

A STUDY OF UREA AND THE MAJOR ELECTROLYTES IN
RELATION TO FEEDING PATTERNS IN KENYAN AFRICAN
INFANTS SEEN AT KENYATA NATIONAL HOSPITAL.

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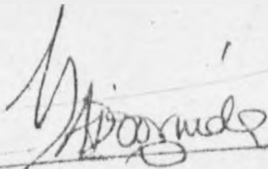
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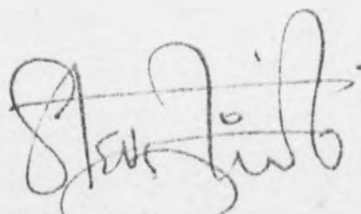
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LIST OF ABBREVIATIONS AND DEFINITIONS

Formula	A breast milk substitute formulated industrially in accordance with applicable codex alimentaries standards to satisfy the normal requirements up to six months of age.
'Combined'	Breast and formula feeding.
KNH	Kenyatta National Hospital.
PDU	Paediatric Demonstration Unit.
mmol/L	Millimoles per litre.
mosm/l	Milliosmoles per litre.
CHO	Carbohydrate.
BUN	Blood urea nitrogen.
S.D.	Standard deviation.

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SUMMARY

The levels of blood urea nitrogen (BUN) were measured in 100 normal infants aged 2,4,8 and 12 weeks. The infants were grouped into three feeding patterns: breast fed only, formula fed only, and combined breast and formula feeding. Associated variations in BUN and electrolytes were sought among the three feeding patterns. No differences were found in sodium, potassium, chloride or calcium levels. Formula fed infants had significantly higher BUN levels when compared with breast fed infants and with infants on combined feeds. Calculated osmolarity was slightly higher in formula fed infants than in the other groups, but these differences were not significant.

INTRODUCTION

The goal in infant feeding includes provision of adequate supply of water, calories and essential nutrients. In most instances the diet supplied to normal infants will include more than the required amounts (1). Most of artificial formulae are based on the cow's milk and have high levels of sodium, potassium, calcium and chloride (2,3). Total protein content is also higher than that in breast milk. The absorption of these electrolytes from the gastro-intestinal tract is always more complete from human milk than from formula or cow's milk (4). They are all important in homeostasis control, for example sodium and chloride play an important role in blood volume control. The excretion of these electrolytes occur mainly in the kidneys (5,6).

Solutes that must be excreted in the urine are referred to as renal solute load. With rare exceptions the main contributors will be nitrogenous substances and the major electrolytes. Sugar, a major component of dietary intake, is ordinarily metabolised to carbon dioxide and water. For this reason the total solute concentration of an infant diet has little predictive value of the renal solute load(7). The estimate of renal solute is based on dietary nitrogen and on the three major minerals, sodium, potassium and chloride. Plasma and extracellular osmolarity are closely related to the plasma sodium concentration. When the water content of plasma is normal the osmolarity is approximately twice the sodium concentration plus the milliosmoles of glucose and urea(6)

Urea is one of the end-products of protein metabolism.

The urea in the cord blood is determined by that of the maternal blood. The serum level of urea is low during the first weeks and it gradually rises depending on the diet. Urea constitutes a major part of renal solute and in the young infant its concentration reflects the combined effects of dietary intake, the degree of hydration and the functional maturity of the kidneys (8).

The kidneys of the mature newborns are perfectly adequate for the well being of the baby provided that an appropriate solute load such as that provided by human milk is ingested. Although the glomerular filtration rate increases in the first two months of life its still low when compared to that of the older child or adult (9). Most tubular transport systems are also incompletely developed in the first three months of life. All these make the functional adaptive capacity of the kidney less in these young infants as compared to older children and adults(10). A greater stress is therefore placed on the kidneys when the baby is fed on artificial feeds.

The normal baby is able to deal with the greatly increased solute and osmolar loads of cow's milk. The fact that most infants tolerate these increased loads does not mean that they are desirable. They may be very dangerous in a child who is fed on cow's milk which contains an excess sodium and osmolar load, when he has diarrhoea (11).

