

**THE EFFECT OF SODIUM SUPPLEMENTATION
ON SODIUM HOMEOSTASIS IN VERY LOW BIRTH
WEIGHT INFANTS FED ON OWN MOTHERS' MILK**

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BY

ROBERT KANGWANA/AYISI

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To

My parents The Late Lawrence Ayisi

and Mrs. Regina Ayisi

for my upbringing.

And to my beloved daughter

Vivian Gloria Khasandi with affection.

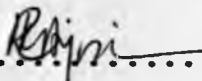
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DECLARATION

I certify that this dissertation is my own original work and has not been presented in any other University.

Dr. R. K. Ayisi

MB. ChB. Cert. Trop. Med. (NBI).

Signature 

This dissertation has been submitted for examination with our approval as University Supervisors.

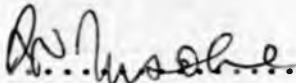
Dr. R. N. Musoke,

MB. ChB., M.Med.(Paediatrics) Makerere,

Senior Lecturer, Department of

Paediatrics, College of Health

Sciences, University of Nairobi.

Signature 

Dr. D. A. O. Orinda,

Ph.D. MSc. Clin. Bioch. DCB (London),


Senior Lecturer, Department of Human

Pathology,

Division of Chemical Pathology,

College of Health Sciences,

University of Nairobi.

Signature 

CONTENTS

Page

1. Declaration	(i)
2. Table of Contents	(ii)
3. List of Abbreviations	(iii)
4. List of Tables	(iv)
5. List of Figures	(v)
6. Summary	1
7. Introduction	2
8. Objectives	6
9. Materials and Methods	6
10. Results	13
11. Discussion	34
12. Conclusions	41
13. Recommendations	42
14. Acknowledgements	43
15. Appendix A	44
16. Appendix B	45
17. References	46

LIST OF ABBREVIATIONS:

1. KNH - Kenyatta National Hospital
2. Meq - Milliequivalent
3. Kg - Kilogramme
4. l - Litre
5. > - greater than
6. < - less than
7. mOsmol - milliosmol
8. Wt - weight
9. VLBW - Very low birth weight
10. gms - grammes
11. % - percentage
12. P.E.T. - pre eclamptic toxæmia
13. mls - millilitres
14. umol - micromoles
15. mmol - Millimoles
16. Na⁺ - sodium
17. K⁺ - potassium
18. Fig. - Figure
19. cm - centimetre
20. GFR - Glomerular Filtration Rate
21. HCO₃⁻ - Bicarbonate
22. H⁺ - hydrogen ion
23. wk - week

LIST OF TABLES

	Page
Table I - Infants' Distribution by sex	14
Table II - Summary of Clinical data	16
Table III - The electrolyte Composition of breast milk from mothers delivering preterm babies	17
Table IV - Mean postnatal growth rates of supplemented and unsupplemented infants	33

LIST OF FIGURES

	Page
Fig. I - Birth weight distribution	15
Fig. II - Mean total fluid intake for each week of the study period between the two groups	18
Fig. III - Mean sodium intake from breast milk	20
Fig. IV - Mean total sodium intake per day compared between supplemented and unsupplemented groups	21
Fig. V - Serum sodium computed for weekly averages	23
Fig. VI - Serum potassium concentration computed for weekly averages ...	24
Fig. VII - Urinary sodium represented as mean values compared between supplemented and unsupplemented groups	26
Fig. VIII - Postnatal changes in urinary potassium excretion represented as mean values compared between supplemented and unsupplemented groups	27
Fig. IX - Plasma creatinine in relation to postnatal age of VLBW preterm infants	29
Fig. X - Post natal values of urinary creatinine	30
Fig. XI - Creatinine clearance compared with postnatal age in both groups	

SUMMARY

Clinical and biochemical effects of supplementing dietary sodium intake were studied. A group of 66 very low birth weight (VLBW) preterm infants were recruited in the study. Forty one of these were supplemented with 3 mmol/Kg/day of sodium chloride for six weeks, and twenty five were not. Weekly serum sodium and potassium were assayed in both groups, in addition to urinary electrolytes. Their mothers' breast milk 24 hrs electrolyte content was also determined. Weekly anthropometric measurements (Head circumference, weight and length) were also carried out.

The mean serum sodium and potassium in the supplemented group were 140 mmol/l and 6.2 mmol/l respectively as opposed to values of 139 mmol/l (Na^+) and 5.7 mmol/l (K^+) in the unsupplemented ones. There was no significant intergroup difference in the mean electrolyte values $p > 0.05$. The mean urinary sodium was 15.7 mmol/l in the supplemented group compared to 7.3 mmol/l in the unsupplemented group. The difference was statistically significant $p < 0.05$. The mothers' breast milk had a mean sodium of 10.8 mmol/l and 16.6 mmol/l of potassium. Hyponatraemia was never recorded in any of the study infants. This study reveals no appreciable influence of sodium supplementation on the infants' electrolyte profiles although weight gain was significantly higher in the supplemented infants. Therefore from this study, we conclude that hyponatraemia is quite rare in VLBW preterm infants fed on own mothers' milk and hence sodium supplementation may not be essential.

INTRODUCTION

Numerous studies have been carried out on nutritional supplementation of VLBW infants with various dietary supplements such as minerals, proteins, carbohydrates and vitamins (1,2,3). Sodium is one of the minerals whose effect on growth and biochemical status has been extensively studied (4).

Sodium is the bulk cation of the extracellular fluid and the principal osmoregulator whose amount in the circulation is the balance between intake and excretion (5). The sodium content of the fetus is relatively higher than that of adults (6). This is due to the fact that the fetus has a relatively higher turnover of cartilage, connective tissue and extracellular fluids (all of which contain considerable amount of sodium) and a relatively small muscle mass (which has a low sodium content) (6).

Sodium homeostasis in the newborn infant is characterised by a positive sodium balance over a wide range of sodium intake (7). It is the newborn kidney's primary function as it is in adults to maintain this state. However, their sodium and volume regulatory mechanisms are functionally limited (8). Excretory capacity of Na^+ is reduced by a relative concentrating defect (maximal urine osmolality approximates 600-700 mOsmol/Kg of water), and therefore obligatory solute load requires extra free water clearance for its elimination (9-11).

A shorter loop of henle may contribute to this urinary concentrating dysfunction (12,13).

The highly anabolic state of the neonate limits the availability of urea for establishing concentration gradient between the medullary interstitium and distal tubule which is necessary for urine concentration (14). Yet it has to ensure positive sodium, potassium and chloride balance necessary for growth.

Abnormalities in tubular reabsorption of sodium are observed frequently with renal impairment. The question of inappropriate renal sodium handling is usually raised by observation of an abnormal urinary sodium value (15). Siegal and Oh (16) as well as Arant et al (17), reported that infants with gestational age of more than 32 weeks, have tubular reabsorption value of more than 99 percent whereas in the less mature infants, it is between 90-99 percent. Engle and Arant (18) in a study on a group of 57 normal preterm and term infants, found values of 96% in infants with conceptional ages of 26-30 weeks and 98-100% percent in more mature ones.

Engelke et al (19) studying 17 consecutive infants weighing less than 1200 grammes found increased sodium excretion. This increased natriuresis was thought to be due to various degrees of illness, high fluid intake or ineffective secretion of aldosterone. Spitzer suggested that renal sodium loss and hyponatraemia often encountered in premature infants appear to be due to an insufficient rise in aldosterone or to a limited responsiveness of the distal tubules to aldosterone stimulation (20-23).

The preterm infant has been characterised as a 'renal salt loser'. Day et al (24) and Roy et al (25) in their studies of 30 and 46 VLBW infants respectively found hyponatraemia to occur in 30% of healthy VLBW infants of less than 1300 grammes between weeks 2-6 of life and this was thought to be due to a combination of factors including high urinary sodium losses relative to plasma levels, insufficient intake due to relatively low Na^+ found in certain infants formulae and coprecipitation of Na^+ with calcium in bone during periods of rapid growth. These findings were corroborated by Aperia et al (26).

Preterm infants have a problem with their sodium homeostasis (25, 26). Basal excretion is high because their adrenal glands do not respond as well as adult glands to elevated levels of renin (27). Their distal convulated tubules are also less responsive to aldosterone (28). Paradoxically when pushed into positive sodium balance by high sodium intake, the preterm infant is unable to rapidly increase sodium excretion (29). This is due to the inability of the preterm infant to shift blood flow away from salt losing cortical nephrons. Hence the preterm infant is susceptible to both sodium loss and sodium and volume overload (30). Lorenz (31) observed that infants receiving a higher fluid and sodium had relatively low serum sodium values due to a dilutional effect.

A study on macromineral balance of preterm infants

fed on own mothers' milk showed that milk from these mothers provided adequate amount of sodium, potassium and chloride to meet the estimated requirements for growth (32, 33). Gross (34) demonstrated a higher sodium concentration in preterm milk as compared to term milk (26.6 ± 3.0 meq/l Vs 22.3 ± 2.4 mmol/l on day 3. In another study on infants fed on preterm and term milk, he also found that hyponatraemia was less frequent in those fed on preterm milk (15% vs 50%) (35, 36). This was attributed to adequate amount of protein, sodium, chloride, potassium and energy in early preterm human milk to support growth.

The recommended daily requirement for sodium in VLBW preterm infants is 2-3 mmol/Kg/day, with an average of 2.5 mmol/Kg/day (37). It is generally considered important to provide sodium supplementation to some VLBW preterm infants especially those who are ill to avert possible hyponatraemia (38).

