PREVALENCE OF HYPONATREMIA IN CHILDREN ADMITTED AT KENYATTA NATIONAL HOSPITAL WITH PNEUMONIA

BY

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A Dissertation submitted in Partial Fulfillment of the requirements for the Masters Degree in Paediatrics and Child Health, University of Nairobi.

Declaration

This dissertation is my original work and has not been presented for the award of a degree in any other university.

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DEDICATION

This dissertation is dedicated to my husband, Peter Wang'ondu for his unwavering support and encouragement and to our three lovely children, Miley, Mitchell and Mikeray.

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ABBREVIATIONS

KNH Kenyatta National Hospital

PEU paediatric emergency unit

ICU intensive care unit

WHO World Health Organization

SIADH syndrome of inappropriate secretion of antidiuretic hormone

ADH Antidiuretic hormone

AVP arginine vasopressin

Na Sodium

K potassium

GLU glucose

BUN blood urea nitrogen

Kgs kilograms

ABSTRACT

Background

Pneumonia remains the leading single cause of childhood mortality. It's associated with several complications the commonest being hyponatremia. Studies done in the western countries have reported a high prevalence of hyponatremia, an indicator also of disease severity No study has been done to evaluate the prevalence of hyponatremia in children admitted at the Kenyatta National Hospital.

Objectives

The objectives of this study were; to determine the prevalence of hyponatremia in children admitted with pneumonia at KNH and to describe the socio-demographic and clinical characteristics of children found to have hyponatremia.

Methodology

A descriptive cross-sectional study was carried out at KNH on children aged 2months to 12years admitted with pneumonia. Those who met the inclusion criteria were recruited. History and physical examination was done to confirm diagnosis and classify the severity of pneumonia. A 2ml blood sample was then withdrawn from the patient and taken to the laboratory for electrolyte analysis.

Results

A total of 135 pediatric patients admitted at KNH were reviewed. Prevalence of hyponatremia was 71.9 %(97/135). Most patient had severe hyponatremia 40.6 %(39/97). Hyponatremia was significantly associated with high temperatures (39.0^0c-41.1^0c), (OR=6.60 [95%CI: 1.62-26.92]; p=0.009. There was a significant association between having very severe pneumonia and hyponatremia (OR=3.45 [95%CI: 1.56-7.69]; p=0.002. A high proportion of children having very severe pneumonia also had hyponatremia (83.8%) compared to those with severe pneumonia (59.7%). Having hypokalemia was significantly associated with hyponatremia (OR=4.08 [95%CI: 1.44-11.57]; p=0.008. A high proportion of children with hypokalemia had hyponatremia (87.2%) compared to those with normal potassium level (62.5%).

Conclusion

There is a high prevalence of hyponatremia in children admitted with pneumonia at KNH. Hyponatremia is an indicator of severe illness and use of hypotonic intravenous solutions is associated with development of hyponatremia .

RecommendationsAll patients admitted with pneumonia should have electrolyte levels analyzed and appropriate management instituted. Caution should be exercised when giving intravenous fluids to children with pneumonia.

1. BACKGROUND AND LITERATURE REVIEW

1.1 Background

Pneumonia remains the leading single cause of childhood mortality. Its accounts for 19 %(2million) of all under five deaths. This however does not include deaths due to pneumonia during the neonatal period; if this were included the overall estimate will rise to 29 % (1). Pneumonia affects children and families everywhere, but is most prevalent in South Asia and sub-Saharan Africa where its account for 85% of deaths. In Kenya alone > 20000 children die each year from pneumonia and 5,000 are debilitated by it.

Despite the various strategies put in place to curb this disease (vaccination, vitamin A and zinc supplementation, exclusive breastfeeding for six months, early detection and treatment e.t.c), prevention and treatment remains a challenge. Most children with pneumonia can be treated safely at home. However studies done have shown that only 27% of these children actually get the appropriate treatment (1). Failure to institute timely treatment results in progression of the disease necessitating hospitalization. Children admitted with pneumonia are critically ill and often times have complications which include electrolyte abnormalities, the commonest being hyponatremia. Studies done in the western countries have shown up to 45.4% of children hospitalized with pneumonia had hyponatremia (2-4).

Hyponatremia in pneumonia has been linked to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) (5). ADH excess results in water retention and volume expansion leading to fall in Serum osmolality below the reference range. Hyponatremia does not develop unless the patient is ingesting or receiving some source of free water. Most children with pneumonia cannot maintain adequate fluid intake due to breathlessness, fatigue, or risk of aspiration (6) necessitating fluid therapy. Administration of hypotonic fluids may lead to development of acute hyponatremia which leads to a rapid shift of fluids into brain cells (16, 20). The resultant cerebral edema is associated with high mortality. Hyponatremia has also been documented as a marker of severe illness and increases mortality (7,8).

It's therefore paramount for clinicians to understand common electrolyte abnormalities, have a high index of suspicion and timely recognize them. This will facilitate institution of appropriate treatment resulting in better outcomes.

1.2 LITERATURE REVIEW

Hyponatremia is defined as serum sodium (Na) concentration of less than 135mEq/L (9-10). Serum sodium concentration and serum osmolarity normally are maintained under precise control by homeostatic mechanisms involving stimulation of thirst, secretion of antidiuretic hormone (ADH), and renal handling of filtered sodium (10).

Serum Na plays a significant role in serum osmolality and tonicity (serum osmolarity = 2Na + Glu/18 + BUN/2.8). Changes in serum osmolality are responsible for the signs and symptoms of hyponatremia and also the complications that happen during treatment in the presence of high-risk factors. Whereas hypernatremia always denotes hypertonicity, hyponatremia can be associated with low, normal, or high tonicity. Hyponatremia is the most common electrolyte disorder encountered in hospitalized patients (11)

Clinical presentation of hyponatremia is uncommon and happens as a result of a rapid fall in serum Na and also the absolute level of serum Na. Clinical symptoms are nonspecific; therefore, the paediatrician must consider the diagnosis in patients presenting with vague constitutional symptoms or with altered level of consciousness. Fifty percent of children develop symptoms when serum Na levels fall below 125 mEq/L, a relatively high level when compared with adults(12,13,14) Although morbidity widely varies, serious complications can arise from hyponatremia and can also happen during treatment. Understanding the pathophysiology and treatment options for hyponatremia is important because significant morbidity and mortality are possible.

1.2.1 PATHOPHYSIOLOGY

Hyponatremia can develop because of (1) excessive free water, a common cause in hospitalized patients receiving hypotonic solutions; (2) excessive renal or extrarenal losses of Na or renal retention of free water; (3) rarely, deficient intake of Na.

