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SERUM IRON, ZINC AND COPPER STATUS OF SEVERELY MALNOURISHED CHILDREN IN WAD MEDANI, SUDAN

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Abstract

Objective: To determine status of iron (Fe), zinc (Zn) and copper (Cu) in severely malnourished children in Wad Medani, Central Sudan.

Methods: Atomic absorption spectrophotometry was used to assess the serum concentrations of iron, zinc and copper in ninety children- sixty severely malnourished children and thirty control. The children were selected randomly from patients admitted to the nutritional section at Wad Medani Children Teaching Hospital in Gezira State, Central Sudan. The age range of the studied children was 3-37 months. The malnourished children were diagnosed and classified into two groups: marasmus and kwashiorkor with 30 patients in each group. Their anthropometric measurements including weight and height were measured. Total serum protein, serum albumin, haemoglobin concentrations and haematocrit were determined using standard methods.

Results: Analysis of variance between the three groups showed highly significant differences in all measured biochemical parameters ($p<0.001$). Positive and significant correlations were observed between serum albumin and zinc levels ($r = 0.4$, $p=0.01$), and between serum copper and haemoglobin levels ($r = 0.3$, $p=0.01$). The nature of the association between these trace elements status and their implications for malnutrition pathophysiology are discussed.

Conclusion: The association is established between trace elements (Fe, Zn, Cu) status and malnutrition in children suffering from marasmus and kwashirkor in the Gezira state.

Key words: serum iron, serum zinc, serum copper, malnourished children, Sudan.

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ملخص:

الأهداف : تحديد وضع الحديد والزنك والنحاس عند الأطفال المصابين بسوء التغذية الوخيم بمدينة ودمدني بوسط السودان ، طرق البحث: استخدام جهاز الامتصاص الذري الطيفي لقياس تركيزات الحديد والزنك والنحاس لتسعين طفلاً – ستون مصابون بسوء التغذية الوخيم وثلاثون أصحاء كمجموعة ضبط– اختير الأطفال عشوائياً من الأطفال المرضي اللذين تم إدخالهم إلي قسم التغذية بمستشفي الأطفال التعليمي ودمدني– ولاية الجزيرة. المدى العمري لأطفال الدراسة يتراوح بين 3–37 شهراً. صنف الأطفال المرضي لمجموعتين: مرازمس وكواشيوركور– 30 طفل لكل مجموعة. شملت القياسات البشرية التي أخذت للأطفال الطول والوزن. تم قياسات تركيزات البروتين الكلي في المصل، البيومين المصل، خضاب الدم، الكسر الحجمي للخلايا الحمر باستخدام الطرق القياسية. النتائج: أوضح تحليل التباين لمتوسطات القياسات في المجموعات الثلاث فروقات معنوية جداً في كل القياسات الكيموحيوية (P<0.001). هنالك ارتباط معنوي موجب بين مستوي البيومين المصل ومستوي الزنك في مصل (r=0.4,p=0.01) وبين مستوي النحاس في المصل ومستوي خضاب الدم (r=0.3,p=0.0). نوقشت طبيعة علاقة هذه العناصر بالفسيولوجية المرضية لسوء التغذية. الخلاصة: تم توضيح العلاقة بين وضع الحديد والزنك والنحاس وسوء التغذية الوخيم عند الأطفال المصابين بالمرازمس والكواشيوركور بود مدني– ولاية الجزيرة بوسط السودان. الكلمات المفتاحيه: حديد المصل، زنك المصل، نحاس المصل، الأطفال المصابين بسوء التغذية، السودان.

Introduction:

Malnutrition is a leading cause of morbidity and mortality worldwide. In Sudan it is estimated that 33% of children under five years are mild to moderately malnourished and 8% are severely malnourished [(1)].

The consequences of malnutrition for human well-being and for socio-economic development are varied and far-reaching in infants and young children. Under-nutrition and growth retardation are associated with reduced physical activity, impaired resistance to infection, impairment of intellectual development and cognitive abilities, and increased morbidity and mortality [(2)]. In marasmus there is a generalized wasting due to deficiency of both energy and protein while in kwashiorkor which is characterized by oedema, energy intake may be adequate but there is a deficiency in both the quantity and quality of protein. However, the two conditions are accompanied by and complicated by deficiencies of vitamins and minerals -including those of iron, zinc and copper- [(3,4,5)].

Trace elements have many diverse and crucial biochemical functions. Commonly, they are involved directly in electron transport, as a cofactor for a wide variety of enzymes (hence involved in a wide variety of biochemical functions), or as vital component of several metalloproteins [(6)].

Iron, Zinc and copper deficiencies in protein energy malnutrition (PEM) have been documented in many studies. This may be due to the fact that these trace elements in serum are bound to proteins and their deficiencies have been attributed to protein depletion [(7)].

