

Electrolyte Abnormalities in Patients with Dengue Infection Admitted to a Tertiary Care Teaching Hospital in Southern India

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Abstract

Introduction: Electrolyte abnormalities are well known in patients with dengue fever.

Aim: The purpose of this study was to detect the electrolyte abnormalities that commonly occur in patients with dengue infection and to correlate them with the severity of illness.

Material and methods: This prospective observational study included 95 patients with uncomplicated dengue fever and dengue haemorrhagic fever admitted to the medical wards and casualty of a tertiary care teaching hospital. Serum sodium and potassium levels were estimated in all the study subjects along with hematocrit and platelet count.

Results: Hyponatraemia was present in 36% of the study subjects, while hypokalaemia was found in 34%. However, statistical analysis showed that only hypokalaemia was found to be significantly associated with the severity of illness.

Conclusion: Hyponatraemia and hypokalaemia are common electrolyte abnormalities in patients with dengue infection.

Keywords: Hypokalaemia, hyponatraemia, dengue fever.

Introduction:

Dengue fever is an acute febrile illness that is caused by a flavivirus, which has four serotypes and has the potential of causing large scale outbreaks. The disease is highly prevalent in tropical countries like India. It is transmitted by *Aedes aegypti* and *Aedes albopictus* mosquitoes. Dengue is an important arthropod-borne disease worldwide, with an average of 50 - 100 million infections that occur every year¹.

Dengue has a wide variety of clinical manifestations. While the majority of patients recover following a non-severe episode of illness that is usually self-limiting, a few of them progress to complications like plasma leakage or haemorrhage. A transient and reversible imbalance of inflammatory mediators like cytokines and chemokines occurs in dengue haemorrhagic fever, which is probably caused by a high viral burden that leads to activation of vascular endothelial cells and derangement of the coagulation system causing plasma leakage, bleeding and shock, respectively².

Assessment of serum electrolytes is routinely done in patients admitted to the hospital with dengue fever (DF) and dengue haemorrhagic fever (DHF). Hyponatraemia is defined as plasma Na⁺ concentration below 135 mEq/l and hypokalaemia is defined as K⁺ concentration below 3.5 mEq/l³. The electrolyte abnormalities in patients with

dengue fever can be attributed to vomiting, haemorrhagic phenomena, and even shock in case of DHF.

Aim

To assess levels of serum sodium and potassium in adult patients with dengue fever and dengue haemorrhagic fever and to correlate their abnormalities with the severity of illness.

Material and methods

This prospective, observational study was done in the medical wards and casualty of a tertiary care teaching hospital in southern India in July and August 2017. The study protocol was approved by the Institute Ethics Committee. The sample size for this study was calculated to be 95 at 5% level of significance and 25% relative precision, based on a previous study that showed the prevalence of hyponatraemia to be 40% in patients with dengue infection⁴.

Inclusion criteria

Adult patients (greater than 18 years of age) with confirmed dengue infection (by NS1 antigen test or IgM antibody by ELISA) admitted to a tertiary care teaching hospital in south India.

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Exclusion criteria

Patients with concomitant diabetic ketoacidosis and chronic kidney disease were excluded from the study.

Patients admitted to the medical wards and casualty of a tertiary care teaching hospital with dengue infection (confirmed by NS1 antigen test or positive IgM antibody to dengue virus by ELISA) were enrolled in this study after applying the exclusion criteria as mentioned above.

Patients were explained about the study procedure in simple terms in a language that they could understand, and only those who agreed to participate voluntarily in this study were included after taking their informed, written consent.

The study subjects underwent a brief clinical examination that included measurement of temperature, pulse rate and blood pressure. Hydration status was assessed clinically by examination of the tongue for moistness, skin turgor and urine output. Examination of the skin was done to look for blanchability (blanching of skin on application of pressure by the fingers) and any bleeding manifestations (petechiae, purpura, or ecchymoses). History of bleeding from other sites if present, were noted (gum bleeding, epistaxis, haematuria, haematochezia/melena, and menorrhagia in females). Clinical evidence of plasma leakage (ascites, pleural effusion) was also noted, if present.

Based on the clinical examination, the severity of illness was graded in patients as uncomplicated dengue fever (DF) and dengue haemorrhagic fever (DHF). DHF was graded as I, II, III and IV⁵.

The laboratory parameters included in this study were haemoglobin, haematocrit, and platelet count. Apart from these, the serum levels of sodium and potassium were also noted in all study subjects. Sodium level below 135 mEq/l was considered as hyponatraemia and potassium level below 3.5 mEq/l was considered as hypokalaemia. Mild hyponatraemia was defined as sodium level between 130 - 134 mEq/l, while moderate and severe hyponatraemia was defined as sodium level between 120 - 129 mEq/l and less than 120 mEq/l, respectively. Similarly, potassium level between 3 - 3.4 mEq/l was taken as mild hypokalaemia, while values of potassium between 2.5 - 2.9 mEq/l and less than 2.5 mEq/l were considered as moderate and severe hypokalaemia, respectively.