Under normal circumstances, the human body is able to maintain serum Na in the normal range (135-145 mEq/L) despite wide fluctuations in fluid intake. The body's defense against developing hyponatremia is the kidney's ability to generate dilute urine and excrete free water in response to changes in serum osmolarity and intravascular volume status (14).

Serum sodium concentration is regulated by stimulation of thirst, secretion of ADH, feedback mechanisms of the renin-angiotensin-aldosterone system, and variations in renal handling of filtered sodium. Increases in serum osmolarity above the normal range (280-300 mOsm/kg) stimulate hypothalamic osmoreceptors which in turn cause an increase in thirst and in circulating levels of ADH. ADH increases free water reabsorption from the urine, yielding urine of low volume and relatively high osmolarity and, as a result, returning serum osmolarity to normal. ADH is also secreted in response to hypovolemia, pain, fear, nausea, and hypoxia (5, 11).

Aldosterone, synthesized by the adrenal cortex, is regulated primarily by serum potassium but also is released in response to hypovolemia through the renin-angiotensin-aldosterone axis. Aldosterone causes absorption of sodium at the distal renal tubule. Sodium retention obligates free water retention, helping to correct the hypovolemic state. The healthy kidney regulates sodium balance independently of ADH or aldosterone by varying the degree of sodium absorption at the distal tubule. Hypovolemic states, such as hemorrhage or dehydration, prompt increases in sodium absorption in the proximal tubule. Increases in vascular volume suppress tubular sodium reabsorption, resulting in natriuresis and helping to restore normal vascular volume

Hyponatremia is physiologically significant when it indicates a state of extracellular hyposmolarity and a tendency for free water to shift from the vascular space to the intracellular space. Although cellular edema is well tolerated by most tissues, it is not well tolerated within the rigid confines of the bony calvarium (14, 16). Therefore, clinical manifestations of hyponatremia are related primarily to cerebral edema. The rate of development of hyponatremia plays a critical role in its pathophysiology and subsequent treatment (13, 15). When serum sodium concentration falls slowly, over a period of several days or weeks, the brain is capable of compensating by extrusion of solutes and fluid to the extracellular space. Compensatory extrusion of solutes reduces the flow of free water into the intracellular space, and symptoms are much milder for a given degree of hyponatremia.

When serum sodium concentration falls rapidly, over a period of 24-48 hours, this compensatory mechanism is overwhelmed and severe cerebral edema may ensue, resulting in brainstem herniation and death (17-18)

1.2.2 TYPES OF HYPONATREMIA

The etiology of hyponatremia can be categorized pathophysiologically in three primary ways, based on the patient's plasma osmolality

(a) Hypertonic hyponatremia- caused by resorption of water drawn by osmoles such as glucose (hyperglycemia or diabetes) or mannitol (hypertonic infusion).

(b) Isotonic hyponatremia- more commonly called "psuedohyponatremia," is caused by lab error due to hypertriglyceridemia (most common) or hyperparaproteinemia.

(c) Hypotonic hyponatremia- is by far the most common type, and is often used interchangeably with "hyponatremia." Hypotonic hyponatremia is categorized in 3 ways based on the patient's blood volume status. Each category represents a different underlying reason for the increase in ADH that led to the water retention and thence hyponatremia

(c1) hypervolemic hyponatremia- wherein there is decreased effective circulating volume even though total body volume is increased (by the presence of edema). The decreased effective circulating volume stimulates the release of ADH, which in turn leads to water retention. Hypervolemic hyponatremia is most commonly the result of congestive heart failure, liver failure (cirrhosis), or kidney disease (nephrotic syndrome).

(c2) Euvolemic hyponatremia- wherein the increase in ADH is secondary to either physiologic but excessive ADH release (as occurs with nausea or severe pain) or is due to inappropriate and non-physiologic secretion of ADH, i.e. syndrome of inappropriate antidiuretic hormone hypersecretion (SIADH), hypothyroidism, adrenal insufficiency or extreme psychogenic polydypsia.

(c3) Hypovolemic hyponatremia - wherein ADH secretion is stimulated by volume depletion.

Table 1: Overall classification of hyponatremia

Hypertonic hyponatremia (i.e., factitious hyponatremia
Isotonic hyponatremia (i.e., pseudohyponatremia)
Hypotonic hyponatremia (ie,"true" hyponatremia
Hypervolemic hypotonic hyponatremia
Euvolemic hypotonic hyponatremia
Hypovolemic hypotonic hyponatremia

NOTE; Classification is based on plasma osmolality and volume status

1.2.3 PREVALENCE OF HYPONATREMIA

The prevalence of hyponatremia has been studied in various patient populations in developed countries and found to occur in 1%-45% of patients with pneumonia.

In India, a study done by S.D.Subba Rao et.al in children admitted in pediatric intensive care unit, found the prevalence of hyponatremia to be 29.8% (2). It was more frequent in summer (36%) than in winter (24%). In another study hyponatremia was found in 27% (3) of children with pneumonia. It was associated with 60% longer hospital stay, two fold increase in complications and 3.5 times higher mortality. Variables were affected further if hypokalemia co-existed with hyponatremia.

In Japan, a study done by Kaneko et al found the prevalence of hyponatremia in children with pneumonia to be 38.7%. This was higher as compared to a prevalence rate of 13.3% found in children who had pharyngitis or laryngitis. The conclusion from this study was that, the deeper the site of inflammation in the respiratory tract, the higher the prevalence of hyponatremia(7).

In Italy, a study done to determine the incidence and the risk factors for hyponatremia in children with community acquired pneumonia found out that the commonest pathogens were mycoplasma

pneumonia, viruses and streptococcus pneumonia in descending order. Hyponatremia was present in 45.4% of patients. The children with hyponatremia had significantly higher mean white blood cell counts, neutrophil proportion, C-reactive protein, procalcitonin levels, and initial temperature. The mean sodium concentration was almost identical in the children with pneumococcal, atypical, and viral pneumonia(8).

Table 2: Summary of prevalence rates of hyponatremia in pneumonia

Study	Site/yr	Sample size	Prevalence of hyponatremia
Frequency and significance of electrolyte abnormalities in pneumonia	India-1987-1989	264	25%-68% secondary to SIADH
Hyponatremia in pediatric community acquired pneumonia (CAP)	Italy-2008	108	45.4%
Hyponatremia in children with respiratory tract infections (pharyngitis, bronchiolitis, pneumonia	Japan-2009	138	38.9%

2. STUDY JUSTIFICATION

Hyponatremia has clearly been shown to be a common electrolyte abnormality in pneumonia. It has also been shown that severe hyponatremia is a marker of severe illness and is associated with high morbidity and mortality.

