

ORIGINAL ARTICLE

Frequency of hypokalemia in pediatric ICU patients with diarrhea and their outcome in a tertiary care pediatric hospital in Lahore, Pakistan.

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ABSTRACT... Objective: To provide comprehensive insight into this issue and determine the frequency of hypokalemia, ultimately offering recommendations for reducing its occurrence among patients suffering from diarrhea. **Study Design:** Cross sectional study. **Setting:** Pediatric Intensive Care Unit (PICU) of Fatima Memorial Hospital in Lahore. **Period:** June 25, 2022 to September 24, 2023. **Methods:** A total of 175 children, encompassing both genders and aged between 1 month to 12 years, who were admitted to the PICU for a minimum duration of 48 hours, were included in the study. The data pertaining to the children's basic demographic information, diagnosis, length of stay, and outcomes were documented on a proforma. The analysis of the data was conducted using SPSS v25, wherein all variables underwent a descriptive analysis. By implementing stratification, we were able to control for potential confounding variables, such as age and gender. Following stratification, Chi-square and Independent t-tests were performed, with a p-value of 0.05 indicating statistical significance. **Results:** Gender distribution showed that 112(64.0%) were males and 63(36.0%) were females. The mean age of the children was 26.32 ± 32.02 months. The mean serum potassium level was 3.19 ± 0.80 mEq/L. Among 175 children with diarrhea, 110(62.9%) had hypokalemia. According to outcome of children, 33(18.9%) were discharged home, 128(73.1%) discharged to the ward, and 14(8.0%) expired. The mean stay in the PICU was 4.69 ± 3.852 days and the mean stay in the hospital was 5.87 ± 3.729 days. **Conclusion:** Hypokalemia, a frequently encountered electrolyte disturbance in pediatric patients afflicted with acute bouts of diarrhea, necessitates the utmost vigilance on the part of the attending physician. To avert the potentially dire consequences of severe hypokalemia, it is imperative for healthcare providers to engage in diligent and sequential surveillance of serum potassium levels while concurrently implementing potassium supplementation for affected children amidst episodes of acute diarrhea.

Key words: Diarrhea, Hypokalemia, Mortality, Pediatric ICU, Serum Potassium Level.

INTRODUCTION

Diarrhea is the primary cause of illness and death among children worldwide, resulting in more than two million deaths annually on a global scale. Moreover, this condition is closely linked to compromised cognitive and physical development in developing nations. In developing countries, diarrhea-related diseases rank as the second leading cause of child mortality, with an annual toll of 760,000 fatalities and 1.7 million instances of illness.^{1,2}

The disease burden is disproportionately elevated for children in low- and middle-income countries. Infants are particularly susceptible

to the development of diarrheal disease, with a substantial proportion of deaths occurring within the first two years of life. On a global scale, the majority of deaths resulting from diarrhea are concentrated in South Asia and Africa. Diarrheal disease constitutes 26.93% of mortalities among children under the age of 5 worldwide, with nearly 90% of these deaths occurring in Sub-Saharan Africa and South Asia.^{3,4}

Sixteen percent of child mortalities in Pakistan are attributed to diarrheal disease. Pakistan has an estimated population of 24 million children under the age of 5, and on average, these children experience 3 to 4 episodes of diarrhea per year,

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resulting in approximately 120 million episodes annually. It is a common occurrence for children with diarrhea to experience imbalances in electrolyte levels and dehydration. The presence of various types of electrolyte disturbances contributes significantly to the increased mortality rate among children suffering from acute diarrhea.^{5,6}

Electrolyte imbalances may go unnoticed; however, prompt detection, coupled with a diligent level of suspicion and comprehensive assessment of prevalent electrolyte disturbances, is imperative for the purpose of monitoring and rectifying such imbalances. In order to uphold homeostasis, potassium serves as the primary intracellular ion, crucial for the normal cellular functioning. It is worth noting that the extracellular fluid constitutes a mere 2% of the body's total content, thereby indicating that serum potassium levels do not reflect the entirety of potassium within the body.^{7,8}