It has been clearly shown that infants fed on formulae or cow's milk, both of which contain approximately four times as much sodium as does breast milk, have a higher risk of developing hypernatraemic dehydration than do breast fed infants when they develop diarrhoea (12,14)

Present infant feeding practices in Kenya favour artificial feeds and early introduction of solid foods at the expense of breast feeding. Happily all efforts are being made in the right direction to encourage mothers to breastfeed their babies. Paediatric advisory groups do not recommend additional foods before three months (13). Most commercial formulae as well as cow's milk with added carbohydrates yield a renal solute load that is lower than that of cow's milk but greater than the renal solute presented by human milk. It has been found that a significant proportion of feeds made at home are too concentrated (14). In 1973 Davies et al found raised serum osmolarity levels in a significant proportion of healthy infants (18). It has also been shown that there are significant differences in plasma sodium, potassium, chloride and urea levels between breast fed and bottlefed infants with gastroenteritis (15).

Here at Kenyatta National Hospital a lot of work has been done on the biochemical status of infants and children with gastroenteritis (16,17,18). There is no study of the effects of different milk feeds on their levels of the blood urea nitrogen and the major electrolytes. Such study is certainly useful in the evaluation and management of sick infants. This is what prompted the present study.

OBJECTIVES

1. To determine the serum sodium, potassium, calcium, chloride and the blood urea nitrogen levels in normal infants attending Paediatric Demonstration Unit (PDU).

2. To relate the observed serum urea nitrogen and electrolytes levels to the following feeding patterns:
 - (i) Breast feeding only.
 - (ii) Formula fed only.
 - (iii) Combined (formula fed and breast fed).

MATERIALS AND METHODS

The study covered the period from May 1984 to September 1984 inclusive.

1. STUDY AREA

The infants included in the study were selected from Kenyatta National Hospital Paediatric Demonstration Unit (PDU), the Child Welfare Clinic. They were selected from Monday to Thursday between 11 a.m. and midday.

2. SELECTION OF INFANTS

Only infants aged 2,4,8 and 12 weeks were included in the study. Each infant admitted in the study had a full medical and dietary history recorded by the author.

The following were noted:-

- Diet of the baby from birth.
- The person who feeds the baby regularly.
- Whether the baby had been feeding normally on that day.
- When the baby was last sick and the treatment given.

A full examination was also done.

2.1 Inclusion Criteria

- 2.1.1 Normal healthy infants.
- 2.1.2 Infants with a fixed feeding pattern.
- 2.1.3 Infants fed only by the mother.
- 2.1.4 Informed consent from parents.

2.2 Exclusion Criteria

- 2.2.1 Presence of any previous major illness at any time from birth.
- 2.2.2 Drug therapy of any kind.
- 2.2.3 Incidental finding of a sign that caused no symptoms e.g. splenomegaly.

The infants were placed into three groups according to their feeding pattern:

Breast fed infants

Formula fed infants

Breast/formula fed infants.

3. SPECIMEN COLLECTION

In each infant a good clean venipuncture was done from the external jugular vein using a scalp vein needle. In most cases only one venipuncture was done. There was no squeezing of blood. Too much suction was also avoided. As soon as 3.0 ml of blood was drawn the needle was removed and the blood placed in the appropriate labelled containers:

2.5 ml was put into a plain biochemistry bottle.

0.5 ml was put into a fluoride bottle.

All specimens were delivered to the laboratory within one hour of collection. During transportation care was taken not to disturb the clotted blood.

4. LABORATORY METHODS

The method described by Wootton (19) using an Eel flame photometer was employed in the determination of sodium and potassium, while the method of Schales and Schales (20) was used for serum chloride estimation. Calcium was determined by Atomic Absorption Spectroscopy (21). Blood urea nitrogen was determined as described by Chaney and Marbach (22). Blood sugar was estimated by the Reflomat method (23). All the analyses were done by one person.

5. The Reference Ranges for Blood Urea Nitrogen and Electrolyte Values.

The values given in the Nelson Textbook of Pediatrics (Nelson, WE, Vaughan V.C., McKay, R.S. and Berhman R.E. editors, 11th Edition, W.B. Saunders, Philadelphia, 1979) were taken as the reference values.