There is a knowledge gap of this condition in our set-up and therefore this study will act as a baseline for other studies in this topic. Describing the burden of this problem will aid in providing useful data that can generate other entry points into studying this condition.

It will also help in raising clinician's index of suspicion in identifying electrolyte abnormalities and more so hyponatremia in patients with pneumonia hence instituting appropriate management resulting in better outcome of the patient.

SIADH has been postulated to be the cause of hyponatremia in pneumonia patients. Management of this condition requires fluid restriction. Most of our patients are not able to take adequately orally and end up being on maintenance intravenous fluids. By doing this study it will open more avenues in studying the appropriate fluids for these patients. Furthermore administration of hypotonic fluids has been associated with hospital acquired hyponatremia which has a poor outcome.

3. RESEARCH QUESTION

What is the prevalence of hyponatremia in children aged two months to twelve years admitted with pneumonia at KNH?

4. OBJECTIVES

Primary objective

To determine the prevalence of hyponatremia in children admitted with pneumonia at KNH.

Secondary objective

1. To describe selected socio-demographic and clinical characteristics of children with hyponatremia.

2. To determine the association of hyponatremia and severity of pneumonia.

5. METHODOLOGY

5.1 STUDY DESIGN

This was a descriptive cross-sectional study

5.2 STUDY SITE

The study was carried out at Kenyatta National Unit (KNH), paediatric emergency unit(PEU) and paediatric wards. PEU is where all the sick children are first seen before admission and those who do not require admission are allowed home on treatment. On average 30 patients are admitted everyday a quarter of which have a diagnosis of pneumonia. This number varies depending on the season rising during the cold season.

On arrival patient are triaged into emergency, priority and those who can queue. The emergency patients are seen by a doctor, stabilized then transferred to the wards to continue treatment. Those in need of mechanical ventilation are admitted in ICU. Patients who are relatively stable are seen by clinical officers.

There are four paediatric wards each with a bed capacity of 70 but admits on average 180-200 children per month. Bed occupancy usually exceeds 100 percent. A quarter of in-patient in each ward are children with pneumonia.

Initial withdraw of blood samples for various investigations is done in PEU. Once admitted subsequent investigations are done from the ward. PEU and paediatric wards are in close proximity with the paediatric department laboratory which runs several tests including electrolytes, urea etc. Results are released to the patients within 20-30 minutes which aids in making a diagnosis. The laboratory is run by qualified laboratory technicians ensuring quality results.

5.3 STUDY POPULATION

Children aged two months to twelve years admitted at KNH with a diagnosis of pneumonia.

5.4 SAMPLE SIZE ESTIMATION

Sample size was calculated using the Fischer's formula

$$N=\frac{Z^2*P(1-P)}{D^2}$$

N the desired sample size

Z the value representing 95% confidence interval

D the precision with which to measure prevalence of the study ±7.5%

P the estimated prevalence (based on a study done in India which is a developing country like Kenya in which the prevalence of hyponatremia was 27%).

Substituting the above formula the sample size for this study was set at 135 patients.

5.5 SAMPLING PROCEDURE

The principal investigator had undergone training on WHO classification of pneumonia in children during a two week course on Emergency Triage And Treatment$^+$ (ETAT$^+$). Patients were identified by the principal investigator at the PEU and the wards during the day, complete history and physical examination was then done to confirm diagnosis. If a child met the inclusion criteria, informed consent was sought from the guardian or the parent after explaining to him or her about the study.

Socio-demographic data and clinical characteristics of each patient were captured in the questionnaire (Appendix i). Clinical characteristics included axillary temperature and respiratory rate were also taken. Patients were then categorized into either having severe or very severe pneumonia based on the WHO classification (Appendix ii).

Using aseptic technique, 2mls of blood was withdrawn from the antecubital fossa of each patient and put in a vaccutainer. The blood samples were then transported to the paediatric department laboratory within an hour of collection for analysis.

5.6 INCLUSION CRITERIA

- Children 2 months to 12 years admitted at KNH with a diagnosis of pneumonia.
- All children for whom consent is obtained from parent(s) or legal guardian(s) to participate in the study.

5.7 EXCLUSION CRITERIA

- All children with signs and symptoms of diarrhea and dehydration. Diarrhea is associated with electrolyte abnormalities.
- All children with known renal disease. Patients with renal disease have fluid retention which results in dilutional hyponatremia.
- All children with a known cardiac disease which results in volume overload leading to dilutional hyponatremia.
- All children whose parent(s) or guardian(s) refuses to give consent.

