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Comparison of Serum Electrolytes between Sickle Cell and Control Group: A Meta-Analysis

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Abstract

Background: Sickle-cell anaemia is an inherited disease in which genes for sickle-cell haemoglobin comes from both parents. Electrolytes such as sodium (Na+), potassium (K+), chloride (Cl-) are essential for the normal functioning of the cells and organs. The present study was carried out to evaluate and determine the relationship between electrolytes values in Sickle cell anaemia patients.

Aim: To compare serum electrolytes levels between Sickle cell and control group.

Materials and Methods: Meta-analysis was carried out on the findings of ten published studies that were related to serum electrolytes levels of sickle cell anaemia patients. The pooled mean for serum electrolytes was estimated by using a random-effects model.

Results: Pooled mean for serum sodium was lower in sickle cell anaemia with p value 0.04. However, potassium levels were higher in patients than controls with p value 0.01.

Conclusion: Pooled mean reported in this study can be useful in working out the management of sickle cell anaemia.

Keywords: Sickle cell; Electrolytes; Sodium; Potassium; Chloride

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Highlights

- Sickle-cell anaemia is an inherited disease in which genes for sickle-cell haemoglobin comes from both parents.
- We evaluate and determine the relationship between electrolytes values in Sickle cell anaemia patients.
- Serum electrolytes focused in this study are sodium, potassium, chloride.
- Pooled mean reported in this study can be useful in working out the management of sickle cell anaemia

Introduction

Sickle-cell anaemia is an inherited disease in which genes for sickle-cell haemoglobin comes from both parents. The erythrocytes become crescent-shaped, thin and long, which appears like the blade of a sickle. After deoxygenation of haemoglobin from sickle cells (called haemoglobin S), they become insoluble and forms polymers those aggregate into tubular fibers, whereas, normal hemoglobin (hemoglobin A) remains soluble [1].

The haemoglobin S changes in the permeability of membrane which changes electrolyte balance. Sodium and potassium fluxes in the spleen is increased with cellular gain of Na+ and loss of K+ and create imbalance in the ionic strength of the cell membrane [2-4].

Sickle cell patients also showed increased and continued obligatory losses of body fluids and electrolytes which cause dehydration and other metabolic disturbances. Electrolytes such as sodium (Na+), potassium (K+), chloride (Cl-) are essential for the normal functioning of the cells and organs. Any imbalance in them leads to serious complications. Dehydration in sickle cell anaemia patients cause imbalance in electrolyte levels, which leads to sickling, sequestration and haemolysis [5,6]. Several studies have been conducted in different regions, which shows varying estimates of the average sodium, potassium and chloride measure with standard deviation among case and control patients as highlights in Table 1 to Table 3 of this study. These results mislead the clinician in decision of the actual measure of the respective parameters i.e., there is lack of systematic review of this major health issue. Hence, the present study was carried out

Table 1: Study Characteristics for sodium measure among case and control patients.

Author, year	Place	Cases			Control		
		Sample	Mean	SD	Sample	Mean	SD
Hagag, 2014	Egypt	60	131.15	8.55	30	137.8	3.32
Antwi-Boasiako, 2019	Ghana	79	135.01	4.71	48	140.72	4.06
Meshram, 2014	Maharashtra, India	50	127	2.1	50	141	1.21
Nnodim, 2014	Nigeria	100	125.7	3.57	100	141.44	3.18
Rath, 2019	Chhattisgarh, India	52	135.2	4.02	20	131.2	4.4
Gupta 2012	Chhattisgarh India	33	122.79	3.59	30	135.23	0.99
Madan, 2016	Wardha, Maharashtra, India)	15	113.25	27.35	15	138.43	18.87
Madhuri, 2019	Telangana, India	30	134.64	3.93	20	130.61	3.59
Yusuf and Hassan, 2017	Nigeria	74	136.04	3.0	20	139.95	4.68

Table 2: Study Characteristics for potassium measure among case and control patients.