Subjects and methods:

Sixty severely malnourished children 3-37 months of age who were suffering from the various forms of PEM were enrolled in this study. These children were diagnosed and classified into two groups: marasmus and kwashiorkor, thirty patients in each group. according to WHO criteria [(8)]. Thirty children who were hospitalized for non-nutritional causes and had minor ailments were included as control subjects; they were matched by age to the study groups. The study was carried out at the Children Teaching Hospital at Wad Medani, Central Sudan. Children of both sexes were included in this study.The laboratory investigations were performed at the Department of Biochemistry and Nutrition,Faculty of Medicine,University of Gezira.

The diet for treatment known as kwash milk was composed of cow's milk, sesame oil and sugar (sucrose) .It was provided in either of two forms: half- strength or full-strength. It was given in 150 ml/kg body weight/day divided into 3 meals. Also given in exchange two eggs or minced meat + rice + orange or banana.

For each child an informed consent was obtained from parents and a questionnaire data form was filled (with the co-operation of the parents) in order to obtain information regarding: age, sex, weight at birth, term of birth, feeding practices (before the current illness), past medical history including immunization status, physical signs

and information about the educational and socio-economic background of the parents in addition to family size and number of children under five years of age.

Blood samples were collected on admission, about 4 ml of blood was obtained by venepuncture from each patient and was divided into two parts; 0.5 ml was put into polythene vials coated with potassium ethylenediamine tetra acetate (K-EDTA)) for the estimation of haemoglobin (Hb) level and packed cell volume (PCV). The other part was transferred to plain centrifuge tube, allowed to stand for ½ hour to clot and after the retraction of the clot, serum was separated and kept frozen at -20 ^{o}C until analyzed for iron, zinc, copper, total protein and albumin.

Anthropometric measurements: weight and height were measured using a standard UNICEF Balance (Detecto baby scale) and non-stretchable tape respectively. The haemoglobin concentration and packed cell volume were determined by cyanmethaemoglobin and microhaemotocrit centrifuge methods respectively as described by Dacie and Lewis [9].

Analyses for serum iron, zinc and copper were made with atomic absorption spectrophotometer (Unicam 929).Total protein and albumin were determined by biuret and bromocresol green manual methods respectively as described by Gowenlock [10].

Statistical Analysis: Analysis of variance (ONE WAY ANOVA) was applied for comparison between mean values in different groups. Differences were considered significant at $P < 0.05$.

Results:

A total number of 90 children were studied; of these 60 were severely malnourished (30 with marasmus and 30 with kwashiorkor). Both sexes were recruited. The age (mean ± SD) in the control group was found to be 17.2 ± 10.8 months compared to 18.6 ± 6.8 and 16.8 ± 8.3 months in the kwashiorkor and marasmus groups respectively .The ratio of males: females were 18:12 for the kwashiorkor group and 15:15 for marasmus and control groups .The mean weight was found to be 8.7 ± 2.0 kg in the control group, 4.5 ± 0.8 kg in the kwashiorkor group and 5.6 ± 1.2 kg in the marasmus group. The mean height in the control group was found to be 74.7 ± 10.5 cm, compared to 72.6 ± 4.8 cm and 70.3 ± 6.6 cm in the kwashiorkor and marasmus groups respectively (Table 1). The biochemical findings are shown as mean ± SD in Table (2). The differences between the mean values in the three groups were highly significant ($P < 0.001$) in all measured parameters. Positive and significant correlations were observed between serum albumin and zinc levels ($r = 0.4$, $p=0.01$), and between serum copper and haemoglobin levels ($r = 0.3$,$p=0.01$).

Table (1): Characteristics of the study and control groups

Criteria (mean + SD)	Kwashiorkor (n = 30)	Marasmus (n = 30)	Control (n = 30)
Age (months)	18.6±6.8	16.8±8.3	17.2±10.8
Sex: M/F	18/12	15/15	15/15
Weight (kg)	4.5±0.8	5.6±1.2	8.7±2.0
Height (cm)	72.6±4.8	70.3±6.6	74.7±10.5

n = number of subjects
SD = standard deviation

Table (2): Biochemical parameters in kwashiorkor, marasmus and control groups (Mean ± SD)