Determining the potassium level is of utmost importance in the acute management of hypokalemia, a condition that can prove fatal. Malnutrition often leads to subclinical potassium deficiency, which lacks observable signs and symptoms. However, individuals experiencing diarrhea face a potential threat of hypokalemia. The body maintains the potassium (K⁺) level within a range of 3.5-5.0mEq/l by carefully regulating intake, distribution, and excretion. Hypokalemia is diagnosed when serum potassium levels drop below 3.5 mEq/l. Mild hypokalemia occurs when K⁺ levels range from 3.0-3.5mEq/l and is typically asymptomatic. Severe hypokalemia, defined as K⁺ <2.0mEq/l, commonly presents with noticeable symptoms in affected patients.^{9,10}

In a research conducted by Nazia Rehana and her team in Nawab Shah, it was observed that among a collective of 246 pediatric patients suffering from acute diarrhea, a notable proportion of 108 children (43.9%) exhibited the presence of hypokalemia.¹ In a research conducted at Children hospital Lahore, Asma Mushtaq and colleagues enrolled a group of 42 children below the age of 5 who presented with the coexistence

of hypokalemia and diarrhea. Evaluation of the degree of hypokalemia revealed that 31% of the patients exhibited mild severity, another 31% displayed moderate severity, while 38.1% were classified as having severe hypokalemia.⁷

A study conducted at the Pediatric Intensive Care Unit (PICU) in Bharati Hospital, located in Sangli, India, revealed that among the 153 admissions during the specified time period, 50 individuals, accounting for 32.7% of the total admissions, exhibited hypokalemia. In terms of severity, it was observed that 40 of these cases, amounting to 80%, displayed mild hypokalemia, while the remaining 10 cases, representing 20%, presented with moderate hypokalemia.¹⁰

Given the aforementioned information and the potential necessity to mitigate both the morbidity and mortality rates prevalent among the pediatric cohort by averting occurrences of hypokalemia resulting from diarrhea, it is imperative to specifically focus on the Lahore region. Therefore, the ensuing investigation is devised to gain comprehensive understanding of this matter and subsequently ascertain the frequency of hypokalemia, thereby offering suggestions to diminish its prevalence amongst patients suffering from diarrhea.

METHODS

After getting approval from ethical review board (IRB No. 13/12/2022-IRB-1152), the study was conducted at Pediatric Intensive Care Unit, Fatima Memorial Hospital, Lahore from June 25, 2022 to September 24, 2023. After taking approval from hospital's Ethical Committee and written informed consent from parents/guardian, total 175 children fulfilling the selection criteria were enrolled in this study. A sample of size 175 was calculated by using 95% confidence level with 7% margin of error and 32.7% anticipated proportion of hypokalemia in diarrhea.¹⁰

All pediatric patients ranging from 1 month to 12 years of age and experiencing a frequency of three or more loose or liquid stools within a 24-hour period were included in this study upon admission to the Pediatric Intensive Care Unit

(PICU). Only those children discharged with oral medications were considered. Exclusions from the study consisted of children admitted to a hospital but not requiring ICU care, infants under one month of age, and patients receiving diuretic therapy. The gathered data encompassed demographic information, admission diagnoses, daily clinical and laboratory data, severity of diarrhea and hypokalemia, as well as outcomes related to hypokalemia such as length of stay (LOS) and overall prognosis.

Hypokalemia was defined as serum potassium levels <3.0 mEq/L. Diarrhea was labeled as per WHO definition for diarrhea i.e., children having ≥ 3 loose or liquid stools in last 24 hours' period. Outcomes were labeled as length of hospital stay (days), length of PICU stay (days), discharged home or death. Data was entered and analyzed using SPSS version 25. A descriptive analysis was conducted on all variables. Variables such as gender and patient outcome (discharged/death) were presented in the form of frequency and percentages, as they are categorical. On the other hand, quantitative variables such as age, length of hospital stay (in days), and length of stay in the PICU (in days) were presented using mean and standard deviation. To assess the association between socio-demographic variables and hypokalemia, a Chi-square test was employed. A p-value of less than 0.05 was considered statistically significant. To control for effect modifiers, such as age and gender, stratification was implemented. Following stratification, a Chi-square test was performed with a p-value threshold of ≤ 0.05 to determine significance.