Author, years	Place	Cases			Control		
		Sample	Mean	SD	Sample	Mean	SD
Hagag et al. 2014	Egypt	60	5.24	0.69	30	4.02	0.32
Antwi-Boasiako et al. 2019	Ghana	79	5.15	0.63	48	4.81	0.6
Meshram, 2014	Maharashtra, India	50	4.7	0.17	50	3.6	0.17
Nnodim JK et al. 2014	Nigeria	100	4.08	0.28	100	2.88	0.13
Rath D et al. 2019	Chhattisgarh, India	52	4.23	0.86	20	3.8	0.3
Gupta V et al. 2012	Chhattisgarh India	33	4.24	1.16	30	4.97	0.73
Madan KA et al. 2016	Wardha, Maharashtra, India)	15	5.72	0.88	15	4.58	0.49
Bernard KFC et. al. 2018	Cameroon	40	5.47	1.72	40	5.02	1.31
Madhuri M et al. 2019	Telangana, India	30	3.99	0.95	20	3.8	0.32
Hassan RYA et al. 2017	Nigeria	74	4.58	0.67	20	3.77	0.31

Table 3 Characteristics for chloride measure among case and control patients.

Author, years	Place	Cases			Control		
		Sample	Mean	SD	Sample	Mean	SD
Antwi-Boasiako et al. 2019	Ghana	79	102.57	12.11	48	103.56	4.16
Rath et al. 2019	Chhattisgarh, India	52	105.1	4.28	20	98.6	3.9
Madan et al. 2016	Wardha, Maharashtra, India)	15	87.3	30.79	15	110	8.56
Madhuri et al. 2019	Telangana, India	30	105.09	3.97	20	98.32	3.23
Hassan et al. 2017	Nigeria	74	96.16	3.23	20	102.95	3.97

to evaluate and determine the relationship between electrolytes values in Sickle cell anaemia patients. The serum electrolytes focused in this study are sodium, potassium, chloride.

Material and methods

Types of studies

The studies related with Case-control, Cross-Sectional and case series published or unpublished before 31 August 2020 were used for meta-analysis, if serum levels of sodium, potassium and chloride were given for comparison between case and control.

Types of participants

Patients of any age with Sickle-cell anaemia.

Study selection

IOM, PRISMA, and MOOSE criteria were used to evaluate the studies. The study selection processes is summarized in Figure 1. PubMed and Google Scholar database was used with using the keywords “Sickle-Cell” AND “Serum electrolyte” for searching the articles. Studies which were written in English and published as full-length were considered for this study. Their references lists were also accessed for additional support.

Types of outcome measures

1. Serum Sodium level
2. Serum potassium level
3. Serum chloride level

Data extraction

The guidelines used for meta-analysis of observational studies were followed and following data was extracted from each study:

1. Last name of 1st author
2. Publication year of the study
3. Population of Patients
4. Mean and Standard Deviation for Sodium, potassium and chloride separately.

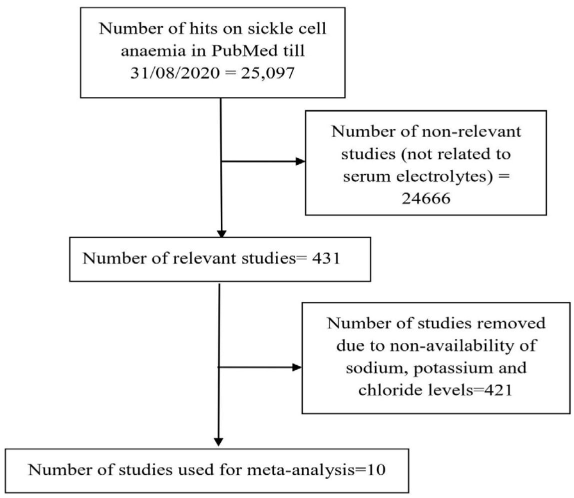

Figure 1 Flow chart in the process of study selection.

Statistical analysis

Separate contingency tables were developed for Sodium, potassium and chloride. A statistical analysis was conducted using STATA-16 statistical software. Forest plots were used for Meta-analyses of Sodium, potassium and chloride levels, which include the summary statistical estimates, 95% confidence intervals and relative weights represented by the middle of the square, the horizontal line, and the relative size of the square, respectively. Heterogeneity across studies was estimated by using I^2 statistic, with values greater than 50% considered as substantial heterogeneity. Random-effects model was used in study because data, which was used in the study, was supposed that selection from all possible studies was random. Bias of the study was evaluated by using funnel graph as shown in Figures 2B, 3B, 4B.

