

# Plasma Renin Activity in Children with Protein Energy Malnutrition (Kwashiorkor)

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## SUMMARY

Plasma renin activity was measured by bio-assay in 100 children with kwashiorkor and in 20 healthy children, and also by radio-immunoassay in another 26 children with kwashiorkor and in another 20 healthy children. Both methods showed that (compared with healthy children) renin activity was significantly increased in children with kwashiorkor; and also that the activity was significantly higher in the patients who subsequently died in hospital, than in those who survived. Increased renin activity probably contributes to the retention of water characteristic of protein energy malnutrition.

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Oedema and a low mass for age are the two cardinal features of protein energy malnutrition (kwashiorkor).<sup>1</sup> In kwashiorkor, there is a failure to balance water consumption and excretion, so that a state of overhydration develops in which the volumes of all three compartments (intravascular, interstitial and intracellular) are increased.<sup>2-25</sup> Since water balance is partly controlled by the renin-angiotensin system, its role in kwashiorkor has now been investigated. A preliminary report has been published.<sup>26</sup>

## PATIENTS AND METHODS

Two groups of patients were studied at Harare Hospital, group B consisting of 100 children admitted consecutively between January and November 1970, and group R of 26 children admitted consecutively during March, April and May 1971. Two healthy contrast groups were also examined; group I consisting of 10 boys and 10 girls aged 11-48 months, and group II consisting of 6 boys and 14 girls aged 11-28 months, attending the Well Baby Clinics serving the same community.

All patients were oedematous owing to malnutrition and underweight for their age (Boston 50th percentile).<sup>17</sup> Before starting treatment, a venous blood sample is taken for routine analysis from all children admitted to Harare Hospital; a portion of this sample was assayed for plasma renin activity. A second venous blood sample was taken

for analysis during each patient's last week in hospital. It was not possible to collect urine before treatment was started, but samples were obtained during the child's first and last week in hospital and also from healthy children at the Well Baby Clinics.

The plasma pH was adjusted to 5.5 with N HCl and it was incubated with angiotensinase inhibitors (EDTA, BAL, hydroxyquinoline) at 37°C for 4 hours. The angiotensin I generated by the action of the plasma renin was estimated by biological assay<sup>18</sup> after fuller's earth extraction<sup>19</sup> for the kwashiorkor patients in group B and in contrast group II; or by radio-immunoassay<sup>20</sup> for the kwashiorkor patients in group R and in contrast group I. Twelve aliquots of a sample of pooled plasma were separately incubated, extracted and bio-assayed. The coefficient of variation for the estimation was found to be 9.7%.

The total white cell and red cell counts were determined with a Coulter counter, the packed cell volume with a microhaematocrit and the haemoglobin by the cyanmethaemoglobin method (Ortho Diagnostics, New Jersey). Blood glucose, serum bilirubin and serum proteins were measured by standard methods,<sup>21</sup> serum and urine sodium and potassium were measured with a flame photometer, and magnesium and zinc by atomic absorption.<sup>22</sup> The serum and urine osmolality were measured with a Mechrolab vapour pressure osmometer 301 A.

Each child was examined by one of us (E.E.K.) and a clinical assessment was made according to McLaren's system (but excluding the serum albumin concentration).<sup>23</sup> This system assigns a score according to the presence of skin, hair and liver changes in addition to oedema. Oedema was measured as the pitting depth in millimetres obtained after applying firm pressure for 15 seconds to the dorsum of the foot. The pressure was sufficient to completely displace the oedema fluid. With the child lying supine, liver enlargement was measured by palpation in the right midclavicular line.

The patients who recovered remained in the hospital or its nutrition centre for 2-5 weeks. Most deaths occurred during the first 3 days in hospital and were usually associated with an overwhelming Gram-negative bacteraemia<sup>24</sup> or with severe gastro-enteritis. Routine treatment was intragastric fortified milk (containing skimmed milk, oil, eggs, Multivite syrup, folic acid and potassium chloride) and magnesium sulphate by intramuscular injection. No iron was given for the first 10 days. Intravenous transfusions of plasma or half-strength Darrow's solution (containing 2.5% glucose) were used only when there was evidence of low output circulatory failure; antibiotics were given only for obvious infections.