RESULTS

Total 175 children admitted at PICU having age 1 month to 12 years who stayed in PICU for ≥ 48 hours were included in study. Gender distribution showed that, 112(64.0%) were males and 63(36.0%) were females. The mean age of the children was 26.32 ± 32.02 months. According to age distribution, 159(90.9%) of the children had ages ≤ 72 months, while 16(9.1%) had ages > 72 months.

The mean serum potassium level was 3.19 ± 0.80 mEq/L. Among 175 children with diarrhea, 110(62.9%) had hypokalemia. According to outcome of children, 33(18.9%) discharged home, 128(73.1%) discharged to ward and 14(8.0%) expired. The mean stay in PICU was 4.69 ± 3.852 days and mean stay in hospital was 5.87 ± 3.729 days.

According to stratification of hypokalemia with respect to gender and age, insignificant difference was observed ($p > 0.05$). According to stratification of stay in PICU and hospital stay with respect to gender and age, insignificant difference was observed ($p > 0.05$).

	Frequency	Percent
Male	112	64.0
Female	63	36.0
Total	175	100.0
Age groups		
≤ 72 months	159	90.9
> 72 months	16	9.1
Total	175	100.0
Hypokalemia		
Yes	110	62.9
No	65	37.1
Total	175	100.0
Outcome of patient		
Discharged home	33	18.9
Discharged to ward	128	73.1
Expired	14	8.0
Total	175	100.0

Table-I. Frequency distribution of demographic variables

	Age (months)	length of stay in PIC U (days)	length of stay in hospital (days)	Serum potassium level (mEq/L)
Mean	26.32	4.69	5.87	3.19
Std. Deviation	32.02	3.85	3.73	0.80
Minimum	1	1	1	2
Maximum	144	38	38	6

Table-II. Mean values of different variables

Variables		Hypokalemia		P-Value
		Yes	No	
Gender	Male	69(61.6%)	43(38.4%)	0.648
	Female	41(65.1%)	22(34.9%)	
Age groups	≤72 months	100(62.9%)	59(37.1%)	0.975
	>72 months	10(62.5%)	6(37.5%)	

Table-III. Stratification of hypokalemia with respect to gender and age

Variables		Outcome of Patients			P-Value
		Discharged Home	Discharged to Ward	Expired	
Gender	Male	16(14.3%)	86(76.8%)	10(8.9%)	0.114
	Female	17(27.0%)	42(66.7%)	4(6.3%)	
Age groups	≤72 months	27(17.0%)	120(75.5%)	12(7.5%)	0.083
	>72 months	6(37.5%)	8(50.0%)	2(12.5%)	

Table-IV. Stratification of outcome of patients with respect to gender and age

Outcomes	Gender	n	Mean	Std. Deviation	P-Value
Length of stay in PICU (days)	Male	112	4.85	3.022	0.458
	Female	63	4.40	5.015	
Length of stay in hospital (days)	Male	112	5.93	2.840	0.777
	Female	63	5.76	4.957	

Table-V. Stratification of length of PICU and hospital stay with respect to gender

Outcomes	Age Groups	n	Mean	Std. Deviation	P-Value
Length of stay in PICU (days)	≤72 months	159	4.64	3.976	0.634
	>72 months	16	5.13	2.306	
Length of stay in hospital (days)	≤72 months	159	5.84	3.853	0.774
	>72 months	16	6.13	2.217	

Table-VI. Stratification of length of PICU and hospital stay with respect to age

Hypokalemia	Outcome of Patients			P-Value
	Discharged Home	Discharged to Ward	Expired	
Yes	20(18.2%)	89(80.9%)	1(0.9%)	0.001
No	13(20.0%)	39(60.0%)	13(20.0%)	

Table-VII. Comparison of outcome of patients with hypokalemia

Outcomes	Hypokalemia	n	Mean	Std. Deviation	P-Value
Length of stay in PICU (days)	Yes	110	4.16	2.356	0.019
	No	65	5.57	5.442	
Length of stay in hospital (days)	Yes	110	5.38	2.201	0.024
	No	65	6.69	5.335	

Table-VIII. Comparison of length of PICU and hospital stay with hypokalemia

DISCUSSION

The condition known as intractable diarrhea of infancy refers to a prolonged period of diarrhea lasting more than two weeks, which typically occurs within the first three months of a baby's life and is unresponsive to conventional treatment, thereby posing a serious threat to the baby's well-being. Nonetheless, progress in the field of nutritional support, particularly in the area of parenteral nutrition, has enhanced the chances of survival and led to the substitution of the term "intractable" with "prolonged," "protracted," or "persistent" to describe diarrhea in infants.