The results were also compared with Kenyatta National Hospital biochemistry normal values.

5.1 Nelson Textbook of Pediatrics,

Serum sodium concentration 134 - 146 mmol/L

Serum potassium concentration 4.1 - 5.3 mmol/L

Serum calcium concentration 2.20 - 2.75 mmol/L

Serum chloride concentration 96 - 106 mmol/L

Serum osmolarity 270 - 295 mosmkg.

5.2 Kenyatta National Hospital biochemistry values,

Serum sodium 135 - 145 mmol/L

Serum potassium 3.5 - 5.0 mmol/L

Serum chloride 95 - 105 mmol/L

Serum calcium 2.13 - 2.63 mmol/L

BUN 1.3 - 3.3 mmol/L.

6. Statistical Analysis

The conditional test on the means using t-test approximation was utilized to test the significance of the differences observed in the results.

RESULTS

140 mothers were explained the purpose of the study, but only 122 agreed to have blood taken from their babies. 22 of the blood samples were not suitable for analysis and only the results of 100 infants were analysed as shown in table I.

Table I THE NUMBER OF SAMPLES ANALYSED,

STUDY VARIABLE	TOTAL NUMBERS OF SAMPLES ANALYSED.
Sodium	100
Potassium	100
Calcium	57
B U N	100
Chloride	86
Blood Sugar	100

Table II: Feeding Patterns and Age Distribution of infants studied,

Age in Weeks	Breast fed	Formula fed	Combined	Total
2	11	-	-	11
4	12	8	8	28
8	9	11	11	31
12	8	11	11	30
Total	40	30	30	100

28 (28%), 31 (31%), 30 (30%), of the infants were aged 4, 8 and 12 weeks respectively. Only 11 (11%) of the infants in the study were aged 2 weeks, and these were all breast fed. Beyond the age of 1 month, only 70% of the infants were still breast feeding. 30 (30%) of the infants were solely on formula.

Table III: Sex Distribution of Infants,

Sex	Breast fed	Formula fed	Combined	Total
Male	19	17	18	54
Female	21	13	12	46
Total	40	30	30	100

The sex distribution of the study infants is shown.

Male infants were more than female infants.

There were no statistically significant differences in sex among the three feeding patterns.

P = 0.01

Table IV: Composition of Infant Milk Foods,

Milk	Protein/ grams/100cc	Sodium mmol/L	Potassium mmol/L	Calcium mmol/L	Chloride mmol/L	CHO/ gram/100
Human	1.2	7	14	8.5	12	7.0
Nan	3.3	18	46	30.5	45	4.7
Lactogen	3.5	16	30	26.5	17	8.2
SMA-26	1.5	7	14	10.5	12	7.2
Similac	1.8	17	31	20.5	17	6.6

The main formula given to the infants were Lactogen and Nan.

SMA-26 was given to 9 infants. 85% were on Lactogen and Nan(32).

Table V: Plasma Sodium Levels in Infants on Different Feeding Patterns,

	Breast fed				Formula fed			Combined		
Age in weeks	2	4	8	12	4	8	12	4	8	12
Number	11	12	9	8	8	11	11	8	11	11
Sodium mmol/L Range	131-140	130-140	133-141	135-140	130-140	131-140	135-145	130-140	134-145	131-141
Mean	137.2	137.0	135.7	137.0	135.0	136.6	137.2	136.3	139.0	135.0
SD	2.5	5.0	2.9	1.9	2.5	1.7	4.4	3.8	2.5	3.1

Only 6 Infants (6%) had a serum sodium above 140 mmol/L, one breast fed and the rest formula fed. The overall sodium range was 130 - 145 mmol/L with an overall mean of 136 mmol/L. The highest (139 mmol/L) and lowest (135 mmol/L) means were observed in infants on combined feeding. There were no significant differences observed between age groups and within the three feeding patterns against serum sodium. $P = 0.01$.