Result

Ten articles that fulfil the eligibility criteria for our study and allocated with the relationship of Sickle cell anemia with serum electrolytes were included in the study. From them 9 were associated with serum sodium [3-11] and ten were associated with serum potassium [2-11] and 5 were associated with serum chloride [4-6,10,11]. Table 1 summarizes the pooled mean, lower limit, upper limit of sodium. Table 2 summarizes for potassium and Table 3 for chloride levels.

Serum sodium

Serum sodium reported in all nine studies dealing with its relationship with Sickle cell anaemia and controls. The pooled mean of sickle cell anaemia was 130.50 mEq/L (95% CI: 126.62–134.38), with I^2=53.40%. However, in control group, pooled mean was estimated as 137.49 mEq/L (95% CI: 134.61–140.37) with I^2=60.40%. These results showed that there were significantly lower sodium levels in sickle cell patients as compared with controls as shown in Figure 1A.

Research publication bias was small because maximum studies were located the on the top and inside of the funnel figure as shown in Figure 1B.

Serum potassium levels

Ten studies dealing with serum potassium levels in Sickle cell anaemia and control group. Overall mean of all studies in sickle cell group was 4.60 mEq/L (95% CI: 4.25 – 4.95) with I^2=16.60%, which was significantly higher as compared with control group 3.87 mEq/L (95% CI: 3.47–4.28) with I^2=75.54% as shown in Figure 2A. Research publication bias was minimal because maximum studies were located the inside of the funnel figure as shown in Figure 2B.

Serum chloride levels

The Pooled mean of studies in sickle cell group was 101.53 mEq/L (95% CI: 95.81–107.25) with I2=32.31%, whereas, in control group was 100.93 mEq/L (95% CI: 97.33–104.53) with I2<0.01%. Five studies reveal an association with serum chloride levels in Sickle cell anaemia and control group. There was no statistically significance difference found between these groups as shown in Figure 3A. Studies have minimal publication bias because maximum studies were located the inside of the funnel figure as shown in Figure 3B.

Discussion

Summary

This meta-analysis work evaluating the prognostic value of electrolyte in patients with sickle cell anaemia. Total 10 studies of sickle cell anaemia were taken in this study, from which 9 studies had shown association with sodium, 10 were shown with potassium, and five chloride were taken in this study. The study used a random effect model, with the assumption that each study used randomly selected samples for analysis. The high heterogeneity observed in the studies of each variable type was due to the different periods in which the studies were carried out, and the diversity of locations, cultures and economic status.

Strengths and limitations

Commonly sodium (Na+), Potassium (K+), Chloride (Cl-) were measured electrolytes in blood testing. In extra cellular fluid