In addition, the syndrome of intractable diarrhea of infancy arises from a variety of disorders that exhibit heterogeneity and lack specificity for infants under the age of three months, thereby engendering controversy regarding its designation. However, it is important to differentiate the syndrome of protracted diarrhea in infancy, also known as non-specific enterocolitis, from the concept of chronic non-specific diarrhea, which denotes a less severe condition. Conversely, the syndrome may also manifest as a secondary consequence of any disease that induces chronic diarrhea.¹¹⁻¹³

Intestinal water absorption is a passive phenomenon that occurs in response to osmotic and hydrostatic pressure gradients across the intestinal tract. Osmosis can be generated through the active transportation of electrolytes or non-electrolytes. The passage of water and electrolytes through the intestinal mucosa can occur passively via the paracellular pathway or actively through the apical and basolateral pathways. The absorption of sodium occurs through at least three mechanisms.

The sodium pump, known as Na-K-ATPase, is situated in the basolateral membrane of the cell and facilitates the efflux of sodium from the cell into the interstitial space (wherein three sodium ions are exchanged for two potassium ions entering the cell). This process leads to a reduced intracellular sodium concentration, which in turn promotes further sodium influx into the cell. Similarly, the exchange of three sodium ions

for two potassium ions generates intracellular electronegativity, thereby facilitating the transport of more sodium from the intestinal lumen into the cell.

The alternative means by which sodium is absorbed is neutral and takes place when sodium exists in the form of sodium chloride or is replaced by hydrogen ion, simultaneously with the exchange of chloride within the cell and bicarbonate within the intestinal lumen. The final means of sodium absorption occurs through transport proteins. In this particular Co-transport mechanism, sodium is associated with D-glucose, D-galactose, amino acids, dipeptides, or tripeptides.¹⁴

Sodium is effectively taken in by the colon predominantly via an electrogenic mechanism through selective sodium pores. This physiological process is regulated by aldosterone, which promotes sodium absorption and potassium excretion. The major ion actively secreted is chloride (Cl⁻). This process is coupled with the Na-KATPase pump, which accumulates Cl⁻ within the cellular structure.

In the intestinal lumen, cyclic AMP or an increase in intracellular calcium stimulate the secretion of Cl⁻. Likewise, certain enterotoxins, bile acids, fatty acids, laxatives, and hormones possess the ability to stimulate the secretion of Cl⁻. Potassium transport is primarily passive, although active absorption and secretion have been demonstrated. Bicarbonate is typically absorbed in the jejunum and secreted by the duodenum, ileum, and colon.¹⁵

Unlike the renal function observed in adults, which ensures stability by safeguarding against alterations in the volume and composition of the extracellular fluid, the kidney of neonates and younger infants sustains a surplus of numerous solutes to facilitate growth. The distribution of fluid compartments varies across different age groups, and the process of growth and maturation of organs enables the maintenance of homeostasis despite the apparent constraints imposed by renal function.¹⁶

The explanation for the low serum potassium levels in children with persistent diarrhea appears to involve several factors. Firstly, the duration of the diarrhea lasting for over two weeks results in a significant loss of potassium in the stools. Secondly, a diet that provides an adequate amount of calories typically contains a sufficient quantity of potassium. Lastly, the administration of 2000 ml of 5% dextrose in distilled water through hypodermoclysis inevitably contributes to the depletion of both sodium and potassium reserves in the body.^{17,18}

It is commonly understood that the administration of hypertonic glucose into the peritoneal cavity has the propensity to attract electrolytes into this specific compartment, resulting in the excretion of certain electrolytes in the urine. Our investigation revealed that the majority, specifically 90%, of the cases observed were within the age range of 72 months. A similar age range was also documented by Lerner GB, et al. It is worth noting that the incidence of diarrhea is at its highest in this particular age group.¹⁹