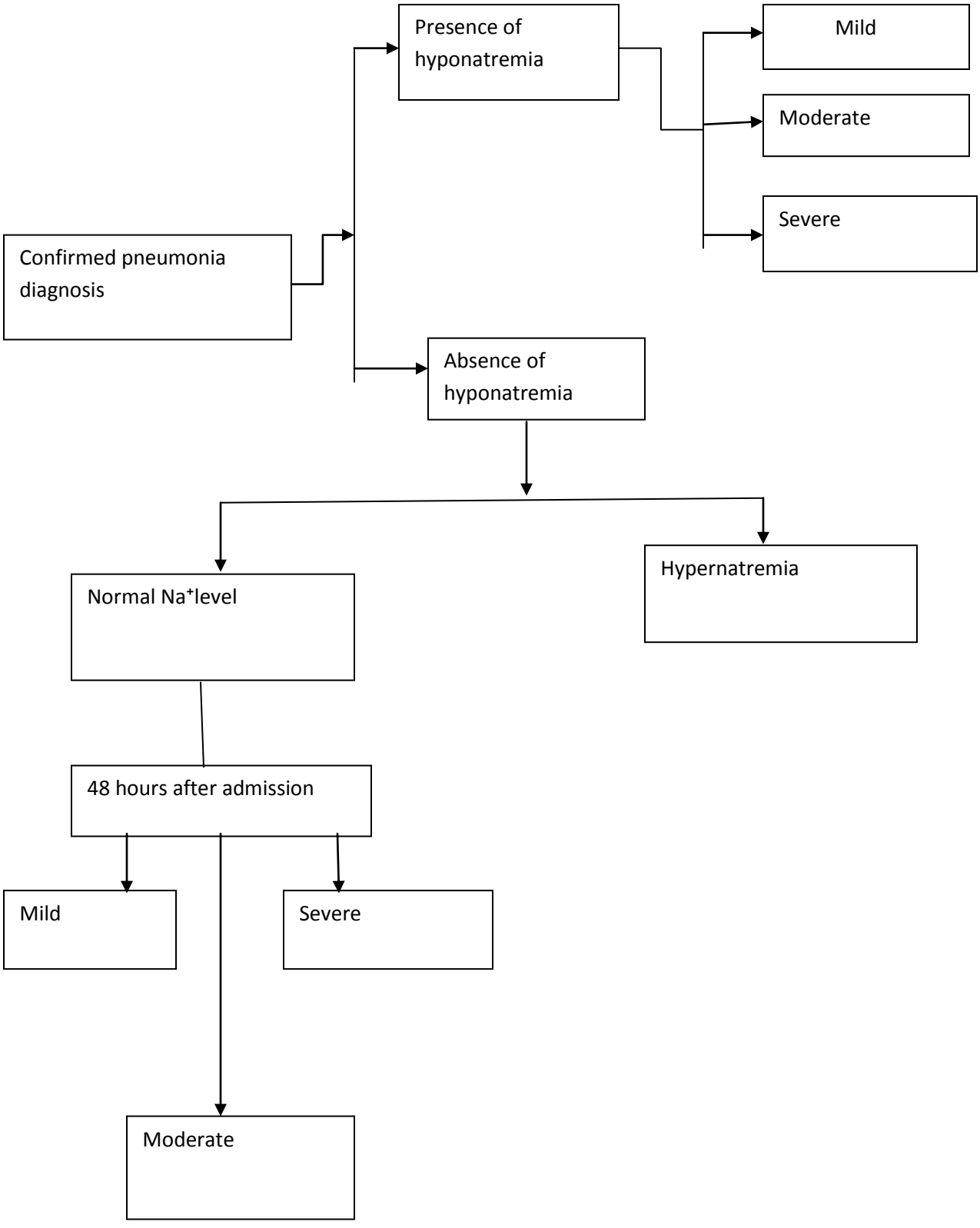
5.8 CASE DEFINATIONS

Hyponatremia was defined as a sodium level of <135mmol/l. The overall prevalence of hyponatremia was calculated as a proportion of all children with hyponatremia to the total number of all children recruited for the study.

Children with hyponatremia were further classified into either having mild, moderate or severe hyponatremia. Mild hyponatremia was defined as sodium levels of 130-134mmol/l, moderate as 125-129mmol/l and severe as sodium levels of <125mmol/l.

Children who had normal sodium levels on admission were followed up over 48hours during which their fluid intake both orally and intravenously were recorded. For those who received intravenous fluid, the type of fluid and amount was also documented. A repeat blood sample was taken 48 hours after admission to determine the proportion that developed hyponatremia in the ward.

FIGURE 1: Flow chart showing the process of defining hyponatremia



5.9 Data management and analysis

5.9.1 Data management

Data from the field was coded and double entered into a computer database designed using MS-Access application. Data cleaning and validation was performed to achieve a clean dataset that was then exported into a Statistical Package format (SPSS). A clean dataset was stored in a computer hard drive disk ready for analysis. Back up files were stored in a flash disc and a CD, this was done regularly to avoid any loss or tampering. All the questionnaires were stored in a lockable drawer for confidentiality.

5.9.2 Data analysis

Data analysis was conducted using SPSS statistical software. Exploratory data techniques were used at the initial stage of analysis to uncover the structure of data and identify outlier or unusual entered values.

Univariate analysis was done where descriptive statistics such as proportions were used to summarize categorical variables and measures of central tendency for continuous variables.

For Bivariate analysis, Pearson's Chi-square test or fisher exact test was used to test for the strength of association between categorical variables. All exposure variables (Independent factors) were associated with the dependent variable (hyponatremia) to determine which ones had significant association. Odds Ratio (OR) and 95% Confidence Interval (CI) were used to estimate the strength of association between independent variables and the dependent variable. The threshold for statistical significance was set at $\alpha = 0.05$ and a two-sided P- value at 95% confidence intervals (CI) reported for corresponding analysis.

Multivariate analysis was done where all independent variables identified to significantly associate with hyponatremia at bivariate analysis were considered together. This was performed using Binary logistic regression where backward conditional method was specified in order to eliminate confounders and effect modifiers. Adjusted odds Ratios (AOR) with their respective 95% Confidence Interval (CI) were used to estimate the strength of association between the retained independent variables and hyponatremia.

6 Ethical considerations

The study was conducted after receiving approval from the Research and Ethics Committee of Kenyatta National Hospital. The parent/guardian was fully explained about the study before his/her child was recruited to the study, and he/she signed the consent form to confirm approval, (Appendix I). The results of each child were handed over to the attending clinician to institute appropriate management

7 Results

7.1 Characteristics of the study population

7.1.1Selected demographic characteristics

A total of 135 pediatric patients admitted in Kenyatta National Hospital were reviewed. Data on selected demographic characteristics as well as clinical presentations were collected as presented in Table 4.1 and Table 4.2. Mean age was 1.8 $\pm$ 2.3 ranging from 0.2 to 12 years, with the majority aged less than or equal to 1 year (59.3%). Gender distribution was fairly comparable, with the proportion of males higher (54.8%) compared to females.

Table 3: Selected socio-demographic characteristics

Variables	n=135	%
Age in years		
<=1 year	80	59.3
>1 - 5 years	44	32.6
>5 years	11	8.1
Gender		
Male	74	54.8
Female	61	45.2

7.1.2 Clinical presentation

A profile of four clinical assessments was done as presented in Table 4.2. All the children (100%) suffered cough as well as difficulty in breathing.

Mean temperature was 38.8 $\pm$ 1.1 ranging between 36.3 and 41.1 ^{0}C. A majority of the children (89.6%) had raised temperatures constituted by 7.4% high grade, 28.9% moderate grade and 53.3% low grade.

Mean respiratory rate was 67.1$\pm$ 13.3 ranging between 28.0 and 96.0 rates per minute. An overwhelming majority (97.8%) had high respiratory rate.

Medical diagnosis revealed comparable proportion of children presenting with severe pneumonia (49.6%) and those presenting with very severe pneumonia (50.4%).

