mean corpuscular haemoglobin were $30.4 \pm 2.8\text{g/dl RBC}$ and $24.3 \pm 10.5\text{fl}$ for subjects and $0.3 \pm 1.8 \text{ g/dl RBC}$ and $25.6 \pm 1.6\text{g/dl RBC}$, for controls and both were comparable ($p > 0.05$) (Table 2),.

The mean value of platelets count were $291.8 \pm 131.7 \times 10^9 /\text{L}$ and $326.4 \pm 133.9 \times 10^9 /\text{L}$ for the subjects and controls respectively and the difference was statistically significant ($p=0.0001$) with PEM children having a lower platelet count compared to the controls (Table 2).

Table 2 : Haematologic profile of the PEM versus the Control.

Haematological Parameters	PEM mean \pm S.D	Controls mean \pm S.D	<i>t</i>	<i>P</i>
RBC ($\times 10^0 \text{ cell/mm}^3$)	4.0 \pm 0.9	4.2 \pm 0.9	2.39	0.123
Haemoglobin (g/dl)	10.1 \pm 2.1	10.9 \pm 15.0	18.58	0.019
Haematocrit (%)	30.4 \pm 6.3	32.0 \pm 6.1	2.97	0.003
MCV(fl)	72.4 \pm 10.9	72.6 \pm 13.6	0.01	0.091
MCH (pg/cell)	24.3 \pm 10.5	25.6 \pm 10.6	0.68	0.41
MCHC(gHb/dl RBC)	30.4 \pm 2.8	30.3 \pm 1.8	0.68	0.411
Platelet count($\times 10^3 \text{ cell/mm}^3$)	291.8 \pm 131.7	326.4 \pm 133.9	180.18	0.0001
White cell count($\times 10^3 \text{ cell/mm}^3$)				
Neutrophils% Lymphocyte%				
	12.8 \pm 11.6	5.9 \pm 8.7	20.38	0.001
	49.5 \pm 12.3	43.8 \pm 5.9	15.64	0.001
	52.7 \pm 12.3	59.4 \pm 7.5	23.80	0.00002

The mean value of WBC in the children with PEM was $12.8 \pm 11.6 \times 10^3$ cell/mm³ and $5.9 \pm 8.7 \times 10^3$ cell/mm³ among the controls ($p = 0.001$) (Table 2). The subjects had higher mean values of total white cell count, neutrophil and lower lymphocytes counts compared with controls ($p < 0.05$) (Table 2).

Children with Kwashiorkor had the highest mean for haemoglobin, (31.6 ± 1.6 g/dl) and haematocrit ($10.7 \pm 0.4\%$), while subjects with marasmus had the lowest mean for haematocrit ($27.6 \pm 5.8\%$), haemoglobin (9.1 ± 2.1 g/dl) and mean corpuscular haemoglobin (22.9 ± 2.3 pg/cell). (Table 2). The subjects with

kwashiorkor and marasmic-kwashiorkor had the highest lymphocyte counts while underweight had the lowest lymphocyte count with a statistical significant difference ($p = 0.0001$) (Table 3). Underweight children had the highest mean of white cell count ($13.8 \pm 14.5 \times 10^3$ cell/mm³) while Marasmic –Kwashiorkor had the lowest mean count, however, the difference is not statistically significant ($p = 0.750$). The neutrophils counts were similar in all the types of Protein Energy Malnutrition ($p = 0.438$) with subjects with kwashiorkor having the highest value. (Table 3)

Table 3 : Haematologic Profile of Children According to the Types of PEM.

Haematologic Parameters	Marasmus n=21 Mean±S.D	Kwashiorkor n=8 Mean±S.D	Marasmic- kwashikor n=11 Mean±S.D	Underweight n=50 Mean±S.D	T	p
RBC($\times 10^6$ cell/mm ³)						
Haemoglobin (g/dl)	3.82±0.91	4.28±0.05	4.28±0.05	4.08±9.5	0.85	0.47
Haematocrit (%)	9.1±2.1	10.7±0.4	10.4±1.7	10.3±2.4	1.89	0.1575
MCH(pg/cell)						
MCHC(hb/dlRBC)	27.6±5.8	31.6±1.6	31.1±5.1	31.08±21	1.77	0.157
MCV(fl)	22.9±2.3	22.4±0.5	23.5±1.3	25.2±13.9	0.36	0.7815
Total WBC ($\times 10^3$ cell mm ³)	31.2±2.9	31.5±2.1	33.1±1.5	29.4±2.9	4.43	0.006
Neutrophils%	68.1±11.9	73.0±3.6	74.4±6.2	73.3±2.1	1.231	0.3015
Lymphocyte%						
Platelet ($\times 10^3$ cell mm ³)	12.9±8.8	11.2±0.7	9.9±1.3	13.8±14.5	0.405	0.750
	47.2±17.9	52.3±13.4	44.7±7.4	51.2±9.8	0.915	0.438
	51.8±13.9	67±4.1	59.9±4.2	49.1±7.1	11.62	0.0001
	273.9±156.2	270.0±5852	226.5±48.7	316.8±137.6	1.7022	0.171