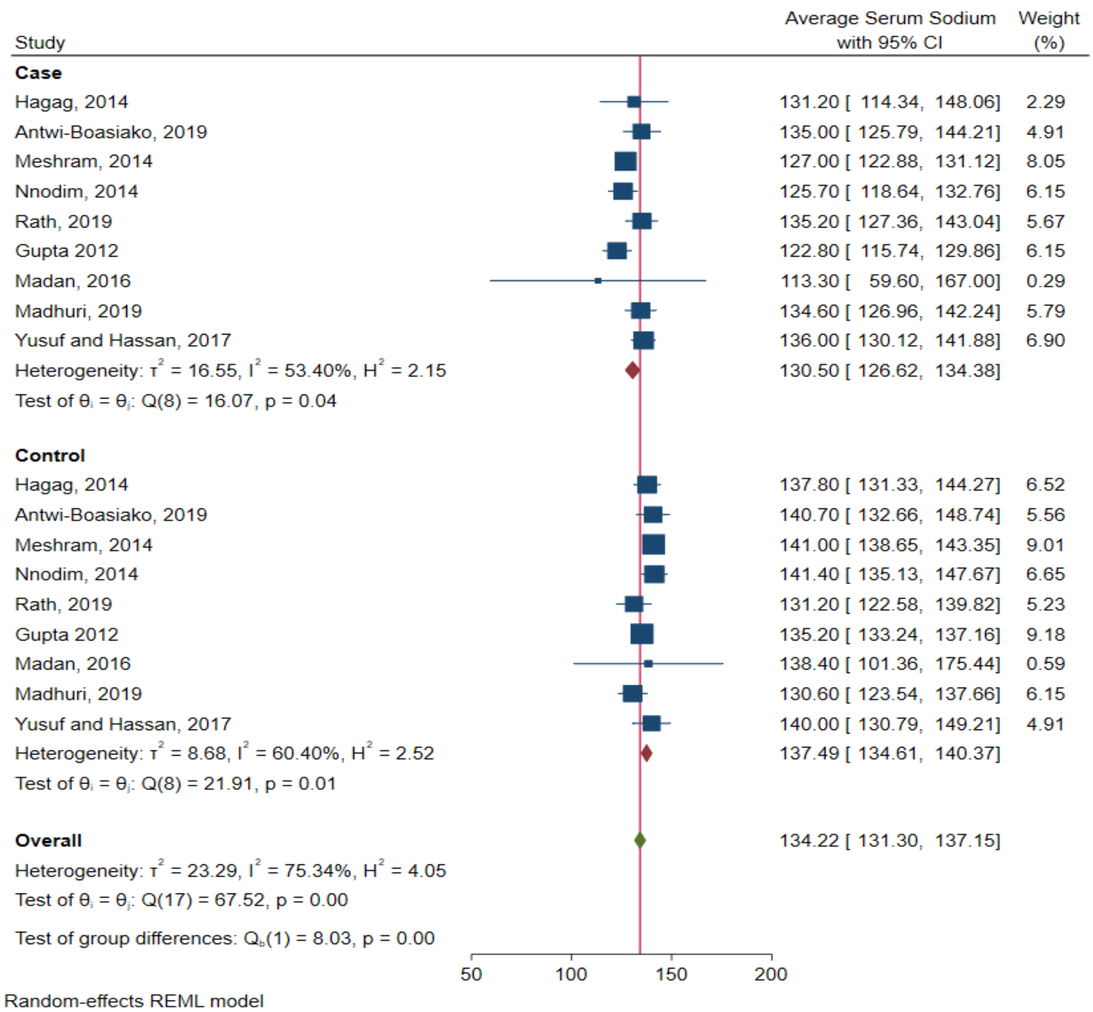

Figure 2A Forest plot of random-effects meta-analysis for Serum sodium in Sickle cell anaemia and control group.

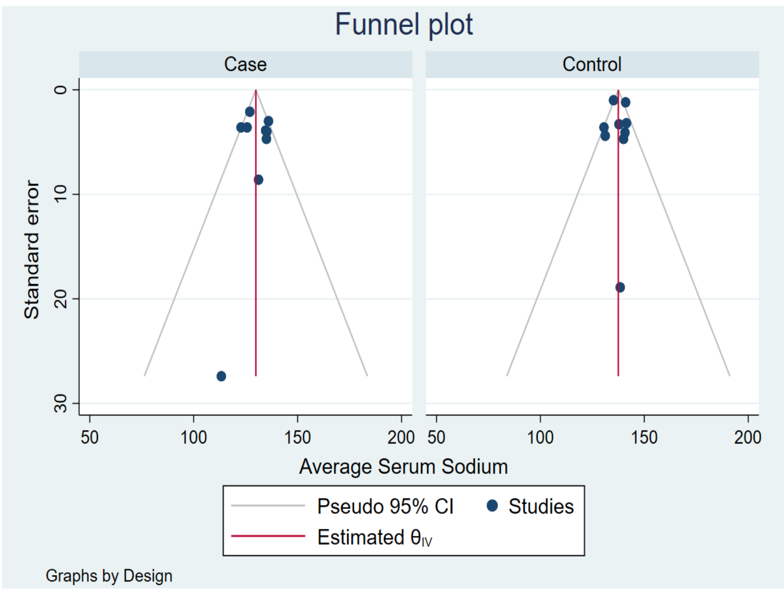

Figure 2B Funnel plot with Pseudo 95% Confidence Interval for serum chloride levels in Sickle cell anaemia and control group.

