TRACE ELEMENT STUDIES ON KARACHI POPULATION, PART II: NORMAL RANGES FOR BLOOD COPPER, ZINC AND MAGNESIUM FOR CHILDREN AND ADOLESCENTS

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Abstract

Normal ranges for copper, zinc and magnesium in whole blood have been established for healthy school going children of Indo-Pak origin. Age groups of 7 to 11 years had slightly elevated levels of these metals when compared with the groups below 7 and above 12 years, except that for females levels increased with age for zinc and decreased for magnesium (JPMA 39:205, 1989).

INTRODUCTION

Copper, zinc and magnesium are three of 25 elements, including 14 trace elements, known to play a vital role in body metabolism. Levels in tissues andbodyfluids depend on diet, state of health, age, sex and ethnic group. Copper is a component of at least 16 metallo proteins[1] , zinc of over eighty[2] and magnesium of about three hundred[3]. Zinc and magnesium metalloenzymes participate in all metabolic pathways, and copper in many. Erythrocyte, blood, plasma or serum levels of these metals give poor indications of status and the estimation of levels in other fluids and tissues are not without their drawbacks. However other tests are sometimes used to add to the validity of blood, plasma or serum estimations[1-8], such as the estimations of zinc dependent enzymes like red blood cell carbotic anhydrase, the zinc taste test and the copper/zinc ratio, and for magnesium, the excretion rate followed by the Magnesium Load Test, and others. For the estimation of copper, zinc and magnesium in blood, plasma or serum, it is not necessary that the subject should be fasting. However, Zinc levels tend to vary with time of day[9]. We are carrying out a series of projects concerning the effects of environmental pollution on the levels of metals inbodyfluids and on health. For logistical reasons, all our studies are on whole blood and not on serum or plasma and as a consequence, normal ranges are required in this fluid. Recently, we established normal ranges in whole blood for copper, zinc and magnesium in healthy adults of Indo-Pak origin[10] and here we are presenting our results for children and adolescents.

MATERIALS, EQUIPMENT AND METHOD

Estimations were carried out using a PyeUnicam SP2900 atomic absorption spectrophotometer. Details of the procedure, materials, treatment of samples, standards and controls, are as described in Part I of this series[10], together with the normal ranges of copper, zinc and magnesium for adults in whole blood.

Subjects

Subjects chosen were boys and girls of various age groups, from two of the grammer schools in Karachi. The determination of the normal ranges for copper, zinc and magnesium in blood was part of an exercise to determine the normal ranges of a variety of biochemical parameters in serum in boys and girls of different age groups. This object was first conveyed to the parents of each child after

consultation with the principal and senior teachers of each school concerned. Written consent of the parents was then sought and fmally full details were recorded from a questionnaire and interview concerning physical data, and health and dietary habits, and to make sure that each child had bad neither an operation nor serious illness during the previous 12 months nor was on any medication. Each subject was of high socioeconomic status, lived in a "good" area of relatively low environmental contamination, and bad both parents of IntoPak origin. Each child on the day of blood sampling presented himself/herself in a fasting condition because of the nature of the overall exercise. This was not actually necessary for the determination of the normal ranges of blood copper, zinc and magnesium, but it was important that for zinc all sampling was carried out at about the same time of day. This was between about 9 and 11A.M. in common with all other samples taken in all our projects. Blood samples for the metal determinations were put in specially treated glass tubes containing 200 ul of 10% EDTA as described previously 10.

Statistical Analysis

In common with work in general involving metal levels in blood, distribution of levels in all groups considered were basically non-Gaussian and hence the Wilcoxon Rank Sum Test11 was used to test for significance of difference between groups of results, the Student's t test being invalid. In the calculation of normal ranges, inspite of the above, in every case there was little difference between the normal range calculated non-parametrically and that as the mean ±2x standard deviation. Hence the latter method was adopted.

RESULTS AND DISCUSSION

Initially, subjects were classified by sex and by the following age groups: 4-6,7-9, 10-13 and 13-19y. As in adults[10],in each age group, there was no significant difference between males and females for blood copper levels but the differences were significant for zinc and magnesium.

Normal Ranges for Blood Copper

The sexes were combined and significant differences in the normal levels were apparent between the age groups 4-6,7-8,9-11,12-19 and between the last of these and the normal range for adults[10]. The highest levels were in the 9-11 age group (Table I).

TABLE I. Normal Ranges for Blood Copper by Age Groups for a Karachi Population.

Age Group (years)	N	Median (ug/dl)	Mean (ug/dl)	Normal Range (ug/dl)	P
4 - 6	59	107.4	106.0	75 - 136.5	--
7 - 8	50	115.0	118.3	67.5 - 169	<0.05 >0.01
9 - 11	87	133.3	131.2	70 - 192	<0.01
12-19	52	106.0	102.8	65 - 140.5	<0.01
Adults[10]	62	94.5	93.5	71 - 116	<0.01

Only in Spain[12] and in Japan[13] have sexual differences in normal range been reported: for 10--19 year old and for adults in the former country and for adults only in the latter. The only other reports we can find concerning copper levels in whole blood were from Bangladesh[14] India[15], Iran[15]. Denmark[16], Finland[15], Sweden[17], Canada[18], U.S.A[19] and Venezuela[19] but for adults only (Table II).