Table 4: Clinical presentation

Variables	n=135	%
History		
Cough and difficulty in breathing	135	100.0
Temperature		
High grade (40.1 - 41.1)	10	7.4
Moderate grade (39.1 - 40.0)	39	28.9
Low grade (37.5 - 39.0)	72	53.3
Normal (<37.5)	14	10.4
Respiratory rate		
High	132	97.8
Normal	3	2.2
Diagnosis		
Severe pneumonia	67	49.6
Very severe pneumonia	68	50.4

7.2 Prevalence of hyponatremia

Analysis of sodium revealed that mean sodium level was 129.7±9.4 ranging between 101 and 157, the highest proportion of children having hyponatremia (71.9%) while 4.4% had hypernatremia. Among 97 patients identified with hyponatremia, 40.6% had severe, 28.1% had moderate while 31.3% had mild (Figure 2).

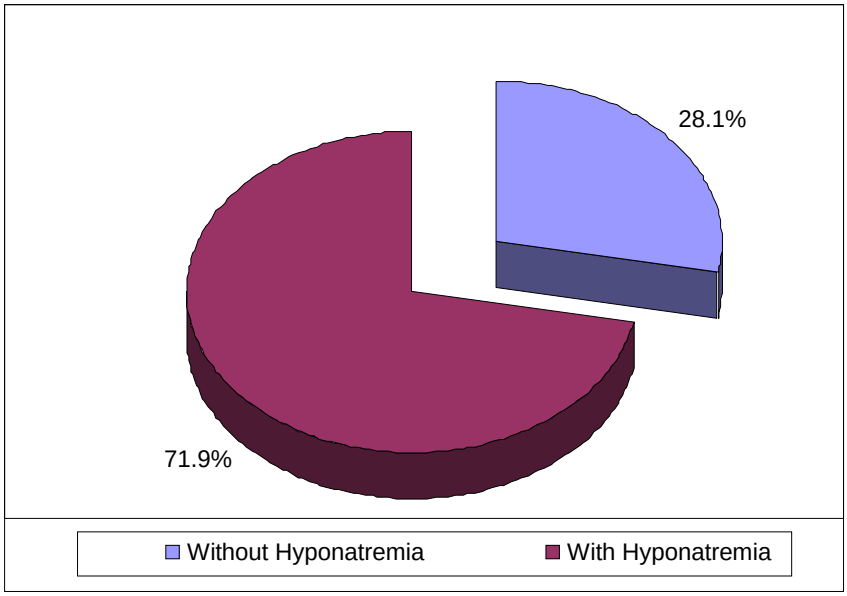


Figure 2: Distribution of children by hyponatraemia at admission

7.3 Hospital acquired hyponatremia

Thirty-two children identified with normal sodium levels at admission were followed-up and reassessed after 48 hours. Mean sodium level was 133.5±4.4 ranging between 124 and 141, out of which 50.0% were identified with hospital acquired hyponatremia; constituted by 28.8% mild hyponatremia, 18.8% moderate hyponatremia and 3.1% severe hyponatremia (Figure 3).

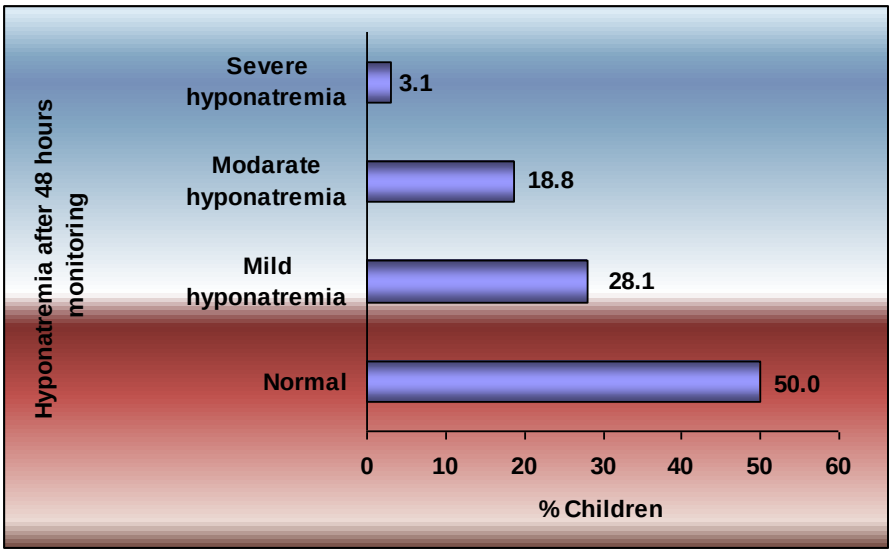


Figure 3: Distribution of children by hospital acquired hyponatraemia

Mean amount of fluid/feed given (amount/kg/day) was 100.3 ± 25.7 ranging between 50 and 150 /kg/day, the highest proportion receiving 100/kg/day (53.1%).

The most common type of fluid given was Half Strength Darrows+5%Dextrose (25.0%) and Ringers Lactate+5%Dextrose (18.8%) while 50.0% received normal feeds (Figure 4).

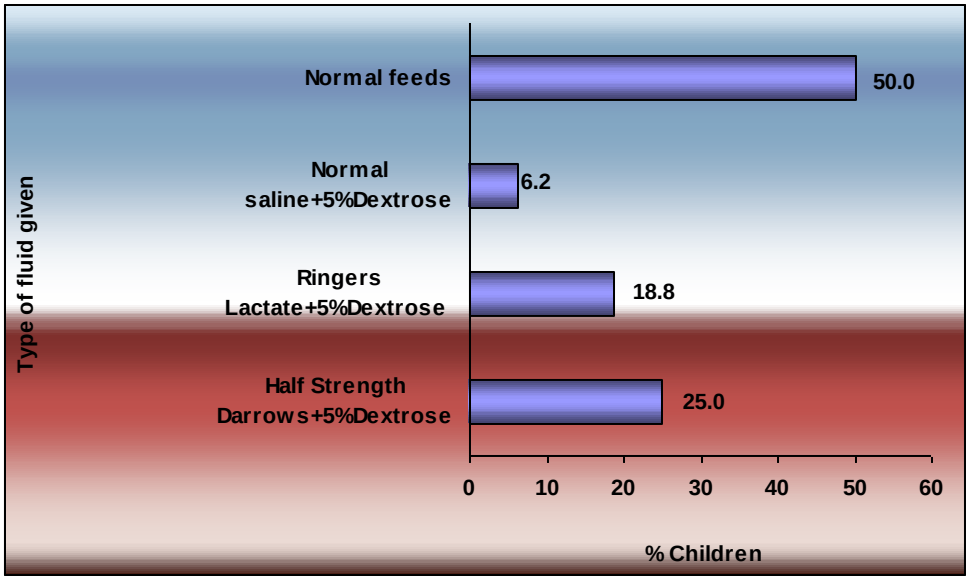


Figure 4: Distribution of children by type of fluid given

7.4 Sodium, potassium assessment

Mean potassium level was 4.1±1.0 ranging between 2.0 and 6.2, with 28.9% of children having hypokalemia while 11.9% had hyperkalemia (Figure 5).