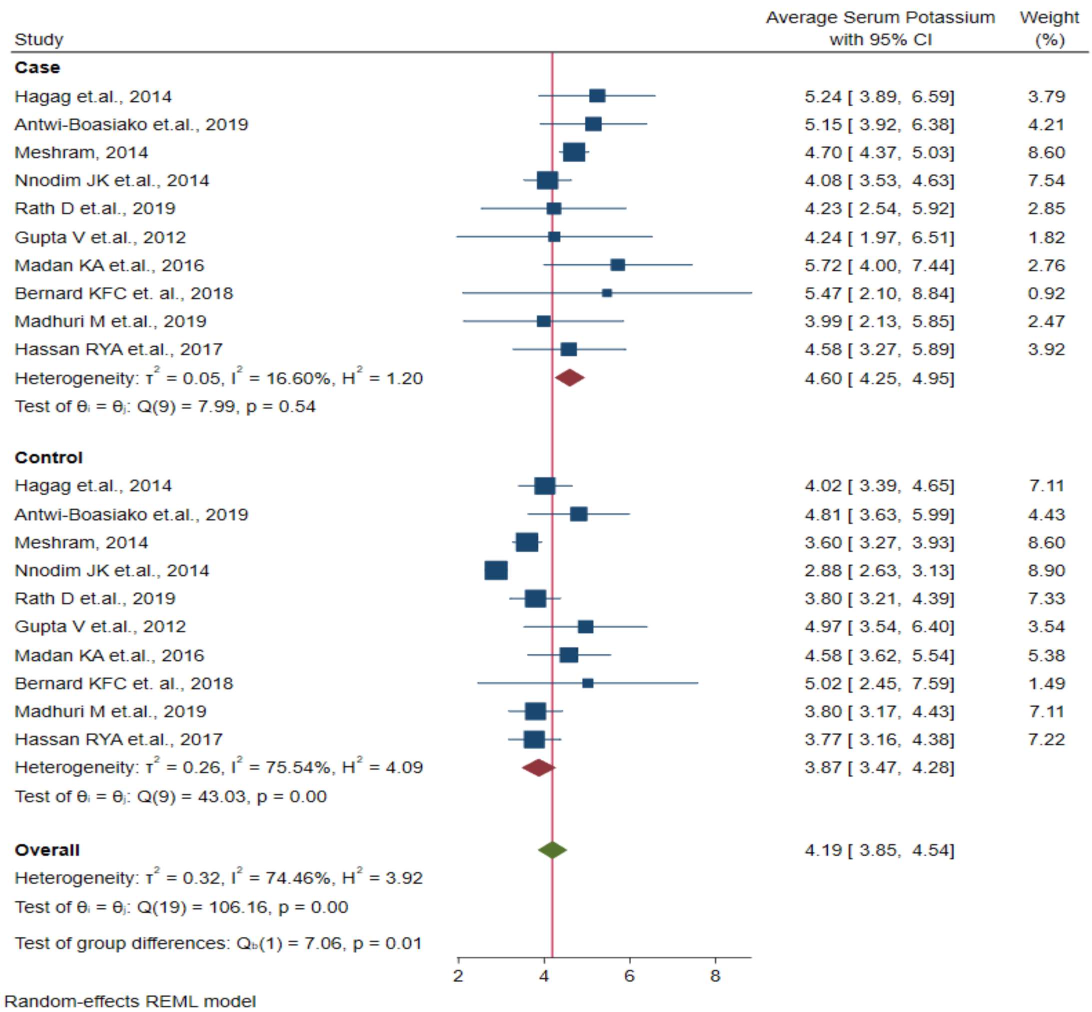

Figure 3A Forest plot of random-effects meta-analysis for serum potassium levels in Sickle cell anaemia and control, group.