Table VI: Potassium Levels in Infants on Different Feeding Patterns,

Age in weeks	Breast fed				Formula fed			Combined		
	2	4	8	12	4	8	12	4	8	12
Number	11	12	9	8	8	11	11	8	11	11
Potassium mmol/L Range	4.3-5.9	4.0-5.7	3.9-5.5	4.6-5.2	4.5-5.9	4.2-5.4	4.4-5.6	4.8-5.4	4.4-5.6	4.0-5.5
Mean	4.9	4.8	5.2	4.8	5.2	4.8	4.9	5.3	4.7	5.1
SD	0.6	0.4	0.4	0.7	1.7	0.4	0.9	0.4	0.4	0.5

The overall potassium range of all the 100 infants was 3.9 - 5.9 mmol/L with an overall mean of 5.0 mmol/L. There were no significant differences observed between age groups and within the three feeding patterns against potassium levels at $P > 0.01$.

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Table VII: Serum Calcium Levels in Infants on Different Feeding Patterns,

	Breast fed				Formula fed			Combined		
	2	4	8	12	4	8	12	4	8	12
Age in weeks										
Number	7	8	5	3	7	7	7	4	4	5
Calcium mmol/L Range	2.0-2.3	2.2-2.5	2.0-2.5	2.2-2.5	2.2-2.3	2.3-2.5	2.1-2.4	2.0-2.4	2.2-2.6	2.3-2.4
Mean	2.1	2.2	2.2	2.3	2.3	2.3	2.1	2.2	2.3	2.2
SD	0.3	0.2	0.3	0.4	0.2	0.2	0.3	0.2	0.2	0.2

The overall serum calcium range was 2.0-2.5 mmol/L with an overall mean of 2.2 mmol/L.

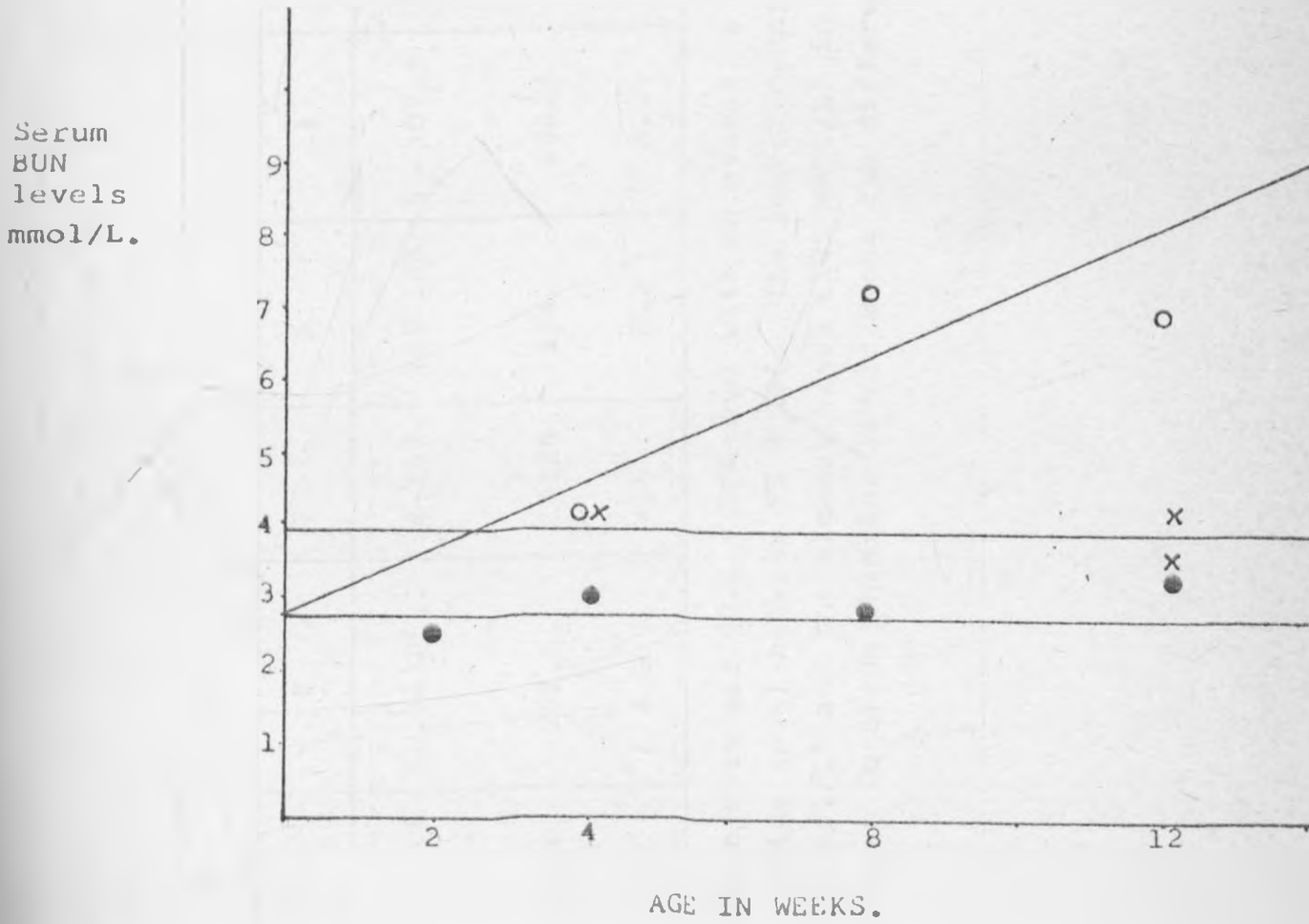
Different milk feeds did not affect serum calcium levels significantly. P = 0.01.