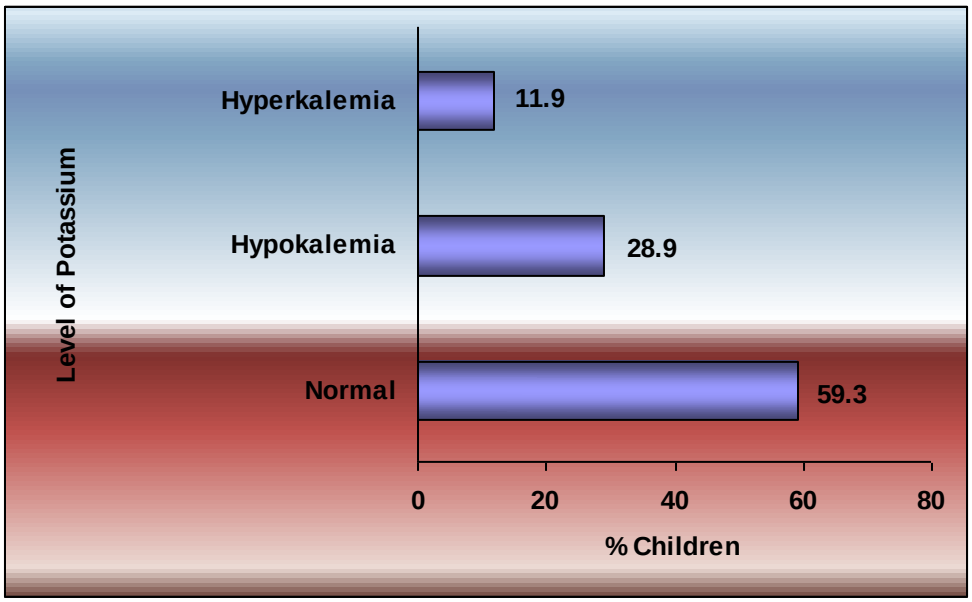


Figure 5: Distribution of children by level of Potassium

Table 5: Sodium, Potassium assessment

Variables	n=135	%
Sodium level category		
Normal	32	23.7
Hyponatremia	97	71.9
Hypernatremia	6	4.4
If hyponatremia, the level		
Mild	30	31.3
Moderate	27	28.1
Severe	39	40.6
Not applicable	39	
Sodium levels 48hours category		
Normal	16	50.0
Mild hyponatremia	9	28.1
Modarate hyponatremia	6	18.8
Severe hyponatremia	1	3.1
Not applicable	103	
Type of fluid given		
HSD+5%Dextrose	8	25.0
RL+5%Dextrose	6	18.8
Normal saline+5%Dextrose	2	6.2
Normal feeds	16	50.0
Not applicable	103	
Amount of fluid/feed given(amount/kg/day)		
>100 kg/day	7	21.9
100 kg/day	17	53.1
<100 kg/day	8	25.0
Not applicable	103	
Potassium Level		
Normal	80	59.3
Hypokalemia	39	28.9
Hyperkalemia	16	11.9

7.5 Bivariate analysis

7.5.1 Hyponatremia in relation to selected demographic and clinical characteristics

Analysis of Hyponatremia in relation to selected demographic characteristics of the children is presented in Table 5. None of the two demographic characteristics was significantly associated with hyponatremia. However, children aged more than 5 years were more likely to have hyponatremia (81.8%), followed by those aged >1 – 5 years (77.3%) and less likely among those aged <=1 year (67.5%). 0ccurence of hyponatremia was high in males (75.7%) compared to females (67.2%).

Table 6: Hyponatremia in relation to selected demographic characteristics of the children

	Hyponatremic (n=97)		Not Hyponatremic (n=38)			95% CI		p
Variables	**n**	**%**	**n**	**%**	**OR**	**Lower**	**Upper**	**value**
Age in years								
<=1 year	54	67.5	26	32.5	0.46	0.09	2.29	0.344
>1 - 5 years	34	77.3	10	22.7	0.76	0.14	4.08	0.745
>5 years	9	81.8	2	18.2	Reference			
Gender								
Male	56	75.7	18	24.3	1.52	0.71	3.22	0.277
Female	41	67.2	20	32.8	Reference			

Table 6 presents analysis of occurrence of hyponatremia in relation to the clinical presentations. Hyponatremia was significantly associated with high temperatures (39.0^0c – 41.1^0c), (OR=6.60 [95%CI: 1.62 – 26.92]; p=0.009). A high proportion of children experiencing high temperatures had hyponatremia (88.1%) compared to those with normal temperatures (57.1%). The level of hyponatremia was comparable between children experiencing moderately high temperatures (59.7%) and those having normal temperatures.

There was a significant association between having very severe pneumonia and having hyponatremia (OR=3.45 [95%CI: 1.56 – 7.69]; p=0.002). A high proportion of children having very severe pneumonia had hyponatremia (83.8%) compared to those with severe pneumonia (59.7%).

Having hypokalemia was significantly associated with hyponatremia (OR=4.08 [95%CI: 1.44 – 11.57]; p=0.008). A high proportion of children having hypokalemia had hyponatremia (87.2%) compared to those with normal potassium level (62.5%). Though not significant, occurrence of hyponatremia among children identified with hypokalemia was high (81.3%) compared to those with normal potassium level.

Table 7: Hyponatremia in relation to clinical presentations of the children

	With Hyponatremia (n=97)		**Without Hyponatremia (n=38)**			**95% CI**		**p**
Variables	**n**	**%**	**n**	**%**	**OR**	**Lower**	**Upper**	**value**
Temperature								
Moderate/high grade	44	89.8	5	10.2	6.60	1.62	26.92	**0.009**
Low grade	45	62.5	27	37.5	1.25	0.39	3.99	0.706
Normal	8	57.1	6	42.9	Reference			
Respiratory rate								
High	94	71.2	38	28.8	UD	UD	UD	0.999
Normal	3	100.0	0	0.0	Reference			
Diagnosis of pneumonia								
Severe pneumonia	40	59.7	27	40.3	Reference			
Very severe pneumonia	57	83.8	11	16.2	3.45	1.56	7.69	**0.002**
Level of Potassium								
Normal	50	62.5	30	37.5	Reference			
Hypokalemia	34	87.2	5	12.8	4.08	1.44	11.57	**0.008**
Hyperkalemia	13	81.3	3	18.8	2.60	0.68	9.87	0.161

Figure 6 presents the occurrence of hyponatremia and hypokalemia combined in relation to severity of pneumonia.