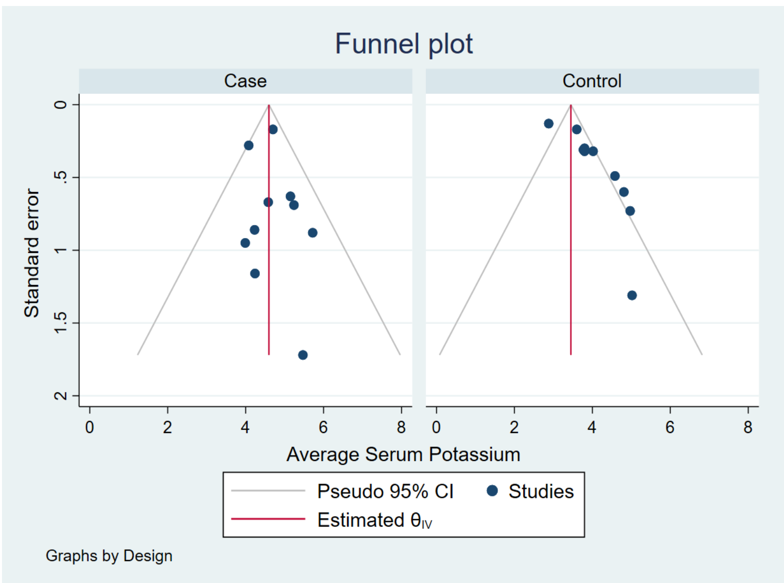

Figure 3B Funnel plot with Pseudo 95% Confidence Interval for serum potassium levels in Sickle cell anaemia and control group.

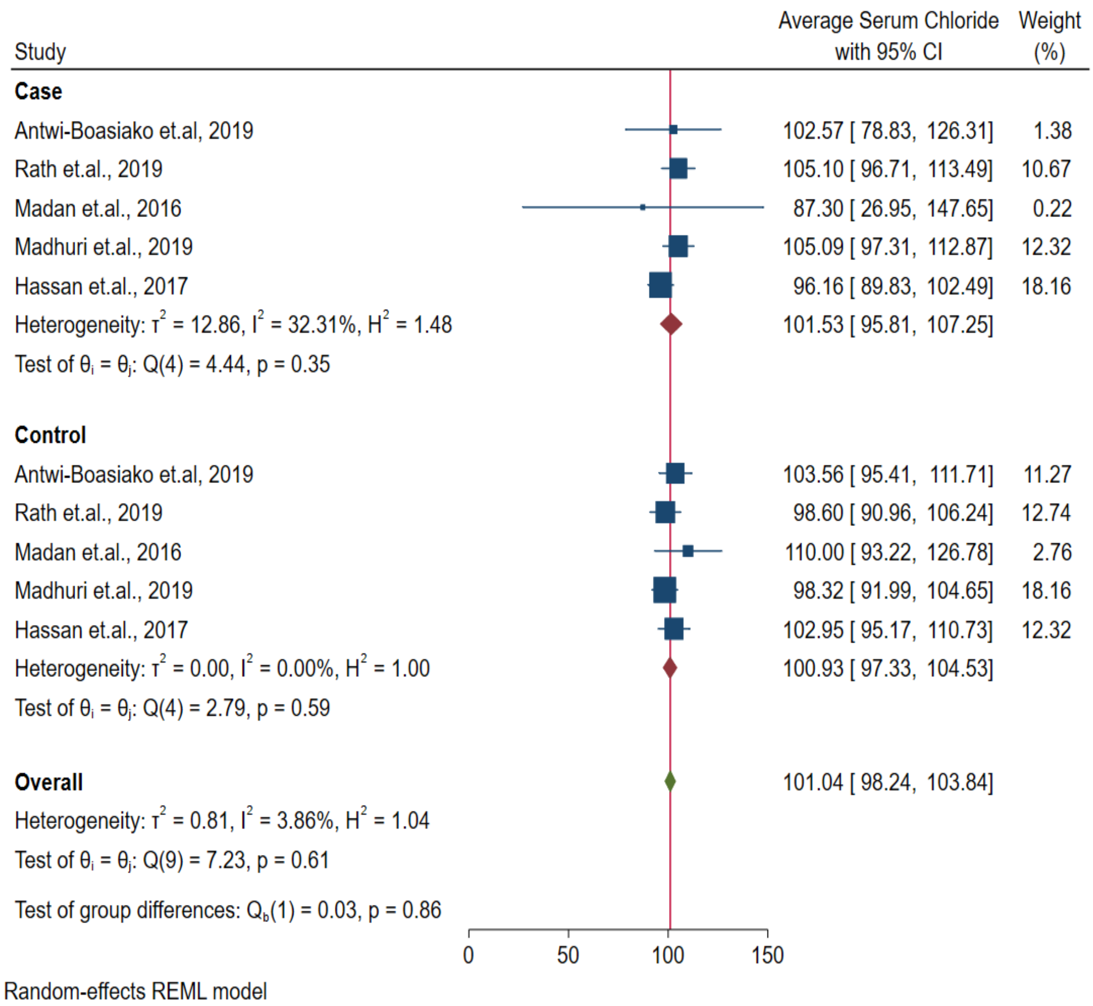

Figure 4A Forest plot of random-effects meta-analysis for serum chloride levels in Sickle cell anaemia and control group.