Though it has been a practice in our newborn unit to supplement all VLBW preterm infants with sodium chloride, it is not known whether this practice is necessary and its efficacy has not been evaluated. There are also no local studies on the significance and incidence of hyponatraemia in VLBW preterm infants in relationship to sodium intake. The sodium content of preterm milk at KNH has also not been studied. It is with this in mind that the author was prompted to carry out this study and make appropriate recommendations.

HYPOTHESIS:

Sodium supplementation has no effect on sodium profiles of VLBW preterm infants fed on own mothers' breast milk.

OBJECTIVES:

- (1) To compare serum sodium levels, and urinary sodium excretion in VLBW preterm infants, between those supplemented and those not supplemented with sodium chloride.
- (2) To compare physical growth of sodium chloride supplemented and that of unsupplemented VLBW preterm infants.

MATERIALS AND METHODS:

1.1 STUDY AREA

This study was undertaken in the Newborn Unit of the Kenyatta National Hospital which is a referral as well as a University teaching hospital for Kenya. The unit admits patients largely from the Kenyatta Hospital Maternity Unit, and a few from other hospitals within the City. It admits all babies weighing less than 2000 gms, and any other high risk neonate requiring specialised care. It has a monthly admission of 150 babies, 20% of whom are VLBW infants.

1.2 STUDY PERIOD

The study was carried out during the months of January through August, 1989.

1.3 REFERENCE POPULATION

All the healthy very low birth weight infants at K.N.H.

1.4 SOURCE POPULATION

Healthy very low birth weight preterm infants aged 7 days.

1.5 STUDY POPULATION

All infants weighing between 1001-1500 gms whose gestational age was assessed using the method by Dubowitz et al (39) and this correlated with obstetrical history were examined at birth. Out of these 66 consecutive infants who were of good clinical state were recruited in the study on day 7 of life.

1.6 STUDY FACTOR

The rationale of sodium supplementation in VLBW preterm infants in our Newborn Unit.

2. STUDY DESIGN:

This being an analytic study, the study population was randomised in two groups. Group 1 consisting of 41 infants were the cases who were supplemented with 3 mmol/Kg/day of oral sodium chloride from day 7 of life. Group II consisting of 25 infants were the controls who were unsupplemented. All these infants were healthy and had been started on own mothers' milk within 24-48 hours after delivery.

The infants were followed up for a period of six weeks postnatally. All infants had blood and urine samples taken on day 7 and thereafter weekly

for five weeks. The mothers' expressed breast milk was also taken on day 7 and thereafter weekly for five weeks. All specimens were biochemically analysed.

2.1 SUBJECT SELECTION

This was done from Monday to Friday every week during the study period. The subjects were selected in the morning hours between 7am and 11am. Every next very low birth weight infant who fulfilled the inclusion criteria was recruited into the study.

2.1.1 INCLUSION CRITERIA

- (i) Normal healthy VLBW preterm infants with no overt features of sepsis.
- (ii) Infants who were exclusively fed on their own mothers' expressed breast milk.
- (iii) Infants whose mothers were on a normal diet without diuretic therapy and with no history of renal disease, PET or hypertension.
- (iv) Infants whose weight was appropriate for gestational age.
- (v) Infants who were retaining at least 80 percent of the prescribed feeds.

2.1.2 EXCLUSION CRITERIA

- (i) Very sick infants.
- (ii) Infants with severe congenital malformations.
- (iii) Infants who became sick during the study were excluded.

2.2 SAMPLE SIZE

Using the reported incidence of hyponatraemia to be 30% in VLBW preterm infants (18) sample size was calculated using the formular as shown in Appendix B.

3. METHODS

3.1 NURSERY ROUTINE

All infants were unclothed and were cared for in incubators. This was continued until their weight was more than 1600 grammes when they were nursed clothed in the cots. Maternal milk was manually expressed by each infant's mother in the newborn unit every three hours. The infants were fed by nasogastric tube basing on a strict protocol based on recommendation cited by Robertson (40). This recommends the feeds on day one to be 60 mls/Kg/day This is gradually increased until maximum of 200 mls/Kg/day by day 14 unless the baby is sick and not tolerating feeds.

The infants were recruited into the study when they were feeding on an average of 150 mls/Kg/day. This was gradually adjusted daily depending on the weight increase of individual infants. This gradually increased to a rate of 200 mls/Kg/day, 210 mls/Kg/day 220 mls/Kg/day and 240 mls/Kg/day by second, third, fourth and fifth weeks of life respectively. As the infants matured, they were weaned off the tube and introduced on cup feeding.

The study group were on addition to breast-feeding given sodium supplementation of 3 mmol/Kg/day. 20% sodium chloride solution was used, which on calculation was found to contain 3 mmol/ml of Na⁺. The sodium was given every day, orally together with the other prescribed medication just before the 9.00a.m. feed.

3.2 ANTHROPOMETRIC ASSESSMENTS

All the measurements were done by the investigator. Infants were weighed weekly using a weighing machine that was accurate to the nearest 50 gms. Weighing was done in the morning between 8-9.00 a.m. before the 9.00a.m. feeds. Crown to heel length was measured weekly using a stadiometer. Head circumference was also measured weekly using a non stretchable tape. Increments in crown to heel length and head circumference were calculated as centimetres gained per week.

4. SPECIMEN COLLECTION

4.1 MILK

One ml aliquot of milk at the end of all stages of expression was taken at every time the mother came to express, put in a plain bottle and refrigerated at 4°C. At the end of 24 hours, the whole 8 ml homogenate was delivered to the laboratory for analysis.

4.2 URINE COLLECTION:

A timed spot specimen of urine was collected from the infants by strapping a plastic paediatric urine collector around the genitalia. This was done after the first morning feed of 6.00 a.m. The collector was removed as soon as the urine was voided. All the urine collected was delivered to the laboratory where it was stored at - 20°C and later analysed in batches.

4.3 BLOOD COLLECTION

The broken needle technique was used in obtaining blood as described by Robertson (41). The hub of an FG 21 or FG 23 needle was broken off and the needle was inserted into a peripheral vein which had been distended in the usual way in the hand. The venous occlusion was gently continued and blood dripped out of the end of the needle into a bottle. 1.5 mls of blood was collected in a plain bottle and was left to stand on a bench until clot retraction occurred and was centrifuged to separate the serum. The serum was stored frozen at - 20°C until analysis was done.

5. LABORATORY METHODS

5.1 Serum, urinary and breast milk sodium and potassium were analysed by flame photometry technique (42).

5.2 Serum and urinary, creatinine were analysed by Jaffe's method by means of end-point determination after deproteinization with trichloroacetic acid (43).

Creatinine clearance was calculated by formular
creatinine clearance = $\frac{38h}{pc}$ (44). Where 38 is
a constant h = height and pc = plasma creatinine.

6. ETHICAL CONSIDERATION

The protocol was accepted by the Kenyatta Hospital Ethical Committee and consent given for research on human subjects. Informed consent was also obtained from parents of the infants for the inclusion into the study and for drawing of blood samples required for analysis.

7. STATISTICAL METHODS

All the information collected was manually analysed using a scientific calculator. Student's-t test was used to test the level of significance. The difference was significant when $P < 0.05$.

8. DEFINATIONS

Hyponatraemia was defined as a serum sodium levels less than 130 mmol/l (45).
Very low birth weight infant was defined as a baby born prematurely, whose weight was less than 1500 gms. (46).

9. REFERENCE RANGE FOR ELECTROLYTE UNDER STUDY

The values given in care of high risk neonate by Klaus Fanaroff was used (47):

Serum sodium concentration 133 - 146 mmol/l
Serum potassium concentration 4.6 - 6.7 mmol/l

Serum creatinine	18 - 35 μ mol/l
Urinary sodium	40 - 220 mmol/l (24 hr. urine)
Urinary potassium	2.5 - 125 mmol/l
Urinary potassium	(24 hr urine varies within diet.
Urinary creatinine	71 - 195 μ mol/l
GFR	28 - 68 mls/min.

RESULTS

The study involved 66 infants. 41 were supplemented with sodium chloride i.e. the cases and 25 were unsupplemented (controls). Table 1 shows the sex distribution of the infants.

TABLE 1 : SEX DISTRIBUTION

SEX	SUPPLEMENTED	UNSUPPLEMENTED
MALE	24 (58.5%)	14 (57%)
FEMALE	17 (41.5%)	11 (43%)
TOTAL	41 (100%)	25 (100%)

There was no statistical significant difference in the sex distribution in the two groups.

Both supplemented and unsupplements were divided into two weight categories i.e. 1001 - 1250 gms and 1251 - 1500 grams as shown in figure 1.

Among the supplemented 17% were between 1001- 1250 while 83% were between 1251 - 1500 gms. While among the ~~unsupplemented~~ 20% were between 1001 - 1250 gms and 80% were between 1251 - 1500 gms.

FIG. 1: BIRTH WEIGHT DISTRIBUTION.