There was a strong association between having very severe pneumonia and occurrence of both hyponatremia and hypokalemia combined (OR=12.50 [95%CI: 4.00 – 33.33]; p<0.001). A high proportion of children having very severe pneumonia had both hyponatremia and hypokalemia combined (44.1%) compared to those with severe pneumonia (6.0%).

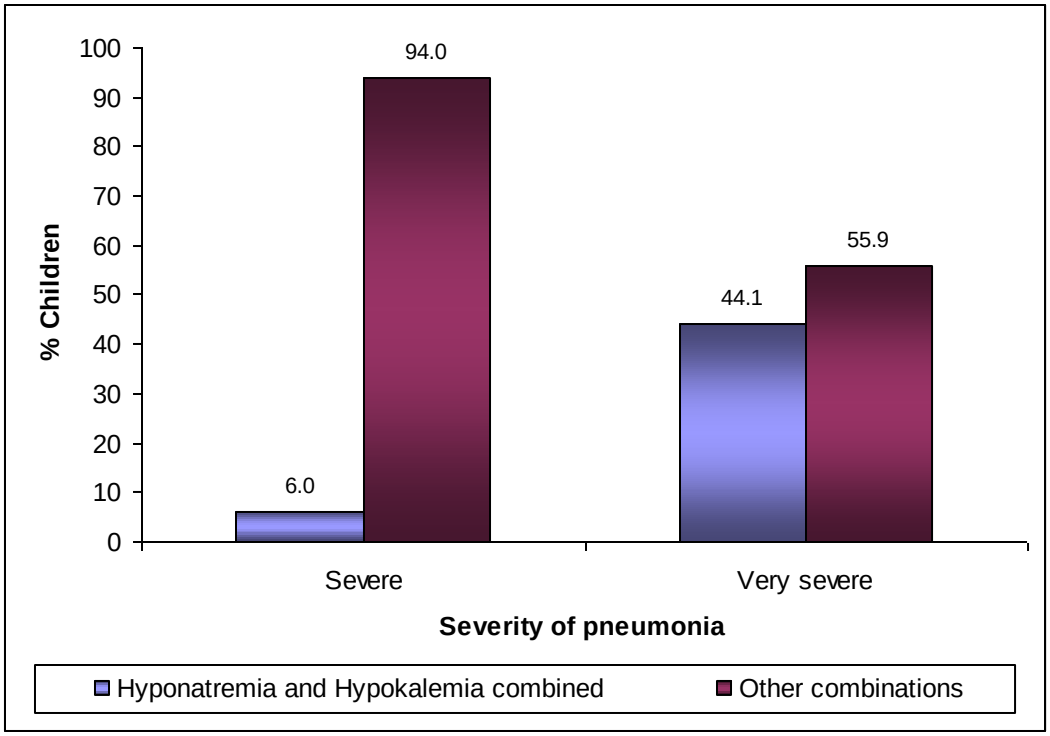


Figure 6: Occurrence of Hyponatremia and Hypokalemia combined in relation to severity of pneumonia

Table 8: presents hospital acquired Hyponatremia in relation to type of fluid and amount administered to the children.

There was a strong association between use of IV fluids and occurrence hyponatremia 48 hours after admission (OR=18.78 [95%CI: 3.18 – 110.84]; p<0.001). A high proportion of children using IV fluids had hospital acquired hyponatremia (81.3%) compared to those that used normal feeds (18.8%).

There was a no significant association between amount of fluid/feed given and occurrence of hyponatremia 48 hours after admission (OR=9.00 [95%CI: 0.94 – 86.52]; p=0.083). However, a high proportion of children using more than 100mls/ kg/day had hospital acquired hyponatremia (85.7%) compared to those that using <=100 kg/day (40.0%).

Table 8: Hospital acquired hyponatremia in relation to type of fluid and amount administered to the children

	With Hyponatremia (n=16)		**Without Hyponatremia(n=16)**			**95% CI**		**p**
Variables	**n**	**%**	**n**	**%**	**OR**	**Lower**	**Upper**	**value**
Type of fluid given								
IV fluid	13	81.3	3	18.8	18.78	3.18	110.84	**<0.001**
Normal feeds	3	18.8	13	81.3	Reference			
Amount of fluid/feed given(amount/kg/day)								
>100	6	85.7	1	14.3	9.00	0.94	86.52	0.083
<=100	10	40.0	15	60.0	Reference			

7.6 Multivariable analysis

Multivariable analysis was performed in order to determine predictors of hyponatremia among the participating children. Three factors associated with hyponatremia at P<0.05 during bivariate analysis were considered for multivariable analysis. They included; (1) Temperature (2) Diagnosis of pneumonia and (3) Level of Potassium. Upon fitting the factors using Binary logistic regression with removal at p<0.1 the final output model is as shown in Table 8.

Adjusting for Level of Potassium, occurrence of very severe pneumonia was significantly associated with hyponatremia (AOR=2.70; 95% CI: 1.15 – 6.25; p=0.022). A child identified with very severe pneumonia was 2.70 times more likely to have hyponatremia compared to one with abnormal levels of Potassium.

Table 9: Predictor of Hyponatremia

		95% CI		
Variables	**AOR**	**Lower**	**Upper**	**p value**
Diagnosis				
Severe pneumonia	Reference			
Very severe pneumonia	2.70	1.15	6.25	**0.022**
Potassium Level category				
Normal	Reference			
Hypokalemia	2.77	0.92	8.33	0.070
Hyperkalemia	2.55	0.66	9.91	0.177

8 DISCUSSION

Hyponatremia has been shown to be the commonest electrolyte abnormality in hospitalized patients. Its complicates many conditions including respiratory, central nervous system, malignancies e.t.c and it's a marker of severe illness resulting in high mortality and morbidity(18,19,21,31).

The goal of this study was to provide a baseline data on prevalence of hyponatremia since no similar study has been done in our set-up.