Variable	washiorkor	Control	Significanc

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	(n=30)	Marasmus (n=30)	(n=30)	e
Serum Iron (µ mol/L)	3.0±0.7	3.4±1.1	5.2±1.3	**
Serum Zinc (µ mol/L)	9.8±2.3	10.3±2.2	12.9±2.1	**
Serum Copper (µ mol/L)	10.9±2.9	12.1±3.3	16.4±3.6	**
Haemoglobin (g/dL)	7.6±1.4	7.3±2.0	10.1±1.0	**
Packed Cell Volume (%)	23.3±3.1	23.1±5.0	30.6±3.6	**
Total Protein (g/dL)	4.5±0.8	5.9±1.0	6.6±0.7	**
Albumin (g/dL)	2.5±0.6	3.2±0.7	4.2±0.5	**
Globulin (g/dL)	2.0±0.5	2.6±0.8	2.4±0.6	**

n = number of subjects SD = standard deviation
** = Significant at p= 0.001

The clinical features and presenting signs and symptoms of the malnourished children are shown in Table (3). Anaemia was seen in 12 (40.0%) of kwashiorkor children compared to 18 (60.0%) of the marasmic ones. Diarrhoea was observed in 15 (50.0%) of the kwashiorkor subjects compared to16 (53.3%) of the marasmic subjects. Anorexia was detected in 24 (80.0%) and 21 (70.0%) of the kwashiorkor and marasmic children respectively; this loss of appetite accompanied a history of
prolonged illness before admission was common in the malnourished children. Mental changes, which ranged from apathy to irritability, were seen in 26 (86.7%) and 22 (73.3%) of the kwashiorkor and marasmic groups respectively. Skin abnormalities were common in the kwashiorkor children 15 (50.0%) compared to 6 (20.0%) of the marasmic ones. These changes included cracked skin, hypopigmentation and mild peeling. Hair changes were observed in 14 (46.7%) of the kwashiorkor children and only one child (3.3%) of the marasmic children; these varied from dyspigmented, thin, easily pluckable hair and loss of its lusture. Fever was present in 18 (60.0%) and 21 (70.0%) of the kwashiorkor and marasmic subjects respectively. Presence of fever indicates an accompanying infection.

Table (3): Presenting signs and symptoms in the malnourished subjects

Signs & symptoms	Kwashiorkor		Marasmus	
	N	%	N	%
Anaemia	12	40.0	18	60.0
Anorexia	24	80.0	21	70.0
Diarrhoea	15	50.0	16	53.3
Mental changes	26	86.7	22	73.3
Skin changes	15	50.0	6	20.0
Hair changes	14	46.7	1	03.3
Fever	18	60.0	21	70.0

n = number of subjects

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Discussion:

The present study has shown that serum levels of iron, zinc and copper were significantly lower in the malnourished children compared to the control subjects. These findings are in conformity with results from other studies indicating
deficiencies of the above mentioned trace elements [11,12,13,14].

Serum zinc is known to fluctuate with factors like infection and diet. In this study children who were infected tended to have still lower levels of serum zinc. Several factors might have contributed to the low levels of zinc seen in malnourished children. The incidence of measles and diarrhoea was a common precipitating factor of malnutrition in most of these children and it is likely that abnormal quantities of zinc might have been lost in their stools thus leading to non-availability of dietary zinc to the tissues. Breast milk is a good source of zinc for infants and children being breast-fed, but usually PEM occurs when breast milk is either insufficient or no longer given to the baby.

Copper is a constituent of many cuproenzymes like cytochrome oxidases, which is involved in energy production via oxidative phosphorylation and protects cell membrane against oxidative damage. Recent advances in studying the causation of kwashiorkor which has not yet been well defined, suggests among many other multi-factors, an imbalance between the production and elimination of free radicals in the malnourished child, resulting in cell damage by oxidative mechanisms [15].

In this study a significant decrease in serum total protein and albumin concentrations was found both in the kwashiorkor and marasmic children; these results are in line with those obtained by Coulter *et al* and Ibrahim *et al*. [15,16]. Marked hypoproteinaemia (i.e. total protein levels of < 4.5 g/dl) and marked hypoalbuminaemia (albumin level < 2.5 g/dl) were observed in the malnourished children. Hypoalbuminaemia, which is believed to result from the lack of dietary protein, is the main cause of oedema of kwashiorkor due to protein deficiency.

The results also showed that haemoglobin concentrations and PCV values for both of the malnourished groups were significantly lower than that of the controls. This agrees with other authors [11,16,17]. Anaemia (Hb < 9.3 g/dl or PCV values<27 %) according to WHO criteria [8] was observed in many malnourished patients. The anaemia of infancy, which occurs most frequently between 6 and 24 months of age, is iron-deficiency anaemia since it normally responds rapidly to iron therapy and is characterized by abnormalities in erythrocyte morphology and in iron metabolites typical of this condition. All the evidence points to a depletion of true iron reserve during the period of rapid growth of the infant, despite the considerable "store" of iron contained in the plethora of haemoglobin in the blood at birth [18] .A positive and significant correlation (r = 0.4, p=0.01) was observed between serum albumin and zinc levels. It is likely that hypoalbuminaemia might have contributed to the low levels of plasma zinc, since 60-70% of plasma zinc is bound to albumin.