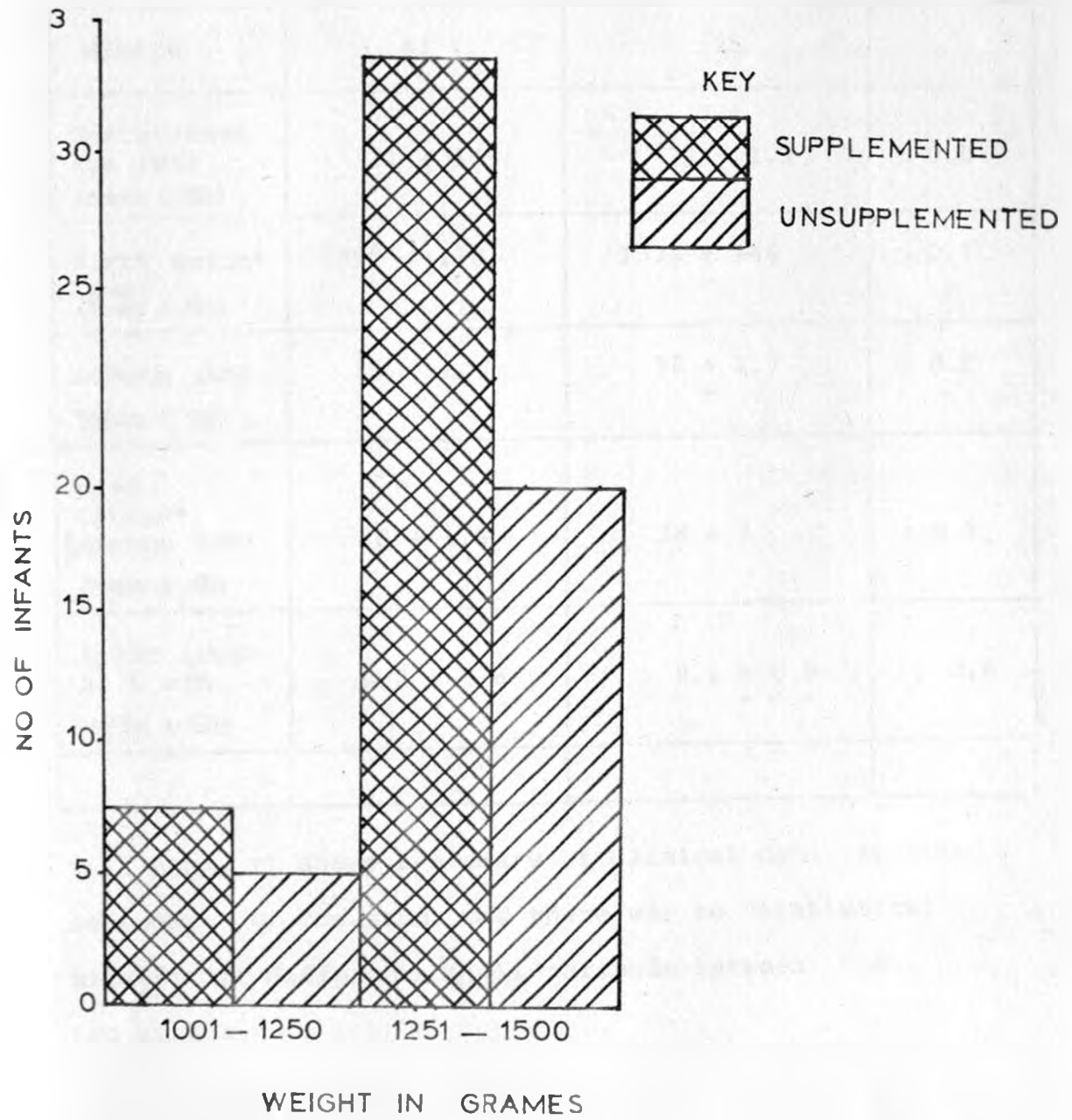


Table II: SUMMARY OF CLINICAL DATA

	SUPPLEMENTED	UNSUPPLEMENTED	P VALUE
NUMBER	41	25	
Gestational age (wk) (mean \pm SD)	31 \pm 1.5	31 \pm 1.9	> 0.8
Birth weight (gms) (Mean \pm SD)	1390 \pm 130	1332 \pm 146	> 0.1
Length (cm) (Mean \pm SD)	38 \pm 1.4	38 \pm 1.7	> 0.8
Head Circumference (cm) (Mean \pm SD)	28 \pm 1.3	28 \pm 2	> 0.8
Apgar score at 5 min. (Mean \pm SD)	9.3 \pm 0.8	9.1 \pm 0.8	> 0.8

Table II shows a summary of Clinical data at the beginning of the study and there was no statistical significant difference in the variable between the two groups.

Table III Electrolyte composition of milk from mothers delivering preterm babies comparing Kenyan mothers with Caucasians in mmols/l mean \pm SD

STUDY POPULATION	ELECTROLYTE	LACTATION DAYS			
		7	14	21	28
KENYAN (Present Study)	Na ⁺	15.5 \pm 5.9	11.4 \pm 4.7	8.8 \pm 3.4	7.7 \pm 2.2
KENYAN (Present Study)	K ⁺	19.4 \pm 3.2	17.1 \pm 3.1	14.5 \pm 3.4	13.8 \pm 2.7
CAUCASIAN (33)	Na ⁺	21.8 \pm 2.7	19.7 \pm 2.3	13.4 \pm 1.8	12.6 \pm 2.5
CAUCASIAN (33)	K ⁺	17.6 \pm 0.5	16.2 \pm 0.5	16.3 \pm 0.9	15.5 \pm 0.6

Note: Caucasian figs. derived from study by Anderson, G.H. et al.

Above table shows the concentration of sodium and potassium in milk from the mothers delivering preterm babies. The contents were analysed weekly up to six weeks postnatally. This was compared with those figures found in Caucasian population (33). Both sodium and potassium decreased with advancing lactation period in both the Kenyan and Caucasian populations. The mean sodium content in Kenyan mothers was 10.8 mmol/l compared with 18.8 mmol/l among the Caucasians ($P < 0.01$). But the breast milk K⁺ content was 16.2 mmol/l, in the Kenyan population and 16.6 mmol/l in the Caucasian population ($P > 0.01$).

FIG. II: Mean total fluid intake for each week of the study period between the two groups.

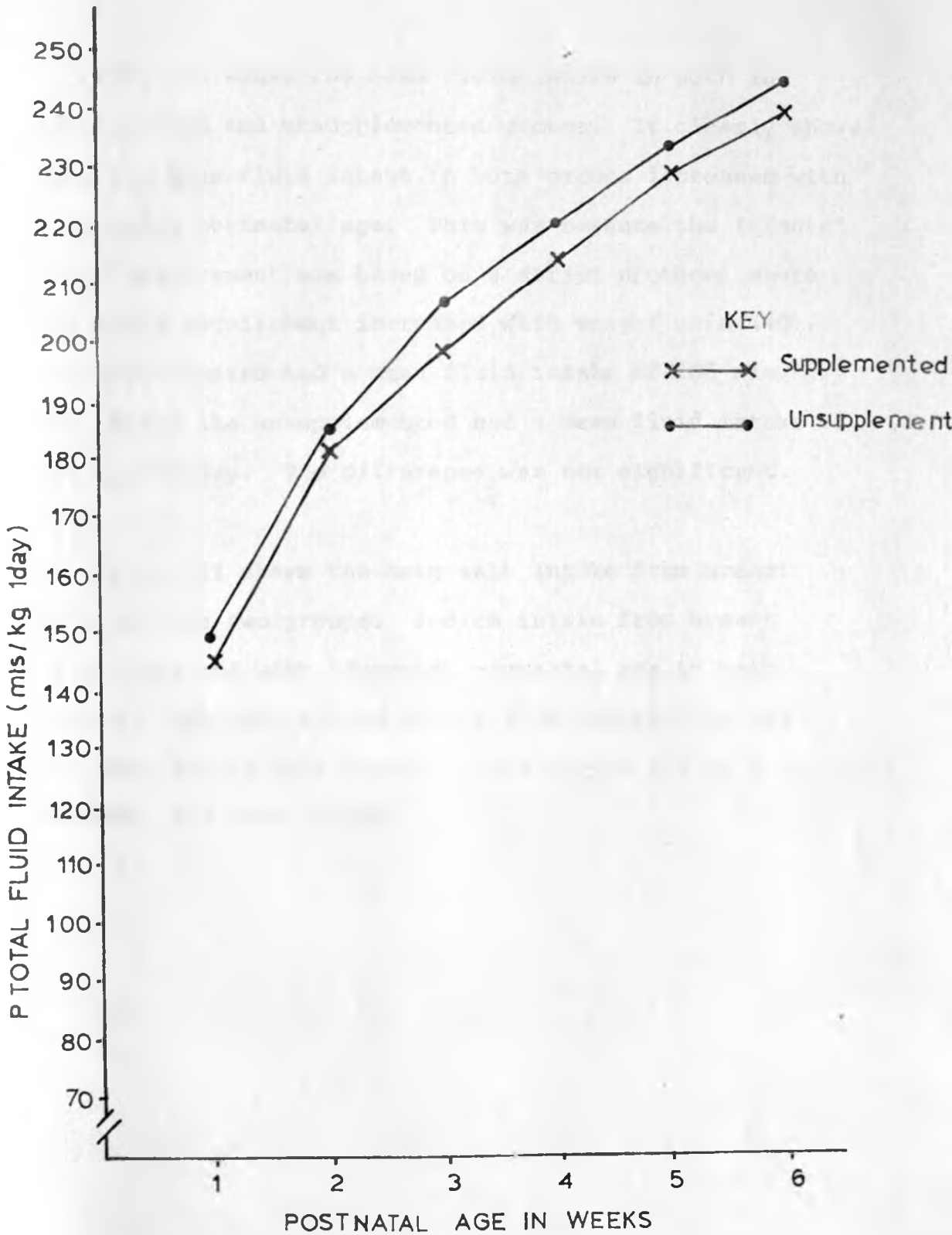


Fig. II shows the mean fluid intake in both the supplemented and unsupplemented groups. It clearly shows that the mean fluid intake in both groups increased with increasing postnatal age. This was because the infants' fluid requirement was based on a strict protocol where the fluid requirement increased with weight gain (40). The supplemented had a mean fluid intake of 206 mls/Kg/day, while the unsupplemented had a mean fluid intake of 202 mls/kg/day. The difference was not significant.