IV. DISCUSSION

This study confirms that anaemia as well as high white cell count are near constant features of protein energy malnutrition as reported by previous studies.^{10,14} Lower mean values were also observed in the haematocrit and haemoglobin values of children with PEM as compared to controls a finding similar to previous studies.^{10,14} Other red cell changes observed from this study includes a significantly lower mean values for MCH, MCV and RBC count in children with PEM when compared to the controls. These red cell changes can be attributed to adaptation to lower metabolic oxygen requirements and decrease in lean body mass seen in PEM.¹⁵ These changes have also been attributed to changes in the plasma volume as well as the intracellular body water in the body.^{16,20} An increase in plasma volume is seen and is said to be responsible for changes in haematocrit and haemoglobin levels while a concomitant decrease in intracellular water is said to be responsible for changes seen in MCHC.²³ Micronutrient deficiencies such as iron, zinc, have also been implicated.^{2,12,13}

This study also found a significant leucocytosis and neutrophilia among children with PEM as compared to controls, this is similar to a previous study where there was a significant rise in leukocyte count in the patients with PEM compared to the controls.¹⁶ Leucocytosis in these children can be a result of infection which is seen commonly in PEM: both PEM and infection, either clinical or subclinical have been reported to act synergistically.¹⁶ This has been an important factor in determining morbidity and mortality attributed to PEM.¹⁴ However, several other studies revealed leucopenia as well as neuropenia as a common finding in malnutrition.^{16,21,22}

Furthermore, a lower lymphocyte count was observed in the malnourished children compared to controls. The lower lymphocyte count can be attributed to changes in the thymus which is greatly reduced in children during severe PEM. The degree of thymic atrophy correlates closely with depletion of lymphocytes and a decrease in the thymic dependent lymphocyte is also associated with impaired immunity.¹⁷

However, among the various classes of PEM, the study found that children with the edematous forms of PEM had the highest mean values for neutrophils as well as lymphocytes count and a significant difference was observed in the lymphocyte count among the various classes of PEM. These findings are not in consonance with that of a previous study which found no difference in the lymphocyte count of children with malnutrition and concluded that a suppression in both granulocyte and lymphocyte functions occurred in malnutrition;¹⁸ another study also reported lower white cell counts in Protein energy malnutrition.¹⁹ The findings in this study can be explained by some possible

adaptive mechanism which attempts to maintain some degree of immunocompetence in the edematous forms of malnutrition. This assumption can be corroborated by that of another study where CD4 counts were higher in malnourished children with edema compared to the non edematous types.¹⁸ No significant changes were observed in the platelet of the various classes of PEM but there was a significant difference in the controls compared to PEM. Children with PEM had a significantly lower platelet count. This decrease in platelets seen in PEM can be attributed to a purported decrease in bone marrow activities which indirectly affect megakaryocyte functions. A similar finding has been reported by a previous study.²⁰

In conclusion, Children with PEM had lower red cell indices and platelet count, and a higher white cell count than the controls. Also the edematous forms of PEM had higher granulocyte and lymphocyte counts when compared to the non edematous forms of malnutrition.

Also, PEM is a condition that constantly modifies the body's defense mechanism and thus altering the haemopoiesis at all levels, thus this studies recommends that more frequent studies be carried out to describe in more detailed the trend of such changes in this part of the world. This would enhance anticipatory care and outcome of the children affected.

V. AUTHORS CONTRIBUTION

Saka AO, Ojuawo A, Abdulkarim and Adeboye MAN, were involved in conceptualizing the research work as well as carrying out the research work. Bilamin and Latubosun were involved in the laboratory analysis while Saka MJ was the biostatistician involved in study design, data collation as well as analysis.

The authors declare that we have no competing interest.

VI. FUNDING

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