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The difference between the groups of data was tested by Wilcoxon's method for ranked observations.

## RESULTS

Plasma renin activity was significantly higher in children with kwashiorkor than in the healthy contrast groups and it was significantly higher in the patients who died in hospital than in those who survived (Fig. 1).

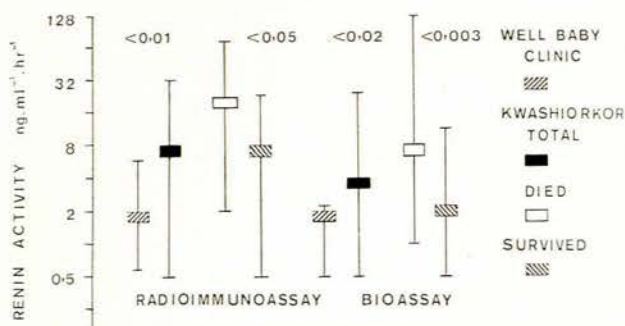


Fig. 1. Median plasma renin activity measured by radioimmunoassay and by bio-assay in the two groups of children from the Well Baby Clinics and in the children with kwashiorkor. Bars represent the 10th and 90th percentiles.

In group R, a significant correlation was found between the plasma renin activity on admission and the serum bilirubin concentration ( $r = + 0.55$ ;  $P < 0.01$ ) and also

between renin activity and liver enlargement ( $r = + 0.43$ ;  $P < 0.05$ ). No other significant correlations were found between renin activity and clinical, biochemical, electrolyte or hormonal changes.

The clinical, biochemical and hormonal data are shown in Tables I and II. They show that all malnourished children had oedema and were significantly underweight. They were more anaemic than the 'well babies' and their albumin concentration was significantly lower. Their serum zinc concentration was also significantly lower than in 95 healthy schoolchildren (aged 8 - 12 years):  $1.0 (0.8 - 1.4) \text{ mg} \cdot \text{L}^{-1}$  ( $P < 0.003$ ).<sup>25</sup>

## DISCUSSION

Increased plasma renin activity in the child with kwashiorkor must be the result either of an increase in renin secretion by the kidney, or a decrease in renin clearance by the liver.<sup>26</sup> In the kwashiorkor patient, the latter is the more likely explanation, since liver damage is characteristic of the disease,<sup>27,28</sup> and also because significant correlations were found between renin activity and hepatic enlargement and between renin activity and serum bilirubin.

Hydration is controlled by the balance between water consumption and elimination. The renin-angiotensin system opposes salt and water elimination by direct action on the kidney<sup>29</sup> and also by releasing vasopressin<sup>30,31</sup> and aldosterone.<sup>32,33</sup> The renin-angiotensin system also increases water consumption by inducing thirst<sup>34-36</sup> and is probably responsible for the overhydration associated with psychogenic malnutrition (anorexia nervosa).<sup>37</sup> Consequently,

TABLE I. CLINICAL AND BIOCHEMICAL DATA IN CHILDREN FROM THE WELL BABY CLINICS (GROUP I) AND IN THE KWASHIORKOR PATIENTS IN GROUP R AND GROUP B. THE MEDIAN (50TH PERCENTILE) IS FOLLOWED BY THE 10TH AND 90TH PERCENTILES (BRACKETED)