Fig. III shows the mean salt intake from breast milk for the two groups. Sodium intake from breast milk increased with advancing postnatal age in both groups. The mean sodium intake from breast milk was 4.2 mmol/day in both groups. This worked out to 2.75 mmol/Kg/day for each infant.

FIG. III Mean total sodium intake from breast Milk.

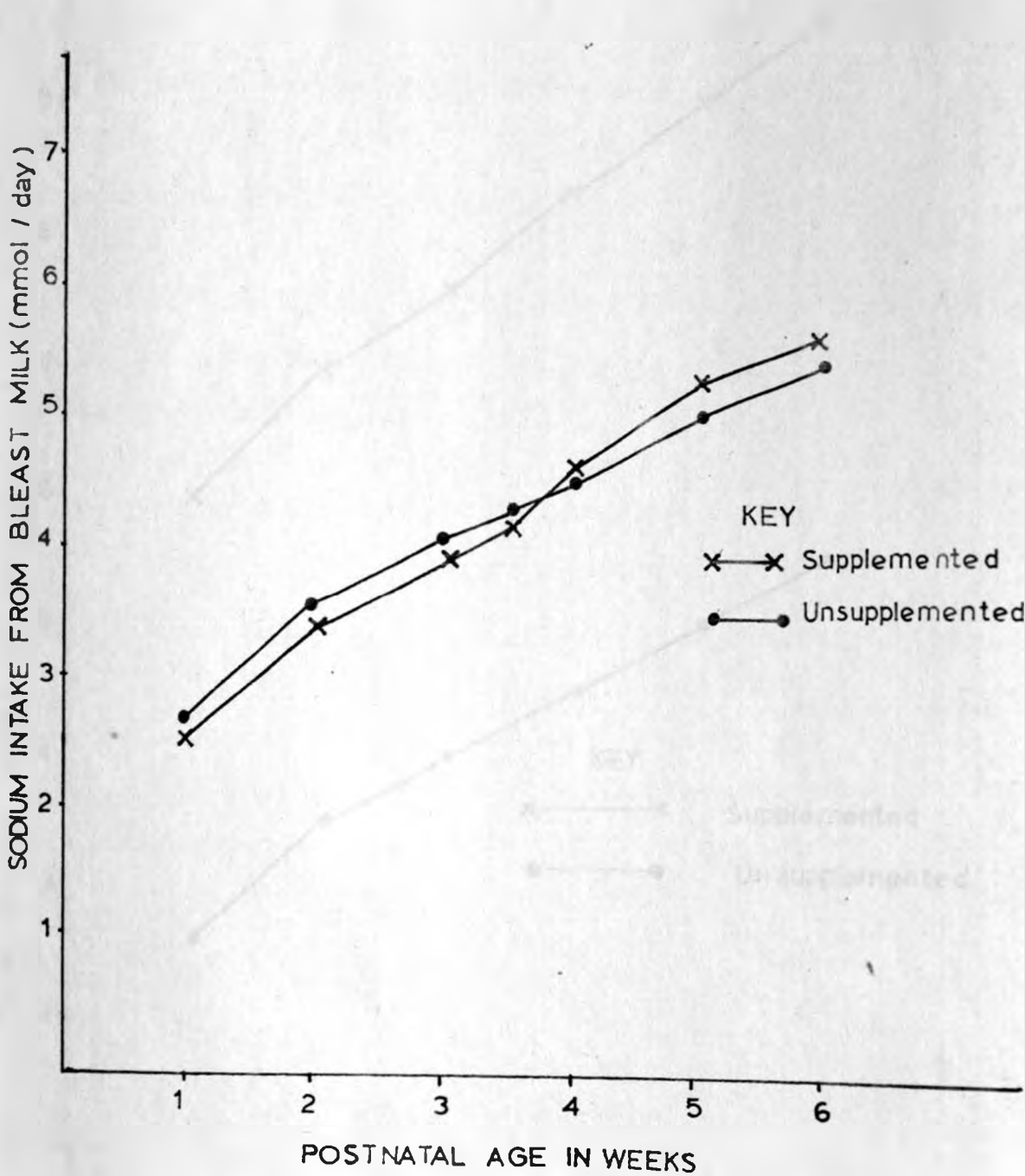


FIG. IV : Mean total Sodium intake per day compared between supplemented and unsupplemented Groups.

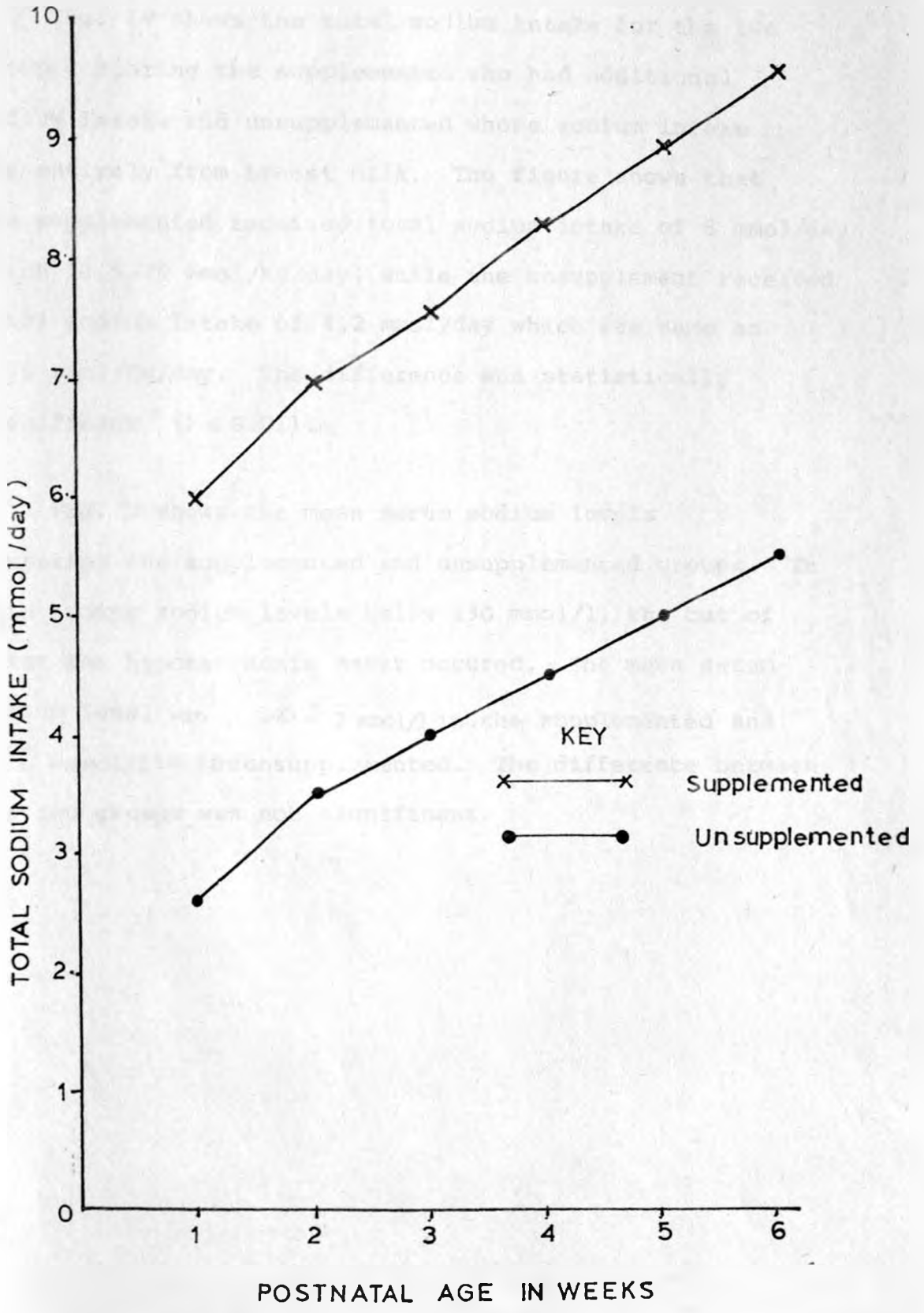


Fig. IV shows the total sodium intake for the two groups comparing the supplemented who had additional sodium intake and unsupplemented whose sodium intake was entirely from breast milk. The figure shows that the supplemented received total sodium intake of 8 mmol/day which is 5.75 mmol/Kg/day, while the unsupplement received total sodium intake of 4.2 mmol/day which was same as 2.75 mmol/Kg/day. The difference was statistically significant ($P < 0.01$).

Fig. V shows the mean serum sodium levels comparing the supplemented and unsupplemented groups. In both groups sodium levels below 130 mmol/l, the cut of point for hyponatraemia never occurred. The mean serum sodium level was 140 ± 2 mmol/l in the supplemented and 139 ± 2 mmol/l in the unsupplemented. The difference between the two groups was not significant.

FIG. v Serum NA^+ computed for weekly averages.