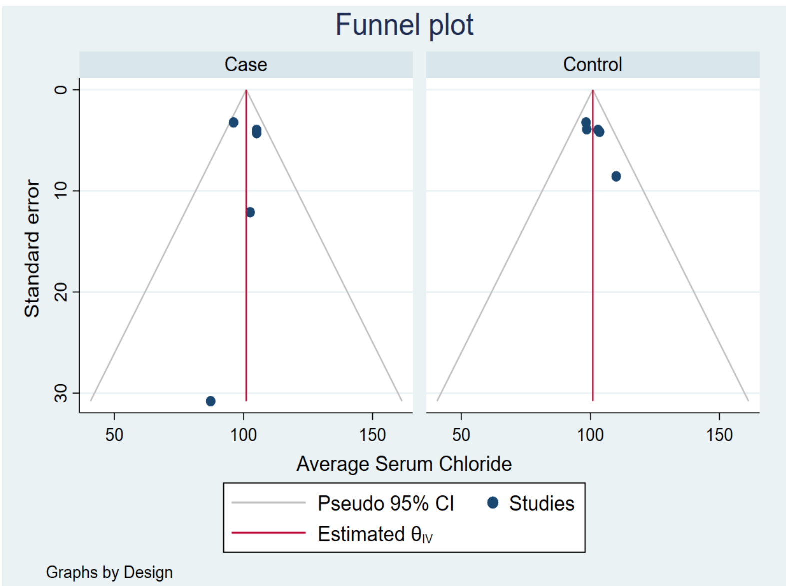

Figure 4B Funnel plot with Pseudo 95% Confidence Interval for serum chloride levels in Sickle cell anaemia and control group.

sodium was the major cation, which is present with anion chloride in the form of NaCl [12,13]. They help in the regulation of total water balance in the body and sodium also helps in the electrical communication between different systems like nervous, muscular and brain. Normal value of sodium in the serum is 135-145 milliequivalent (meq/L) [12,14]. Major intracellular cationic potassium, which is important for the normal function of cell. Most important function is regulation of heart beat and muscles function. Normal blood level is 3.5-5.0 milliequivalent (meq/L) [12,15]. In sickle cell anaemia due to deoxygenation, there is defect in the cation permeability of sodium and potassium. Due to dehydration in sickle cell there is increase in the loss of electrolytes by urine [12,15].

Comparison with existing literature

This study reveals that pooled mean sodium levels in sickle cell anaemia patients had lower than control patients, which was due to dehydration which triggered by movement of sodium into the sickle cell. These were in confirmation with studies done by Hagag AA et al. [7], Meshram AW [3], Nnodim JK et al. [8], Gupta V et al. [9], Madan KA et al. [5] and Madhuri M et al. [10]. However, studies conducted by Antwi-Boasiako C et al. [6], Rath D et al. [4], Hassan RYA et al. [11] shown contradicting results with our study.

This study also indicates that potassium pooled mean level was reported higher in sickle cell patients as compare to control but both were within the normal range (3.5-5.0 mEq/l). The possible mechanism was that sickle cell patients usually encountered Cell dehydration and hypoxia, which leads to the loss of potassium from the cell into the extracellular fluid [6,16-20]. studies done by Hagag AA et al. [7], Antwi-Boasiako C et al. [6], Meshram AW [3], Nnodim JK et al. [8], Rath D et al. [4], Madan KA et al. [5], Bernard KFC et al. [2], Madhuri M et al. [10], Hassan RYA et al. [11] showed similar results with our study, however, study done by Gupta V et al. [9] showed contradicting results.

Conclusion

The pooled mean for serum sodium, potassium and chloride levels in sickle cell anaemia patients are most commonly measured electrolytes in routinely. Levels of serum sodium in sickle cell anaemia decreased, whereas, potassium levels were increased, suggest that routinely quantification estimation of sodium and potassium will help in the management of sickle cell anaemia.

Conflict of interest

None

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