	Kwashiorkor					
	Well Baby Clinic (group I)	Died	Group R—survived		Group B	
			On admission (SA)	On discharge (SD)	Died	Survived (S)
Number of subjects	20	4	22	22	26	74
Age in months	13 (12 - 30)	18	12 (12 - 30)		14 (12 - 27) <sup>a</sup>	18 (12 - 48)
Clinical assessment	0	6	6 (2 - 9) <sup>b</sup>	4 (2 - 8)	6 (4 - 7) <sup>c</sup>	4 (3 - 7)
Mass deficit (%)	14 (5 - 18)	41 <sup>d</sup>	22 (19 - 40)	23 (5 - 39)	33 (18 - 51)	32 (13 - 38)
Infection (%)	0	50	59	0	77 <sup>e</sup>	47
Haemoglobin (g/L)	119 (116 - 133)	68	98 (68 - 122) <sup>f</sup>	95 (82 - 116)	95 (62 - 122)	92 (68 - 112)
White blood cells ( $10^3/\text{mm}^3$ )	9.5 (8 - 11.5)	9.5	7.5 (5 - 11.5)	9 (8 - 12)	13 (3 - 22) <sup>g</sup>	9 (5 - 16)
Serum sodium (mEq/L)	128 (125 - 130)	136	133 (128 - 138)	131 (125 - 139)	132 (122 - 140)	135 (125 - 142)
Serum potassium (mEq/L)	4.6 (4.0 - 5.2)	4.6	4.6 (3.8 - 5.4)	4.5 (4.1 - 5.7)	4.5 (3.7 - 5.8)	4.9 (4.0 - 5.9)
Serum magnesium (mEq/L)	1.8 (1.6 - 1.9)	1.7	1.7 (1.5 - 1.8)	1.7 (1.4 - 2.0)	1.7 (1.2 - 2.1)	1.7 (1.3 - 2.3)
Serum zinc (mg/L)					0.7 (0.4 - 1.5)	0.8 (0.6 - 1.3)
Serum albumin (g/L)	38 (36 - 42)	13	17 (12 - 36) <sup>h</sup>	30 (26 - 39)	17 (14 - 26) <sup>i</sup>	23 (16 - 37)
Serum globulin (g/L)	27 (23 - 31)	26	25 (21 - 33)	32 (26 - 34)	22 (15 - 33)	26 (17 - 39)

a = less than in S, ( $P < 0.05$ ); b = more than in SD, ( $P < 0.05$ ); c = more than in S, ( $P < 0.05$ ); d = more than in I or SA, ( $P < 0.05$ ); e = more than in S, ( $P < 0.05$ ); f = less than I, ( $P < 0.05$ ); g = more than S, ( $P < 0.05$ ); h = less than I or S, ( $P < 0.05$ ); i = less than S, ( $P < 0.05$ ).

TABLE II. CLINICAL AND BIOCHEMICAL DATA IN CHILDREN FROM THE WELL BABY CLINICS (GROUP I) AND IN THE KWASHIORKOR PATIENTS (GROUP R)

	Well Baby Clinic (group I)	Kwashiorkor (group R)		
		Died	Survived	
			On admission	On discharge
Number of subjects	20	4	22	22
Oedema (mm)	0	3,5	2 ( 1 - 3)	0 ( 0 - 1)
Liver enlargement (cm)	0	6	4 ( 2 - 6)	3 ( 2 - 4)
Mean cell volume ( $\mu\text{m}^3$ )	70 ( 63 - 77)	79	80 ( 70 - 91) <sup>a</sup>	81 ( 78 - 89)
Mean cell haemoglobin (pg)	24 (21 - 26)	27	27 ( 24 - 31) <sup>b</sup>	28 ( 26 - 30)
Blood glucose (mg/L)	800 (640 - 900)	1 150	750 (520 - 980)	840 (680 - 1 150)
Serum osmolality (mOsm/kg)	256 (236 - 278)	264	264 (258 - 276)	269 (243 - 286)
Urine sodium (mEq/L)	42 ( 18 - 164)		138 ( 67 - 240) <sup>c</sup>	70 ( 20 - 240)
Urine potassium (mEq/L)	18 ( 5 - 88)		62 ( 15 - 108) <sup>d</sup>	48 ( 22 - 138)
Urine magnesium (mEq/L)	2,5 (0,5 - 4,6)		2,3 (0,5 - 5,0)	3,1 (0,1 - 5,3)
Urine osmolality (mOsm/kg)	274 ( 76 - 626)		536 (231 - 840) <sup>e</sup>	472 (201 - 716)

a = more than 1, ( $P < 0,05$ ); b = more than 1, ( $P < 0,05$ ); c = more than 1 or on discharge, ( $P < 0,05$ ); d = more than 1, ( $P < 0,05$ ); e = more than 1, ( $P < 0,05$ ).

the increased activity of the renin-angiotensin system in the child with kwashiorkor is likely to contribute to his state of overhydration both by increasing thirst and water consumption, and also by opposing the renal elimination of salt and water.

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