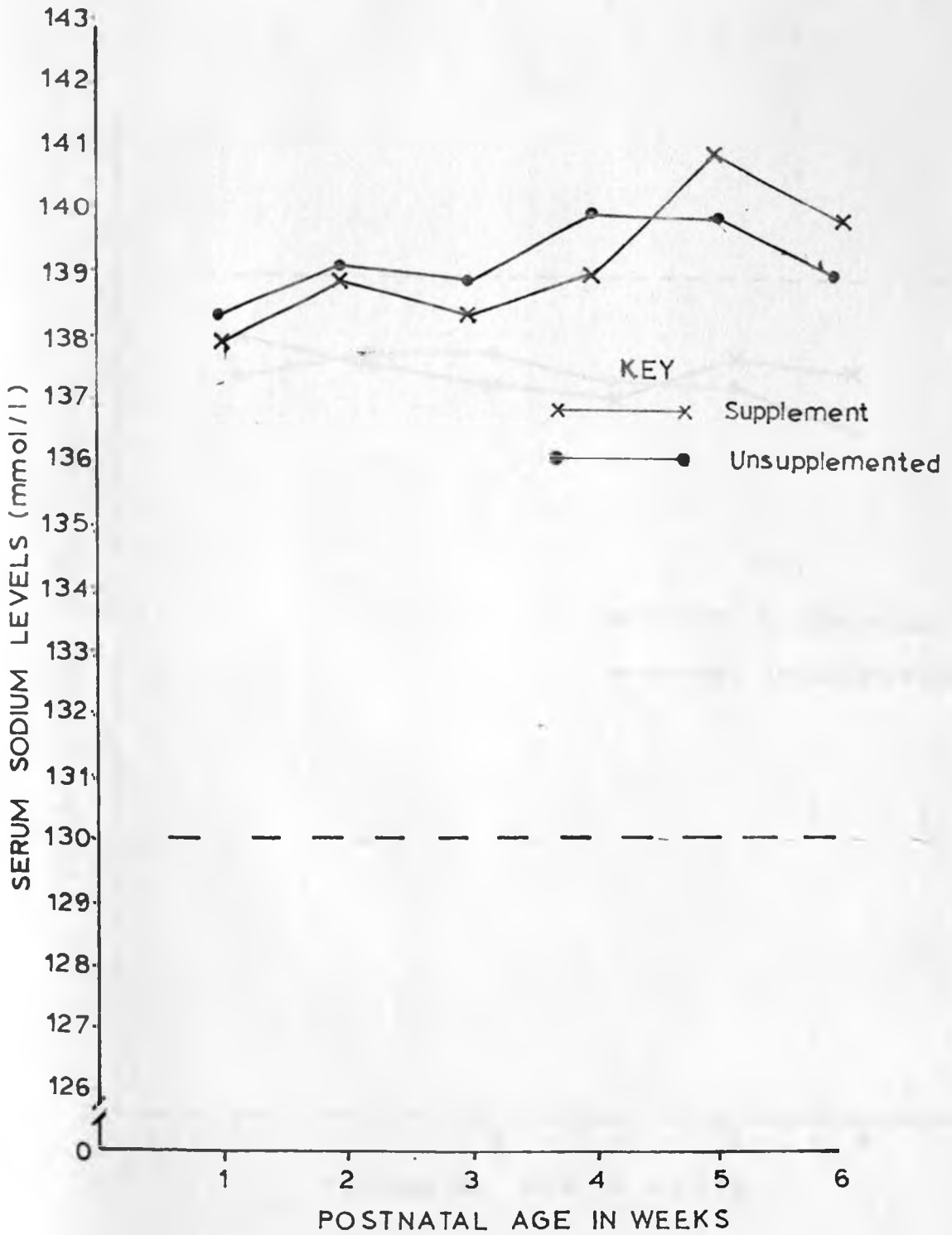


Fig. VI Serum K^+ concentration Computed for weekly averages .

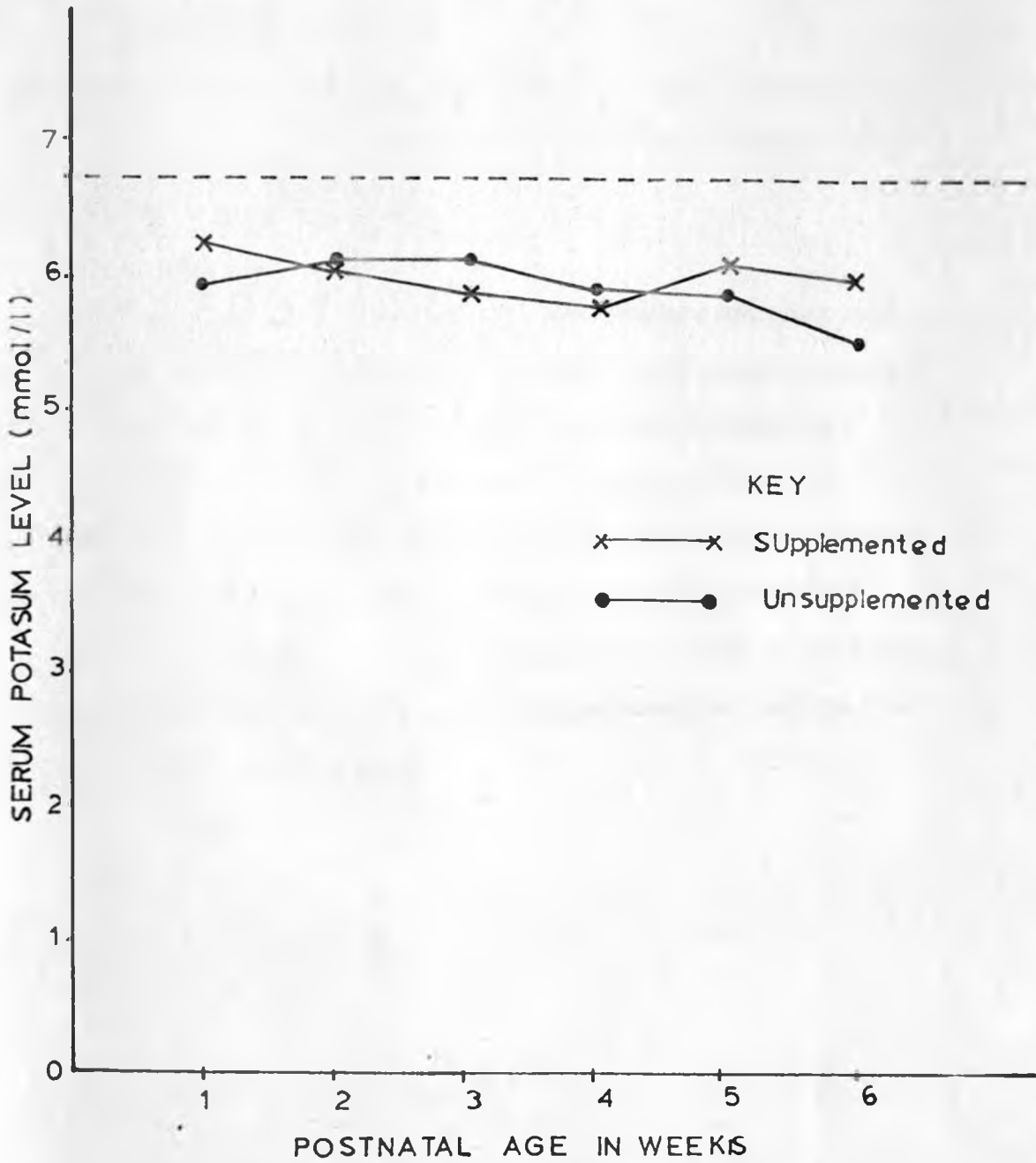


Fig. VI shows the mean serum potassium levels in the two groups. The supplemented had a mean serum potassium levels of 6.0 mmol/l compared with 5.85 mmol/l in the unsupplemented group.

Though the supplemented had a slightly higher potassium level, there was no significant statistical difference between the two groups.

Fig. VII shows the mean urinary sodium amongst the two groups. It was clearly noted that the supplemented had a higher urinary sodium than the unsupplemented. The supplemented group had a mean urinary sodium of 15.7 mmol/l, the unsupplemented group had a mean urinary sodium of 7.3 mmol/l. The difference was significant $P < 0.05$. This shows that the supplemented had a markedly higher urinary sodium than the unsupplemented due to the increase renal sodium load.

FIG VII Urinary sodium represented as mean Values compared between Supplemented and Unsupplemented Groups.