A positive and significant correlation (r = 0.3,p=0.01) was observed between serum copper and haemoglobin levels. It is known that copper has many roles in both blood formation and iron metabolism; and that anaemia has been observed in copper-deficient humans and animals [18]. Any factor such as copper that limits erythropoiesis will also limit haematopoiesis because haemoglobin is confined to the red cells and the haemoglobin content of the individual red cell cannot be increased beyond normal levels [18].

Hair changes (dyspigmentation, sparseness, dry and thin hair fibers and easy pluckability) and skin changes (dryness, cracked skin, hypopigmentation and peeling) were found to be more common in kwashiorkor patients than in marasmus patients; and they may be attributed (among other factors) to zinc and copper deficiencies.

References

1- UNICEF. The state of the World's Children, Unicef, Oxford University Press, 1998.
2- FAO and WHO. Nutrition and Development - a global assessment. International Conference on Nutrition: Italy, 1992.
3- Nelson, W.E.; Behrman, R.E.; Kliegman, R.M. and Arivn, A.M. Nelson Textbook of Pediatrics. 15th

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ed. Philadelphia: W.B.Saunders, 1996:167.
4- Hathaway, W.E.; Hay, W.W.; Groothuis, J.R. and Pailey, J.W. Current Pediatric Diagnosis and Treatment, 11th ed. Connecticut: Appleton and Lange, 1993: 243.
5- Murray, R.K., Granner, D.K., Mayes, P.A.and Rodwell, V.W.Harper's Biochemistry, 25th ed. Connecticut: Appleton and Lange, 2000:656.
6- Bishop, M.L.; Duben-Engelkirk, J.L. and Fody E.P. Clinical Chemistry. 3rd edition. Philadelphia : Lipincott – Raven, 1996: 279- 288.
7- Sandstead, H.H.; Vo-Khactu H.F. and Solomons, N. In: Trace Elements in Human Health and Disease vol. 1. edited by Prasad. A,S. and Oberleas, D.P. New York: Academic Press, 1976: 33-34
8- World Health Organization. Severe Malnutrition. In: Management of the Child with a serious infection or severe malnutrition: Guidelines for care at the first-referral level in developing countries, 2000 : 80.
9- Dacie, J.V. and Lewis, S.M.. Practical Haematology 8th edition. Edinburgh: Churchill Livingstone, 1995: 57.
10- Gowenlock, A.H.; McMurray, J.R.and McLauchlan, D.M. Varley's Practical Clinical Biochemistry. 6th edition. London: Heinemann Medical Books. 1988: 664-665.
11- Alemnji, G.A.; Thomas, K.D.; Durosinmi, M.A.; Tarwo, O. and Fakunle, J.B. Haematogram and serum iron status of malnourished Nigerian children. East-Afr-Med-J 1995; 72 (9): 605-8.
12- Laditan, A.A.and Ette, S.I. Plasma zinc and copper levels during the acute phase of protein –energy malnutrition and after recovery.Trop.Geogr.Med. 1982; 34 (1): 77-80.
13- Tanzer, F. and Ozalp, I. (1988). Plasma and Leucocyte zinc and copper levels in patients with Protein Energy Malnutrition. J-Trop. Pediatr.1982; 34: 306-308.
14- Subotzky, E.F.; Heese, H.D.; Sive, A.A.; Dempster, W.S.; Sacks, R. and Malan, H.. Plasma zinc, copper, selenium, ferritin and whole blood manganese concentrations in children with kwashiorkor in the acute stage and during refeeding. Ann Trop Paediatr 1992 ;12 (1): 13-22.
15- Coulter, J.B.; Suliman, G.I.; Omer, M.I.A.; Macfarlane, S. B.J.; Moody, J.B. and Hendrickse, R.G. Protein-Energy Malnutrition in Northern Sudan:
16- clinical studies. European Journal of Clinical Nutrition 1988;42(9): 787-796.
17- Ibrahim, S.A.; Eltom, A.M.; Abdul-Rahman, A.M. and Saeed, B.O. Correlation of some biochemical parameters with clinical features of Protein Energy Malnutrition. East. Afr. Med-J. 1994; 71 (2): 77-82.
18- Singla, P.N.; Chand, P.; Kumar, A. and Kachhawaha, J.S. Serum zinc and copper levels in children with protein- energy malnutrition. Indian-J-Pediatr. 1996; 63(2): 199-203.
19- Underwood, E.J. Trace Elements in Human and Animal Nutrition. 3rd edition. . New York:Academic press, 1971.