TABLE II. Regional Values for the Normal Range for Copper in Whole Blood in Adults.

Country	Sex	Normal Range (ug/dl)	Mean (ug/dl)	Reference
Spain	M	80-125	105	12
	F	97-137	117	
Japan	M	50-113	82	13
	F	70-114	86	
Bangladesh	M+F	40-276	98	14
India	F	55-170	93	15
Iran	M+F	100-220	130	15
Denmark	M	71-255	83	16
Finland	M+F	72-132	93	15
Sweden	M+F	50-250	100	17
Canada	M+F	78-160	111,122	18
U.S.A.	M+F	31-281	100	19
Venezuela	M+F	43-260	99	19

There were no sexual differences indicated. It may be seen from Tables I and II that the adults normal range in Karachi is narrower than that in any other country, except in Japan, but the mean value of the former is higher than some and lower than others. Our 12-19 year olds have a higher and wider range than Spanish males (10 years old and above) and a wider but lower range than the corresponding Spanish females.

Normal Ranges for Blood Zinc

The sexes were treated separately. Significant differences between the normal ranges for males of the age groups 4-7,8-10,11, 12-14 and 15-19 years of age were apparent. However, the levels of the 15-19 age group were not significantly different from those for adult males. Hence this age group was combined with adult males and the normal range found as being that for a 15 + age group. Normal ranges increase up to 11 years of age and then decline. Female age groups were found similarly: 4-6, 7-9, and 10±, the highest range being at 7-9 years of age. It may be seen that mean levels are higher for females than males between the ages of 7 and 14, except for 11 year olds (Table III).

TABLE III. Normal Ranges by Sex and Age Group for Blood Zinc for a Karachi Population.

Age Group (Years)	N	Median (μg/dl)	Mean (μg/dl)	Normal Range (μg/dl)	P
Males					
4 - 7	49	568	573.3	338 - 808	–
8 - 10	47	635	636.9	353 - 977	$<0.05, >0.01$
11	17	952	909.3	353 - 1279	<0.01
12 - 14	19	617	630.1	364.5 - 896	<0.01
15 +	39	726	726.0	602.5 - 850	<0.01
Females					
4 - 6	24	543	533.3	321 - 745	–
7 - 9	35	626	653.4	371 - 936	<0.01
10+	78	695.5	685.9	591 - 859	$<0.05, >0.01$

Only in Spain[12] and Japan[13] have sexual differences in the normal ranges been reported: in the former, 10-19 year old males have a higher range than females, and in the latter adult males have a higher mean value but the upper end of the normal range is lower than that for females. The other reported values in whole blood axe from Banglades[14], India[15], Iran[15], Finland[16], Sweden[17] and Canda[18] but no sexual differences are given (Table IV).

TABLE IV. Regional Values for the Normal Range for Zinc in whole Blood for Adults.

Country	Sex	Normal Range (ug/dl)	Mean (ug/dl)	Reference
Japan	M	420 - 720	620	12
	F	430 - 800	580	
Spain	M*	338 - 814	576	13
	F*	345 - 729	537	
	M + F	339 - 831	600	
Bangladesh	M + F	300 - 630	440	14
India	F	270 - 920	490	15
Iran	M + F	490 - 750	640	15
Finland	M + F	420 - 870	630	15
Sweden	M + F	400 - 800	600	17
Canada	M + F	200 - 1030	620 - 660	18

*10 -19 age group

Our 15 + age group for males and the 10+ age group for females have higher mean values than reported for any country for adults, although the upper normal limits for both groups are exceeded by India, Finland and Canada. The lower limits for India and Canada are very low and perhaps are due to zinc deficiency in the soil.

Normal Ranges for Blood Magnesium

As significant differences had been found in blood magnesium levels between males and females, the sexes were treated separately. The results for males were treated similarly to those for the zinc, results for males and normal ranges were established for the age groups 4-6,7-U and 13+, the last resulting from a combination of the results for the 13-19 age group and adults which were not significantly different. The 7-12 age group has the highest normal range. Similarly, females fell into the age groups 4-11 and 12+, the former having the higher normal range. Normal ranges are higher for females than males up to the age of 11 years (Table V).

TABLE V. Normal Ranges by Sex and Age Group for Blood Magnesium for a Karachi Population.

Age Group	N	Median (mg/dl)	Mean (mg/dl)	Normal Range (mg/dl)	P
Males					
4 - 6	35	3.50	3.60	2.30 - 4.90	--
7 - 12	86	4.20	4.35	2.41 - 6.29	<0.01
13+	50	3.80	3.78	2.97 - 4.80	<0.05, >0.01
Females					
4 - 11	82	4.30	4.43	2.40 - 6.47	--
12+	55	3.515	3.50	2.65 - 4.66	<0.01

We have found no data in the literature concerning magnesium levels in whole blood, but serum levels were found to be higher in males than females in adult black and white Americans, levels for blacks being higher than for whites, according to a comprehensive survey[20] carried out between 1971 and 1974. Other differencesbetweenraces for serum levels have been recorded, males having higher levels than females in several countries those in Denmark[21] and in eastern parts of India[22] being exceptional.

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