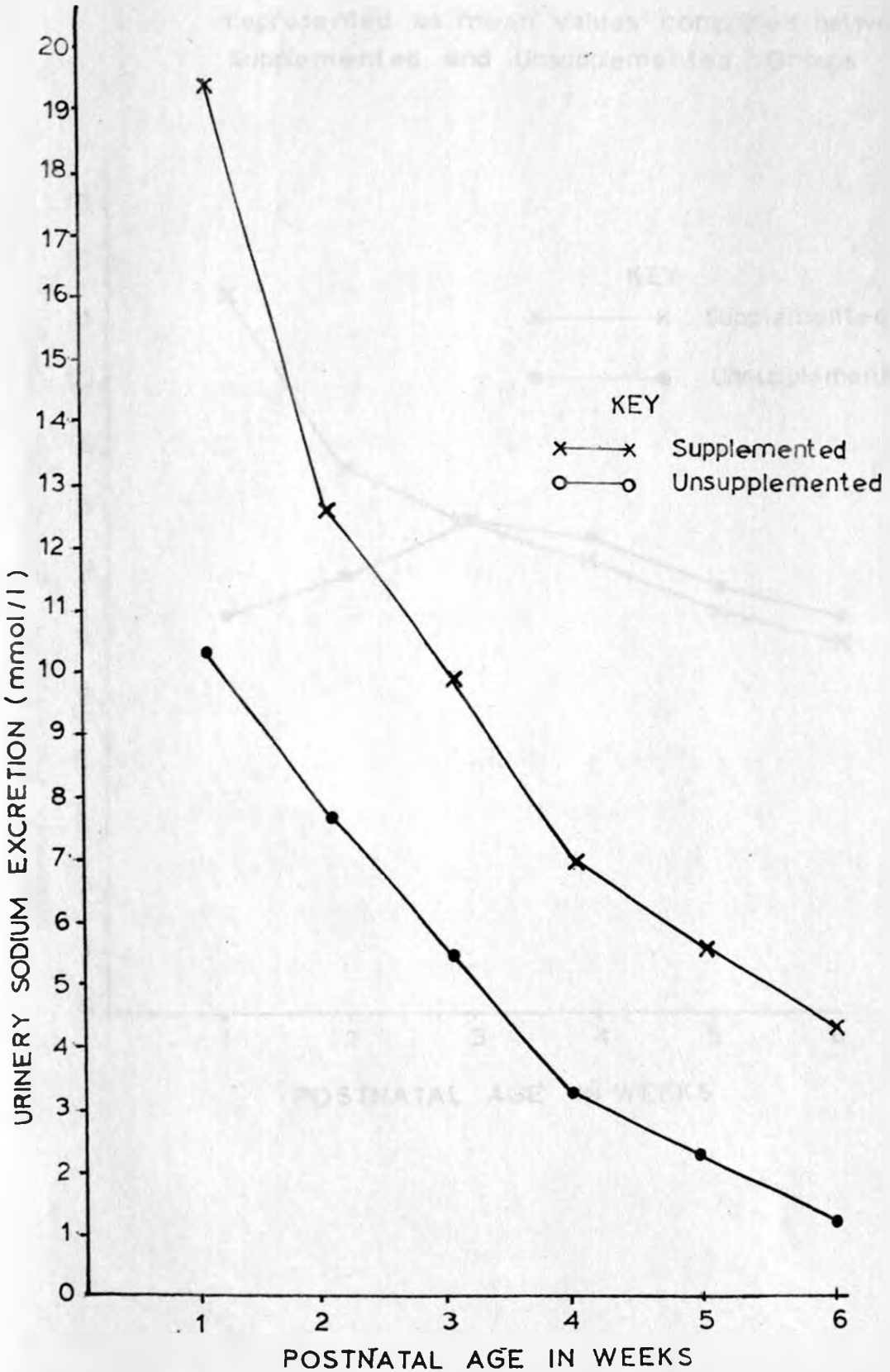


FIG. VIII Postnatal changes in urinary Potassium excretion represented as mean values compared between Supplemented and Unsupplemented Groups.

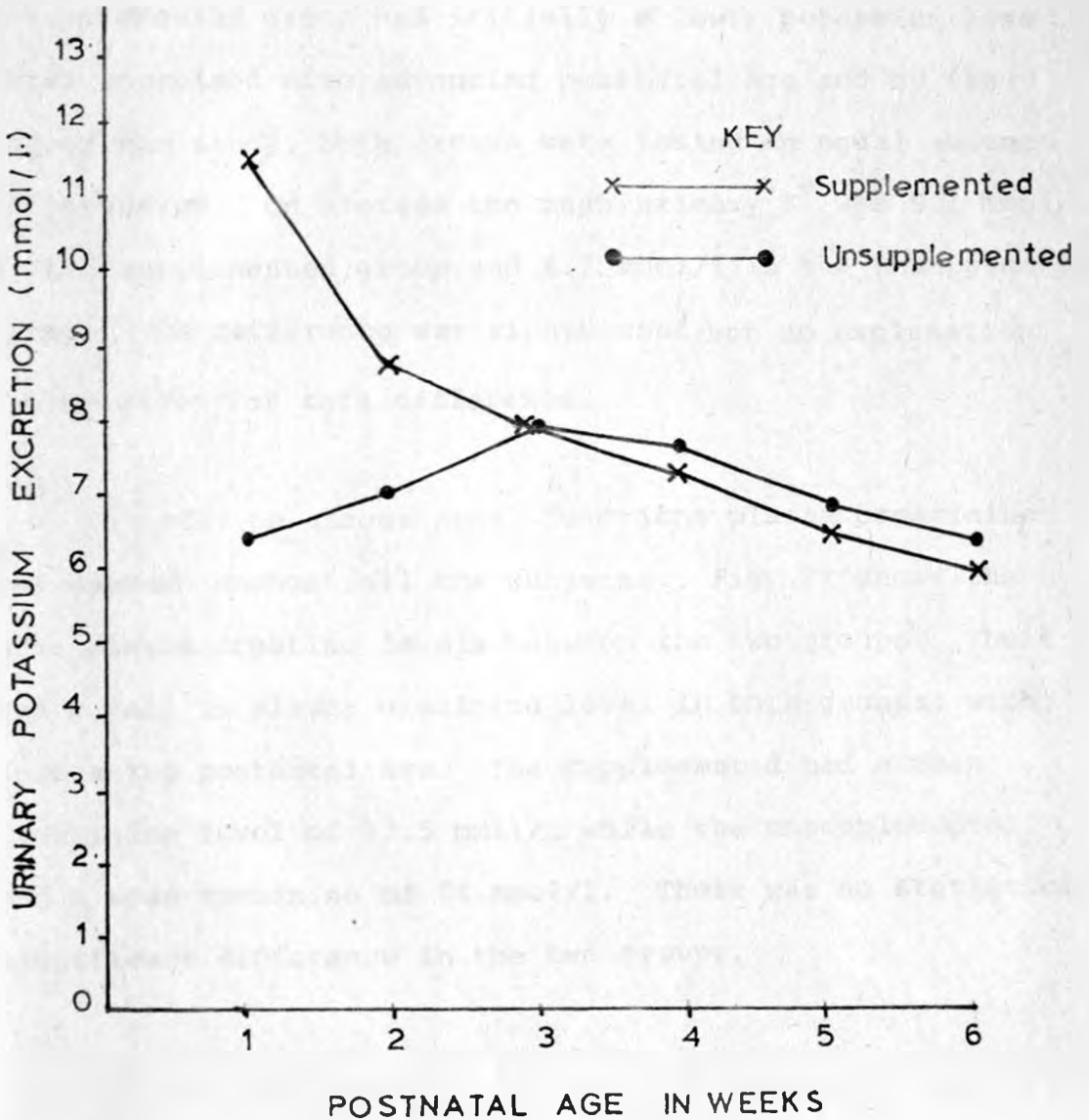


Fig. VIII shows the mean urinary potassium between the supplemented and unsupplemented groups. There was initially a high potassium loss in the supplemented group, which decreased with an increasing postnatal age. The unsupplemented group had initially a lower potassium loss which increased with advancing postnatal age and by the end of the study, both groups were losing an equal amount of potassium. On average the mean urinary K^+ was 9.1 mmol/l in the supplemented group and 6.7 mmol/l in the unsupplemented group. The difference was significant but no explanation can be given for this difference.

In order to assess renal functions plasma creatinine was assessed amongst all the subjects. Fig. IX shows the mean plasma creatine levels between the two groups. There was a fall in plasma creatinine level in both groups, with increasing postnatal age. The supplemented had a mean creatinine level of 93.5 mmol/l while the unsupplemented had a mean creatinine of 84 mmol/l. There was no statistical significant difference in the two groups.

FIG.IX: Plasma creatinine in relation to Postnatal age of VLBW Preterm infants

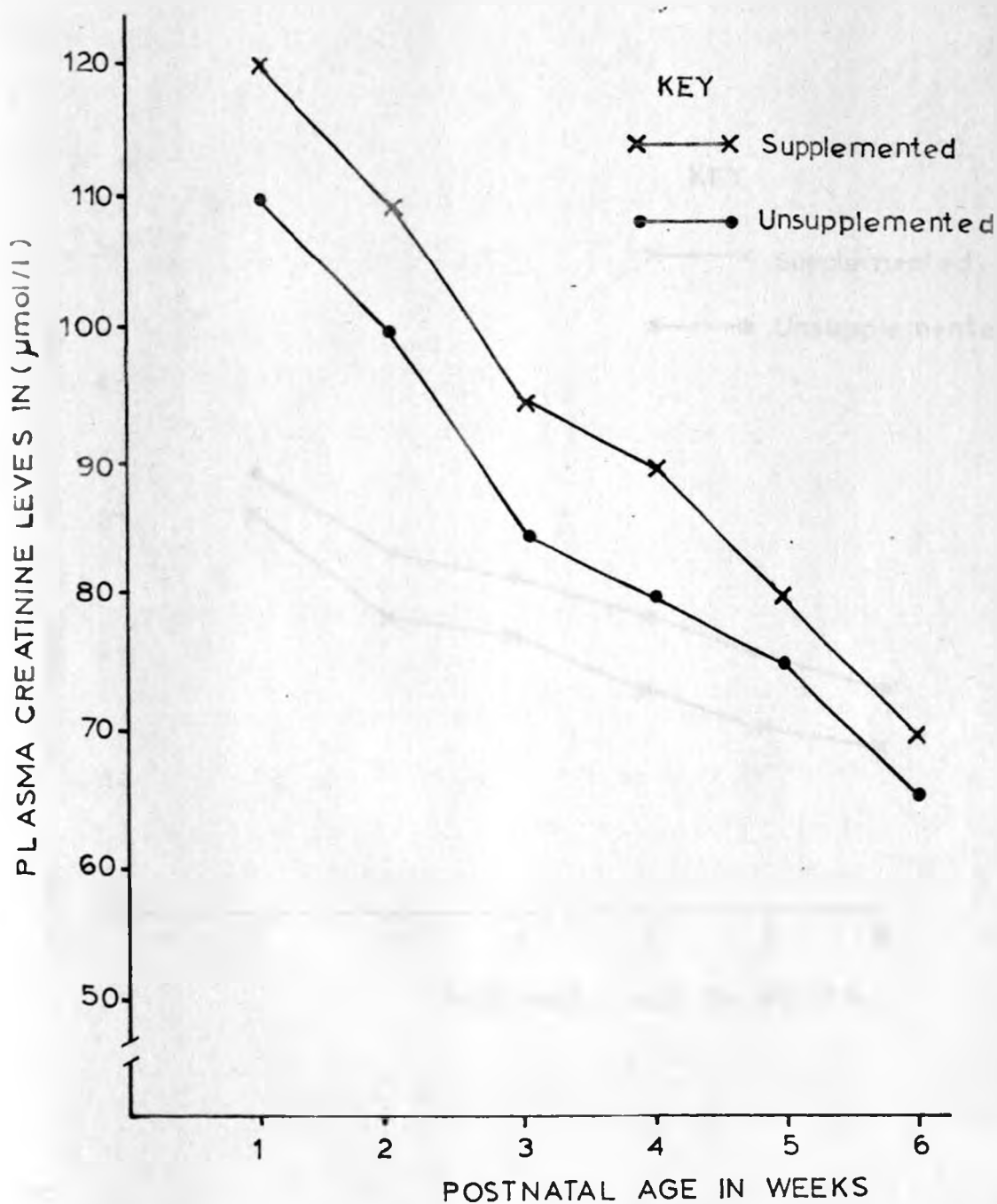


FIG. X : Postnatal Values of Urinary creatinine .