Table VIII: Influence of Different Feeding Patterns on Serum BUN Levels,

	Breast fed				Formula fed			Combined		
	2	4	8	12	4	8	12	4	8	12
Age in weeks	2	4	8	12	4	8	12	4	8	12
Number	11	12	9	8	8	11	10	8	11	11
BUN mmol/L Range	1.3-3.3	2.0-3.6	1.5-4.2	1.7-5.3	1.5-7.1	1.8-8.9	2.0-9.0	1.9-7.1	2.1-7.9	1.7-4.5
Mean	2.6	3.0	2.7	3.4	4.9	7.4	7.0	4.9	5.8	3.5
SD	4.8	3.9	3.9	3.5	8.1	10.8	15.0	8.8	8.4	5.5

The range of BUN was 1.5 - 9.0 mmol/L in the 30 infants on formula while that of the 40 infants on breast milk was 1.3 - 7.4 mmol/L. The highest BUN mean value was observed in 11 infants on formula and aged 2 months (7.4 mmol/L) and the lowest BUN mean (2.6 mmol/L) was observed in the 11 infants aged 2 weeks. There were significantly higher BUN values found in babies on formulas and combined feeding than babies fed on breast milk. $P = 0.01$.

Graph showing the effect of the feeding pattern on Serum BUN,



- Breast fed
- Formula fed
- × Combined

Table IX. Plasma Chloride Levels in Infants on Different Feeding Patterns,

	Breast fed				Formula fed			Combined		
Age in weeks	2	4	8	12	4	8	12	4	8	12
Number	9	10	8	8	7	9	11	8	10	10
Chloride mmol/L Range	91-107	95-106	98.4-106	98.3-106.1	98-107	100-108	95-107.5	97.7-105	90.6-108	96-107
Mean	105	103.0	103.0	101.6	102.6	104.	101.8	103.0	98.2	99.6
SD	7.1	4.5	4.3	4.6	4.5	3.2	3.2	3.2	3.0	5.1

The range of serum chloride in 86 infants was 90.6 - 108 mmol with an overall a means of 101.2 mmol/L.

79 (92%) of the infants had a chloride level between 95 - 106. The lowest means were observed in infants on combined feeding (98.2 mmol/L) and the highest means (105 mmol/L) in breast fed infants.