The overall prevalence of hyponatremia was 71.9%. This rate was 1.5 times higher than that reported in similar studies elsewhere. In Indian a developing country from which this study is linked, the prevalence of hyponatremia was 27% which is 2.5 times lower than that found in the current study(2). These findings could be attributed to the fact that hyponatremia was defined as sodium level of <130mmol/l in the study done in Indian compared to a level of <135mmol/l in this study. Moreover KNH being a referral centre receives critically ill children who already have complications.

Children with very severe pneumonia were more likely to have hyponatremia a proportion of 81.8% compared to those with severe pneumonia (59.7%). A significant association between very severe pneumonia and hyponatremia (p=0.002) was observed. Children with hyponatremia also had very high temperatures (39.1-41.1) p=0.09. It's been postulated that hyponatremia in pneumonia is related to syndrome of inappropriate secretion of ADH which results in retention of fluid despite normal plasma osmolarity(5,23,26). ADH secretion increases in proportion with the extent of lung parenchymal involvement. Hence the significant association of very severe pneumonia with hyponatremia. In addition, severe infections are associated with release of inflammatory cells e.g. interleukin 6 which stimulates ADH production. Inflammatory markers also stimulate thermoregulatory centre resulting in reset of the thermostat hence the high temperatures(31,32,33). Moreover, fever stimulates non-osmotic release of ADH. These observations compares to a study done by Don M Valerio et.al that found hyponatremia to be associated with significantly higher mean white blood cell count, neutrophils,c-reactive protein and initial temperature in children with pneumonia(8).

Studies have also demonstrated that, respiratory compromise is a cormorbid factor in patients with hyponatremia markedly increasing the risk of death from pneumonia(35-37). The underlying mechanism is probably hypoxia, a major risk factor for the development of hyponatremic encephalopathy(38). Studies of hyponatremic animals have revealed that hypoxia impairs volume regulation of brain cells, decreases cerebral perfusion, and increases the probability of neuronal lesions developing (39). Adaptation of the brain to hyponatremia largely depends on extrusion of sodium from the intracellular space via sodium–potassium ATPase pumps. This energy-dependent process is impaired under hypoxic conditions. The combination of systemic hypoxia and hyponatremia is more deleterious than is either condition alone, because hypoxia impairs the ability of the brain to adapt to hyponatremia, worsening hyponatremic encephalopathy (40).

Although the study was not powered for analysis of hospital acquired hyponatremia due to the low numbers of children who had normal sodium levels on admission, half of those who had normonatremia on admission developed hyponatremia. It was also observed that children who received intravenous fluids were more likely to develop hyponatremia compared to those who were on oral fluids (OR=18.78 [95%CI: 3.18 – 110.84]; p<0.001). This could be attributed to the fact that the commonest fluid given was Half Strength Darrows +5% dextrose a hypotonic fluid. Studies have shown that use of hypotonic fluids is associated with development of hyponatremia which has a poor outcome(5,30,31).

There was no significant association between amount of fluid/feed given and occurrence of hyponatremia 48 hours after admission (OR=9.00 [95%CI: 0.94 – 86.52]; p=0.083). However, a high proportion of children given more than 100mls/ kg/day developed hospital acquired hyponatremia (85.7%) compared to those given <=100mls/ kg/day (40.0%). These observations supports the fact that the main cause of hyponatremia in pneumonia is SIADH(). In SIADH the release of ADH is not inhibited by a reduction in plasma osmolality when the individual ingests water and the osmolality of the plasma drops. As the main solute of plasma is sodium, this hypoosmolar state is usually detected as a low sodium level on laboratory testing. SIADH is therefore primarily a condition that results in the abnormal handling of water loading and not a problem with excessive solute loss. This is why it is usually treated with fluid (in particular water) restriction.

9. CONCLUSION

1. There is a high prevalence of hyponatremia in children admitted with pneumonia at KNH

2. Children with very severe pneumonia are more likely to have hyponatremia as compared to those with severe pneumonia indicating that hyponatremia is a sign of severe illness.

3. Use of hypotonic intravenous fluids is associated with development of hyponatremia.

10. RECOMMENDATIONS

Based on the results of this study we recommend that;

1. All children admitted with pneumonia at KNH to have their electrolytes analyzed and appropriate management instituted.

2. To closely monitor electrolytes for children on intravenous fluid.

A study on the appropriate fluid/amount to give per day is recommended.

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APPENDICES

APPENDIX I: QUESTIONNAIRE
PREVALENCE OF HYPONATREMIA IN CHILDREN ADMITTED WITH COMMUNITY ACQUIRED PNEUMONIA AT KNH

QUESTIONAIRRE NO…….. DATE OF INTERVIEW…….

NAME OF INTERVIEWER…….

1 PERSONAL DATA FOR THE CHILD

Age……. year's ……. months……

Gender male ☐ female ☐

2 CLINICAL DATA

History: - cough or ☐

Difficulty in breathing ☐

Temperature ☐ °C

Respiratory rate ☐ /min

Diagnosis:

Severe pneumonia ☐

Very severe pneumonia ☐

3 LABARATORY DATA

a) Sodium levels ☐ Mmol/l

Normal ☐

Hyponatremia ☐

Hypernatremia ☐

A1) If hyponatremia classify further into

Mild

Moderate

Severe

B) Potassium level Mmol/l

Normal

Hypokalemia

Hyperkalemia

C) Sodium levels 48 hours after admission Mmol/l

Normal

Mild hyponatremia

Moderare hyponatremia

Severe hyponatremia

4) Type of fluid given

5) Amount of fluid/feed given (amount/kg/day)

APPENDIX II: WHO CLASSIFICATION OF SEVERITY OF PNEUMONIA

Severe pneumonia

Cough or difficulty in breathing (age>60days) plus at least one of the following

A lower chest wall in drawing ☐

B grunting ☐

C nasal flaring ☐

D 'AVPU'=A ☐

Very severe pneumonia

Cough or difficulty in breathing (age >60days) plus at least one of the following

A central cyanosis ☐

B inability to breastfeed or drink, or vomiting everything ☐

C convulsions, lethargy or unconsciousness. AVPU='V','P' or'U' ☐

☐

D severe respiratory distress

☐

TACHYPNEA

2-11 months ≥50 /minute

1-5 years ≥40 /minute

SODIUM LEVELS

Normal 135-145mmol/l

Hyponatremia <135mmol/l

Hypernatremia > 145mmol/l

Hyponatremia will further be classified as

Mild	130 – 134mmol/l
Moderate	125mmol/l – 129mmol/l
Severe	< 125mmol/l

Potassium levels

Normal	3.5 – 5 mmol/l
Hypokalemia	<3.5 mmol/l
Hyperkalemia	>5 mmol/1