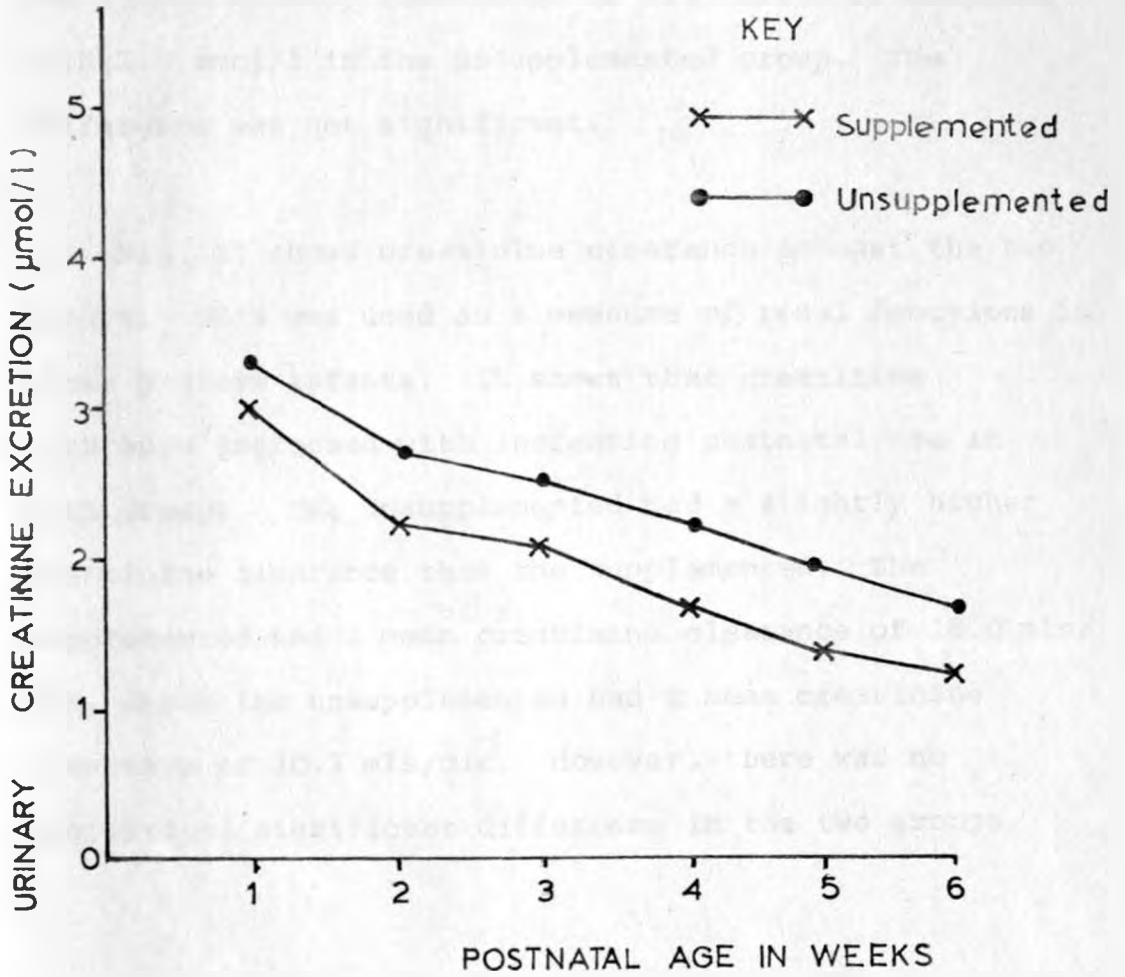


Fig. X shows the mean urinary creatinine in the two groups. It shows decreasing urinary creatinine with advancing postnatal age, this may be a reflection of decreasing plasma creatinine levels. The supplemented had a mean urinary creatinine of 2.4 mmol/l as compared with 2.6 mmol/l in the unsupplemented group. The difference was not significant.

Fig. XI shows creatinine clearance amongst the two groups. This was used as a measure of renal functions in these preterm infants. It shows that creatinine clearance increased with increasing postnatal age in both groups. The unsupplemented had a slightly higher creatinine clearance than the supplemented. The supplemented had a mean creatinine clearance of 18.0 mls/min, while the unsupplemented had a mean creatinine clearance of 20.3 mls/min. However, there was no statistical significant difference in the two groups.

FIG.10: XI Creatinine clearance compared with Postnatal age in both the supplemented and unsupplemented

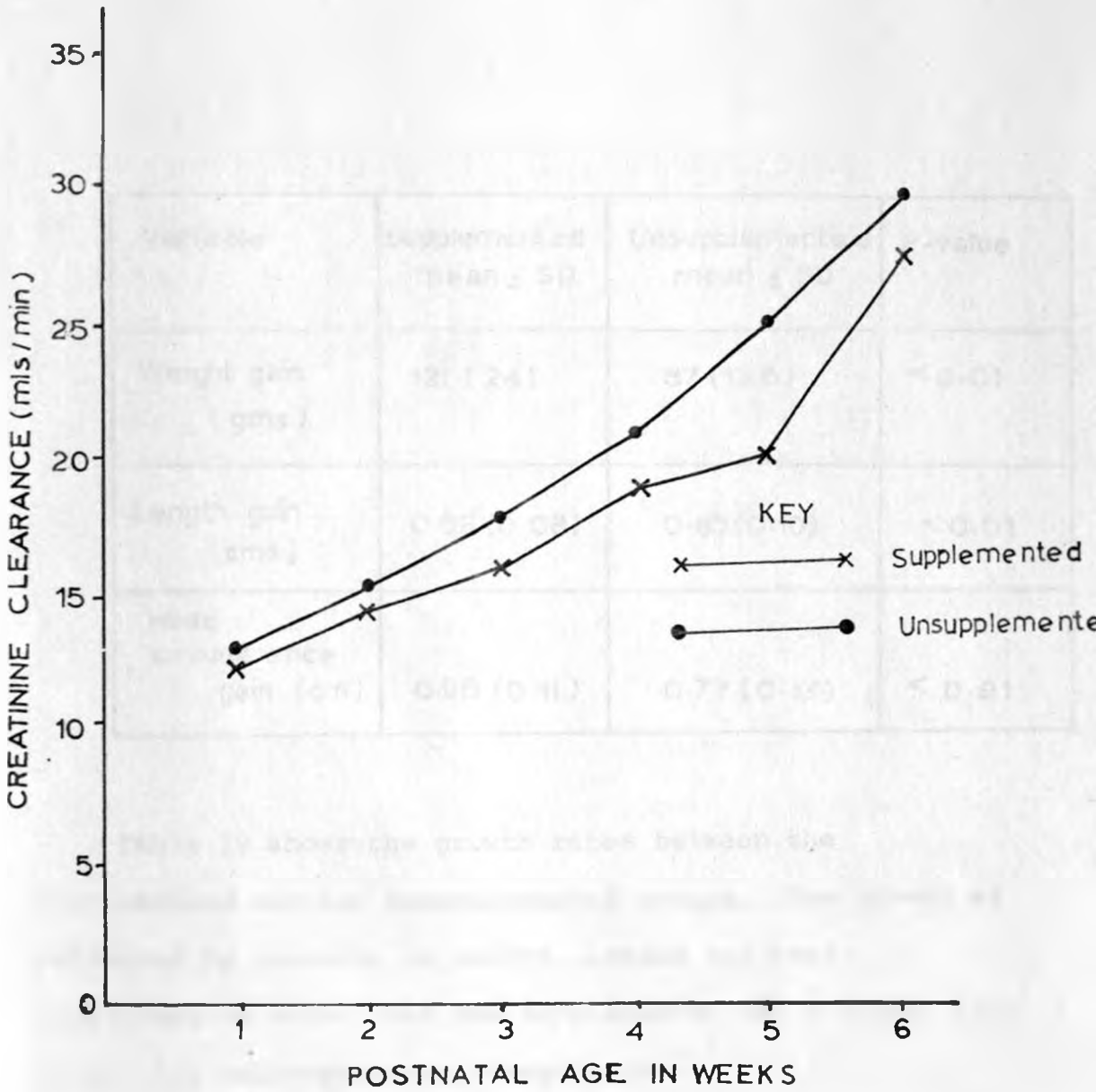


Table VI Mean Postnatal growth of supplemented and unsupplemented infants

Variable	Supplemented mean \pm SD	Unsupplemented mean \pm SD	P-value
Weight gain (gms)	121 (24)	87 (13.5)	< 0.01
Length gain (cms)	0.96 (0.08)	0.85(0.10)	< 0.01
Head circumference gain (cm)	0.95 (0.11)	0.77 (0.13)	< 0.01

Table IV shows the growth rates between the supplemented and the unsupplemented groups. The growth as reflected by increase in weight, length and head circumference shows that the supplemented had a higher gain in all the anthropometric measurements.