There were no significant differences in serum chloride levels among the different feeding patterns. $P = 0.01$

Table X: Study Values compared to Reference Ranges in Nelson Textbook of Pediatrics and Kenyatta National Hospital reference range,

Study Variable mmol/L	Number	Study Values mmol/L			Reference Range mmol/L	Normal Values K.N.H. mmol/L
		Range	Mean	SD		
Sodium	100	130-145	136.0	3.3	135-146	135 - 145
Potassium	100	3.9-5.9	5.0	0.4	4.1-5.5	3.5-5.0
Calcium	57	2.0-2.5	2.2	0.5	2.2-2.75	2.13-2.63
Urea (BUN)	100	1.3-9.0	4.7	8.2	2.5-6.8	1.3-3.3
Chloride	86	90.6-108	101.2	4.1	98-106	95 - 105

The sodium reference range (135 - 146 mmol/L) is higher than that in the study. (130 - 145 mmol/L). 94% of the infants had serum sodium levels between 130 - 140 mmol/L, while 79 (92%) of the infants had serum chloride between 95 - 106 mmol/L. The study chloride range was 90-108 mmol/L with a mean of 101.2 mmol/L. The potassium study values (3.9 - 5.9 mmol/L) are similar to potassium reference values (4.1 - 5.5 mmol/L) but higher than the normal values for KNH (3.5 - 5.0 mmol/L). Similarly BUN study values were higher than the reference values (2.5 - 6.8 mmol/L). The upper most BUN value (9.0 mmol/L) is much higher than the normal range of values. The serum calcium mean was 2.2 mmol/L. No marked differences were noted between the study values (2.0 - 2.5 mmol/L) and the reference values (2.2 - 2.75 mmol/L).

Table XI: Calculated Serum Osmolarity in Infants on different Feeding Patterns,

	Breast fed				Formula fed			Combined		
Age in Weeks	2	4	8	12	4	8	12	4	8	12
Number	11	12	9	8	8	11	11	8	11	11
Mean Sodium mmol/L	137.2	137.0	135.7	137.0	135.0	136.6	137.2	136.8	139	135
Mean Potassium mmol/L	4.9	4.8	5.3	4.8	5.2	4.8	4.9	5.3	4.7	5.2
Mean Blood Sugar mmol/L	3.6	3.8	3.6	3.6	3.9	4.3	3.9	4.4	3.9	3.9
Mean BUN mmol/L	2.6	3.0	2.7	3.4	4.9	7.4	7.0	4.9	5.8	3.5
Mean Osmolarity osm/kg	290.3	290.5	288.5	292.1	290.0	294	294.7	293.0	297.1	287
SD	3.5	4.8	3.4	3.4	7.0	3.7	6.9	7.8	3.2	5.4

There is slightly higher osmolarity values on formula fed infants. There was no significant difference within the age groups or among the different feeding patterns. P = 0.01.

DISCUSSION

The retention of the major electrolytes from the milk feeds is only sufficient to maintain growth and homeostasis and the rest are excreted (25). All milk formula contain a higher concentration of the major electrolytes than human milk (table IV). At the present time mothers are being advised and encouraged to breast feed their babies. 70% of all the infants were on breast milk (40% on breast milk only and 30% on combined feeding). At two weeks all babies were on breast milk but at one month some had been started on formula (table II). No mother had been advised on medical grounds not to breast feed. This suggests that early introduction of artificial milk feeds is still common (26). The two main reasons given for not breast feeding were; the baby had refused to breast feed or the mother felt that she did not have an adequate milk supply. 85% of the infants on formula were on Lactogen and Nan, which are less costly than SMA-26.

The absorption of sodium, potassium and chloride is not affected by other dietary components (29). The serum sodium range in this study was 130 - 145 mmol/L with a mean of 136.0 mmol/L (Table X). This is quite low when compared to the adult values (28). The poor renal tubular concentrating ability in early infancy could cause low levels as the different feeding patterns did not affect the serum levels significantly. (table V). About 26% of the intake of sodium, chloride or potassium is excreted in the stools (4). The mean serum sodium concentration was highest in the infants on combined feeding. The 11 infants aged two months had a mean of 139 mmol/L. Five formula fed infants, aged 2 months had serum sodium levels of 140 mmol/L. To keep within the normal ranges of the major electrolytes the formula fed infants must excrete more of these electrolytes. Significant amounts of sodium,

Chloride and potassium are lost through the skin and through the gut during diarrhoea. High intakes of these mineral result in high skin losses than do lower intakes (27). Formula fed infants excrete more of the electrolytes than do breast fed infants to keep within the normal ranges. Thus disturbance of the excretory mechanism in formula fed infants as in dehydration due to gastroenteritis may easily result in hypernatraemia (30).