Hypokalemia was observed in 62.9% of the cases examined within the scope of this particular investigation. In a separate study conducted by Hojte, et al, it was discovered that 75 out of 100 cases exhibited a reduction in the levels of sodium and potassium within their serum. Additionally, Iqbal, et al. demonstrated that 28% of cases involving acute gastroenteritis displayed abnormal levels of electrolytes. Furthermore, Anand S, et al. noted that 80% of patients experiencing diarrhea and dehydration showcased electrolyte abnormalities, with 46% of these individuals presenting with hypokalemia.²⁰⁻²²

The prevalence of hypokalemia exhibited a higher occurrence in the present investigation in contrast to other studies, where the researchers witnessed a frequency of hypokalemia around 14%. Nevertheless, the authors encompassed a range of conditions, including diarrhea, within their examination. In the context of diarrheal disease, these same authors observed hypokalemia in 20% of the cases. The hypokalemia identified in our patient could potentially be attributed to the

heightened loss of potassium through diarrhea. In addition, the loss of bicarbonate also plays a partial role in the development of hypokalemia within these patients.²³⁻²⁵

Roshni S, demonstrated a heightened prevalence of hypokalemia, unveiling the occurrence of mild, moderate, and severe cases in 39%, 26%, and 2% of instances, respectively. They revealed a notably elevated degree of hypokalemia among malnourished children in comparison to their healthier counterparts. Singh N, on the other hand, indicated no statistically significant disparity in the duration of hospitalization or the presence of hypokalemia when compared to normokalemia. Islam, et al revealed a mortality rate of 19%, with a direct correlation between the overall mortality and the decrease in serum sodium concentration. Consequently, there remains an absence of explicit evidence regarding the optimal timing for the measurement of serum electrolytes in children suffering from diarrhea.²⁶⁻²⁸

If possible, it is advisable to assess the serum electrolytes of children in need of intravenous rehydration. Moreover, considering that the occurrence of hypokalemia can surpass 60% in children hospitalized due to diarrhea, it is important to measure their serum electrolytes and glucose levels. This is particularly crucial if they are malnourished, have impaired consciousness or seizures, are below three months of age, or are experiencing dehydration or persistent diarrhea.²⁹⁻³¹

Similarly, in cases where dysentery is present, it is advisable to conduct an examination of stools in order to identify any enteric pathogens. Moreover, in situations where persistent diarrhea occurs, it is recommended to test the stools for reducing sugars. Among patients in the Pediatric Intensive Care Unit (PICU), the occurrence of hypokalemia is a prevalent issue. Detecting this condition early on through regular monitoring and promptly addressing it can potentially contribute to an improved outcome. A study revealed that 14.8% of patients experienced a total of 54 episodes of hypokalemia.³²

The management of hypokalemia is contingent upon the severity of the condition and the underlying factors. Certain authors do not advocate for the treatment of mild hypokalemia, whereas others support the use of oral supplements or rectal administration of potassium chloride solution. Intravenous potassium infusion is typically recommended for cases of severe hypokalemia. However, even in this scenario, there is no consensus regarding the appropriate concentration of potassium solution to be utilized, as well as the optimal rate and duration of therapy.^{33,34}

CONCLUSION

Hypokalemia, a frequently encountered electrolyte disturbance in pediatric patients afflicted with acute bouts of diarrhea, necessitates the utmost vigilance on the part of the attending physician. To avert the potentially dire consequences of severe hypokalemia, it is imperative for healthcare providers to engage in diligent and sequential surveillance of serum potassium levels, while concurrently implementing potassium supplementation for affected children amidst episodes of acute diarrhea. Potential future directions include accurate and convenient potassium monitoring, individualized supplementation plans specific to risk profiles, and novel therapeutic strategies to minimize potassium losses and enhance absorption. Education programs and international health campaigns further seek to improve public perception and availability of appropriate treatment for hypokalemia in childhood diarrhea.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

1	Nida Ahmad: Study conception, design, data collection, data analysis, discussion writing.
2	Abid Rafiq Chaudhary: Study conception, design, data analysis, interpretation, results.
3	Muhammad Usman: Review of article.
4	Muhammad Rashid Ayub: Review of article.