DISCUSSION

From this study it is clearly seen that early preterm milk contains a high sodium and potassium and these minerals decreases with an advancing lactation period. These findings agree with those of other workers, where Gross et al (34) found that milk produced by mothers delivering preterm infants had a higher sodium and potassium contents and these minerals decreased with advancing period of lactation. Fomon et al (48) in their study showed that the concentration of sodium in early preterm milk may be as high as 20 mmol/l and this decreased with increasing period of lactation averaging 5.7 mmol/l by day 84. The explanation for this variation in the mineral content is not clear, however, it may be that early preterm milk is less in volume and hence relatively more concentrated or it may be just a natural phenomenon to suit the preterm infants.

But when the electrolyte content of the preterm milk in the Kenyan mothers was compared with caucasians, the sodium contents were lower in the Kenyan population than the caucasian ones. However, the potassium contents were similar in both groups. The reason for this difference is not clear, but it may be nutritional with Kenyan mothers consuming a lower salt diet than the Caucassian,

The higher sodium content in the preterm milk would be of great advantage to the rapidly growing preterm infant,

whose kidneys are also still immature to conserve enough sodium for growth and homeostasis. Therefore preterm milk is adapted to suit the well-being of the preterm infant. All the infants received an equal amount of sodium from the breast milk, however the supplemented cumulatively received more sodium with extra supplementation.

The serum sodium and potassium levels in the infants studied remained within normal limits. No hyponatraemia was recorded in any of the infants during the study period. This differs from the findings of Day et al (24) and Roy et al (24) who found hyponatraemia to occur in 30% of their cases. This may have been due to the fact that the infants they studied were not all healthy. Those who were sick may have been predisposed to excessive urinary sodium losses culminating in hyponatraemia. Aperia et al (26) also found hyponatraemia to occur in some of the cases they studied. In their study the infants were fed on pooled breast milk from mothers who had delivered term babies. The sodium content of this milk averaged 5 mmol/l and the sodium intake from this milk was considerably lower for the preterm infants who have increased urinary sodium losses. In their infants sodium supplementation is required to maintain normal serum levels and prevent hyponatraemia. Also the majority of the infants we studied had birth weight above 1250 gms, unlike those in the previous studies who were below 1250 gms.

The causes of low serum sodium levels in VLBW preterm infants has been speculated to be combined influence of renal immaturity which permits relatively high urinary loss, low intake from pooled mature milk with low sodium content or different infant formulae based on mature milk and co-precipitation with calcium in the growing bones during the period of rapid growth (24, 25, 26). The role of aldosterone as to whether the amount produced is low or the immature tubules are unresponsive to its effect is still unresolved (24, 26). Supplementation of sodium in the VLBW preterm infants fed on pooled mature milk or some infant formulae based on mature milk is to provide daily sodium intake of 3 mmol/Kg/day, but this is supplied if the preterm infant is fed on own mothers' preterm milk, which has a higher sodium content 15.5 mmol/l as compared with 5.0 mmol/l of mature milk (35, 36). This study support the view that preterm infants can maintain serum sodium levels within normal range if fed on early preterm milk, which has adequate sodium content required for growth and homeostasis (33, 48, 50, 51).

Like sodium, the infants also maintained normal serum potassium levels. Hyperkalaemia was not observed in this study as had been reported by Roy et al (25). They defined hyperkalaemia as levels greater than 5.5 mmol/l which was lower than our definition of levels greater than 6.7 mmol/l (47).

As concerns urinary sodium, it was observed that the urinary sodium decreased progressively with increasing

postnatal age. However, the supplemented group were losing more sodium than the unsupplemented ones. The mean urinary sodium was 15.7 mmol/l and 7.3 mmol/l in the supplemented and unsupplemented groups respectively. This showed a significant increase in urinary sodium loss in the supplemented ($P < 0.05$). This finding agrees with Aperia et al (26) and Sulyok et al (27) who found that preterm infants respond to an increased oral sodium load by increased natriuresis. The high sodium excretion in these infants has been attributed to prematurity of the kidneys (27). Since extra sodium load needs extra free water clearance for its excretion, this in itself may be disadvantageous to the VLBW preterm infants who may be pushed in a state of intracellular dehydration.

The urinary potassium was quite different in the two groups in initial stages. The supplemented had a higher urinary potassium loss and this progressively decreased. While the unsupplemented initially had low urinary potassium loss and this progressively increased and by week three, the two groups had an equal urinary potassium losses. Initially there was a significant difference in the urinary potassium loss but in the later days, it was the same. This interesting observation is unexplained and no meaningful conclusion can be drawn from it.

The study shows that plasma and urinary creatinine decreased with increasing postnatal age. This is in

agreement with other workers (10, 12). This may be due to the fact that the plasma creatinine levels in the early postnatal life of VLBW preterm infants, reflect the maternal creatinine levels and this falls with increasing postnatal period as more is excreted in urine. This is said to continue even up to age 2 weeks when the infants attain their own plasma creatine level (12). This may account for the wide variation in creatinine ranges.

Creatinine clearance was used as a measure of glomerular filtration rate. The result shows that creatinine clearance increased in both the supplemented and unsupplemented groups with advancing postnatal age. It was as low as 12.5 mls/min by first week of life. The result obtained in this study agrees with those of other workers (14, 16, 17, 18). During the first week of life there is a rapid, almost two fold increase in GFR. The continued rise reaches adult values as related to body surface area between first and second year of life. The low GFR at birth may be due to the small glomerular capillary area available for filtration. The structural immaturity of the glomerular capillaries associated with a low water permeability, a low arterial blood pressure, a high haematocrit and renal vasoconstriction which result in a low glomerular blood flow. (49).

The results in this study also demonstrate that for the healthy VLBW preterm infants fed with preterm human milk, and who were given sodium supplementation had

significant growth advantage over the unsupplemented. The results of this study agree with those of other workers (50, 51). However, the recorded weight gain for both groups was less than 20 gm/day that was previously recorded in the same neonatal unit (52). This may have been due to an inaccurate weighing machine used in the present study. The one used before was a much more accurate weighing machine measuring to the nearest 10 gms as compared to 50 gm of the present study, giving a smaller possible observer error.

The reason why there was superior growth rate in those supplemented with sodium chloride was because sodium together with calcium co-precipitate in the bones during growth and this leads to rapid growth rate (24, 25). Additional sodium has been shown to increase the rate of H^+ excretion and HCO_3^- secretion and this results in raised PH, therefore reducing acidosis and creating favourable buffering conditions for calcium deposition in bone forming matrix. Schunk et al (54) and Epstein et al (55) have also shown that calcium and sodium share same transport and excretory mechanisms, in cases of high sodium levels, favours calcium deposition into the bone hence superior growth rates in the supplemented than the unsupplemented groups.

However, the data has not been presented in sufficient details to permit fully satisfactory evaluation of the results. In particular there seems little basis for the

conclusion that the weight gain would have been due to increased mineral intake and fluid retention. This could only be concluded if the growth was not sustained after the supplementation had been withdrawn. No side effects attributable to sodium retention and fluid overload were observed in this study.

CONCLUSION

From the study it could be concluded that:-

1. Hyponatraemia is quite rare in VLBW preterm infants fed on own mothers' breast milk as seen at Kenyatta National Hospital.
2. When challenged with an increased oral sodium load, VLBW preterm infants respond by an increased urinary sodium loss.
3. Early preterm milk has a higher mean sodium content, and this decreases with increasing lactation period.
4. Infants given sodium supplementation have a significantly higher growth rates than the unsupplemented ones.
5. Plasma creatinine levels decrease with increasing postnatal age.
6. Creatinine clearance in VLBW preterm infants increases with increasing postnatal age.
7. Sodium supplementation has no influence over serum and urinary sodium profiles of VLBW preterm infants so long as they are healthy and getting adequate feeds.

RECOMMENDATIONS

1. Sodium supplementation may not be essential in VLBW preterm infants so long as they are healthy and getting adequate feeds.
2. A study should be done to determine the effect of sodium supplementation on protein and bone metabolism in VLBW preterm infants, since growth rates were found to be higher in the supplemented.
3. Additional studies will be necessary to define the optimal sodium intake of sick VLBW preterm infants.

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APPENDIX A

BLODATA/LABORATORY RESULT SHEET

NAME.....
 SEX.....
 APGAR SCORE AT 5MIN.....
 BIRTH WEIGHT.....
 LENGTH.....
 HEAD CIRCUMFERENCE.....

WEEKS	1	2	3	4	5	6
WEIGHT						
LENGTH						
HEAD CIRCUMFERENCE						
TOTAL VOL. FEEDS/ DAY						
Na+ SUPPLEMENTATION meq/kg/day						
		RESULTS				
SERUM Na+						
SERUM CREATININE						
SERUM K+						
URINARY CREATININE						
URINARY Na+						
URINARY K+						
BREAST MILK Na+						
BREAST MILK K+						

APPENDIX B

SAMPLE SIZE

$$\text{Prevalence} = 30\% = P_2$$

$$\text{Relative Risk (RR)} = 2$$

$$P_1 = \text{RR} \times P_2$$

$$\text{RR} = \frac{P_1}{P_2}$$

$$\text{Level of significance} = 5\%$$

$$\text{Power of Test} = 90\%$$

$$n = \frac{\left\{ Z_{1-\frac{\alpha}{2}} \sqrt{2P(1-P)} + Z_{1-\beta} \sqrt{P_1(1-P_1) + P_2(1-P_2)} \right\}^2}{(P_1 - P_2)^2}$$

$$= 41.$$

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