The range of serum chloride in 86 infants was 90.6 - 108mmol/L with a mean of 101.2 mmol/L. (table IX) 79 (92%) of the infants had a serum chloride level range of 95-106 mmol/L. The feeding pattern did not affect the serum chloride levels significantly. Chloride is an important ion in maintaining electrical neutrality in acid base disturbances. It tends to rise if bicarbonate is reduced as in metabolic acidosis. Hypochloraemia occurs if there is hyponatraemia due to immature kidney functioning as occurs in early infancy. A balance of these two opposing factors may possibly explain why there is no change in chloride levels in early infancy.

Like sodium the different dietary patterns did not affect the serum potassium significantly. The potassium range 3.9 - 5.9 mmol/L with mean of 5.0 mmol/L is higher than that for adults (table X). The reduced renal functions in the first three months of life may affect the potassium and acid excretion. This may be one cause of the higher potassium levels observed in early infancy. There is more acid production in formula and as acidosis makes potassium shift out of cells into serum one would have expected higher levels in formula fed infants. The study values were very comparable to the standard reference value

Unlike the other major electrolytes calcium absorption

depends in part to the presence of accompanying salts. The presence of excessive phytates, phosphates and oxalates in the diet decreases the calcium absorption as they form insoluble complexes with calcium. Serum proteins were not measured in this study. The serum calcium values measured included protein - bound calcium, calcium complexed to organic molecules and free ionized calcium. Without serum proteins values it was not possible to measure ionized calcium. However in the present study there was no significant difference in the calcium values within the three feeding patterns. The calcium means 2.2 mmol/L and range 2.0-2.5 mmol/L is similar to that of the standard reference values (table VII). Calcium excretion is almost entirely through the large intestine and only 10% of the intake appears in the urine (31) It has been shown that the amount of calcium excreted in urine by infants on breast milk and cows milk does not vary greatly but the amount which appears in the faeces varies greatly depending on the diet and the body needs (4).

In this study the notable findings were in the blood urea nitrogen. The higher end of the range of BUN 1.3 - 9.0 mmol/L was higher than expected. The mean BUN was 4.7mmol/L (table X). There were statistically significant differences among the three feeding patterns against BUN. The formula fed infants have a greater protein intake than those who are breast fed (see graph pg 22) However at three months infants on combined feeding

are possibly getting diluted milk feeds. The high BUN values suggest that protein intake in many infants at one and two months is still excessive and overloads the kidneys functional capacity (8). The finding of such levels in clinical practice must be interpreted with caution.

Human milk contains water and osmolar loads which enables the infant to survive under varying conditions. The calculated osmolarity values were slightly high in formula fed infants although not significant. These infants had higher potassium, sodium and BUN than breast fed infants (table VII VI VII).

The high BUN appears to cause no ill health in normal babies. Babies on formula have an increased incidence of napkin rash (33). The association of high BUN and infections is not known. Its not also known how the high BUN affects the distribution of water and solutes in dehydration states. One does not always get hypertonic dehydration from elevated BUN, but hypertonic feeds predispose to hypernatraemic dehydration in small babies when they get diarrhoea. This means that protein intake should be a greater cause of concern in our local setting.

CONCLUSION

The study has shown that diet is an important component to consider in infants when interpreting the BUN, major electrolytes and serum osmolarity in clinical practice

- (i) Serum sodium levels in infants are lower than those observed in older children and adults.
- (ii) Serum potassium levels in infants are higher than those observed in older children and adults.
- (iii) Formula fed infants have higher serum sodium and potassium than breast fed infants.
- (iv) The present protein content in formula is higher.
- (v) Formula fed infants have higher osmolarity values than breast fed infants.

RECOMMEDATIONS

Further necessary studies are

- (i) Direct measurement of serum osmolarity in infants with different feeding patterns.
- (ii) A study to find whether there is any association of high BUN and infections.
- (iii) Measure total serum proteins and calculate ionized calcium levels.
- (iv) Measure stool electrolytes and correlate with feeds.
- (v) Measure blood pH and correlate with protein content of feeds.
- (vi) Quantify content of feeds further.

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