Statistical analysis

Continuous variables like haemoglobin, haematocrit and serum electrolyte values were expressed as mean with standard deviation (SD) or median with interquartile range (IQR). Categorical variables like severity of dengue infection, hydration status, blanchability, cutaneous bleeding (presence of petechiae/purpura/ecchymoses) and mucosal

bleeding (presence of gum bleeding, epistaxis, haematuria, haematochezia/melena, and menorrhagia) were expressed as percentages. One way ANOVA test was used to compare electrolyte levels with the severity of dengue infection. All statistical tests were carried out at 5% level of significance and p value less than 0.05 was considered as significant.

Results

The mean serum sodium level was found to be 135.92 ± 5.53 mEq/l and mean serum potassium was 3.84 ± 0.55 mEq/l in the study subjects. Haemoglobin was 14.16 ± 2.03 g/dl and haematocrit (PCV) was 42.63 ± 6.43 % (Table I).

Table I: Laboratory parameters of patients with dengue infection.

Laboratory parameter	Mean \pm standard deviation
Serum sodium (mEq/l)	135.92 ± 5.53
Serum potassium (mEq/l)	3.84 ± 0.55
Haemoglobin (g/dl)	14.16 ± 2.03
Haematocrit (%)	42.63 ± 6.43

Table II shows the clinical manifestations of patients on presentation to the hospital. Many of them had bleeding from multiple sites. Among the 41 patients who had mucosal bleeding, only 9 had cutaneous bleeding. Rest of the 19 patients had no evidence of mucosal bleeding. Out of the 95 subjects, 50 (52.6 %) had either cutaneous or mucosal bleeding manifestations. Table II shows the trends in bleeding manifestations among the study subjects. Some patients had bleeding from only one site, whereas some had bleeding from multiple sites. Most common type of bleeding that occurred in patients was melena (10.5 %), followed by gum bleeding (8.4%), menorrhagia in females (4.21%), and epistaxis (3.16%). Haematuria was always accompanied by bleeding from other sites. Out of 31

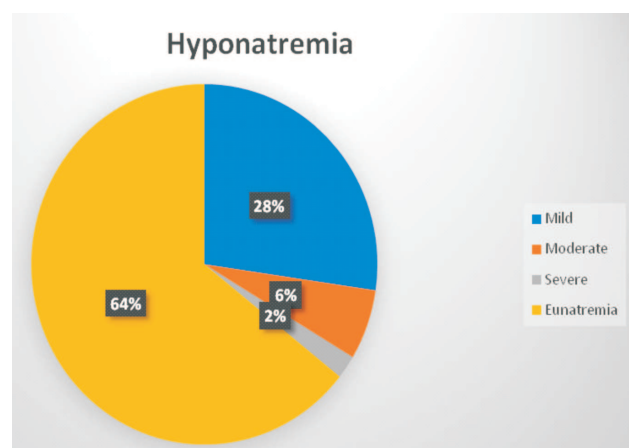


Fig. 1: Proportion of patients with hyponatraemia.

patients, 6 had bleeding from multiple sites.

Table II: Trends in bleeding manifestations.

	Cutaneous bleeding		Total
	Present	Absent	
Mucosal bleeding			
Epistaxis	1	2	3
Gum bleeding	0	8	8
Gum bleeding + epistaxis + melena	1	0	1
Gum bleeding + haematuria	1	0	1
Gum bleeding + haematuria + melena	0	1	1
Epistaxis + gum bleeding + haematuria	2	0	2
Melena	2	8	10
Melena + gum bleeding	1	0	1
Menorrhagia	1	3	4
No mucosal bleeding	19	45	64
	28	67	95

All 95 study subjects were categorised according to the severity of their illness as uncomplicated dengue fever (DF) and dengue haemorrhagic fever (DHF) grades I, II, III, IV according to the guidelines proposed by NVBDCP (National Vector Borne Disease Control Programme). Majority of the patients had uncomplicated dengue fever (54.73%), followed by DHF II (43.16%). Only one patient each had DHF I and DHF III. No patient had DHF IV (Table III).

Table III: Grading of severity of dengue infection.

Dengue fever (DF)/ dengue haemorrhagic fever (DHF)	Grade	Number of patients (%)
DF	-	52 (54.73)
DHF	I	1 (1.05)
DHF	II	41 (43.16)
DHF	III	1 (1.05)
DHF	IV	0

Fig. 1 shows serum sodium levels of the study subjects. Almost two-third of the patients (64%) had normal serum sodium level ($>= 135$ mEq/l). 26 out of 95 patients (28%) had mild hyponatraemia (130 - 134 mEq/l), 6 patients (~6%) had moderate hyponatraemia (120 - 129 mEq/l) and 2 patients (~2%) had severe hyponatraemia (< 120 mEq/l).

Fig. 2 depicts serum potassium levels of the study subjects. Out of the 95 subjects, 63 patients (66%) had normal serum potassium level (> 3.5 mEq/l). 28 patients (30%) had mild hypokalaemia (3 - 3.5 mEq/l) and 4 patients (~4%) had

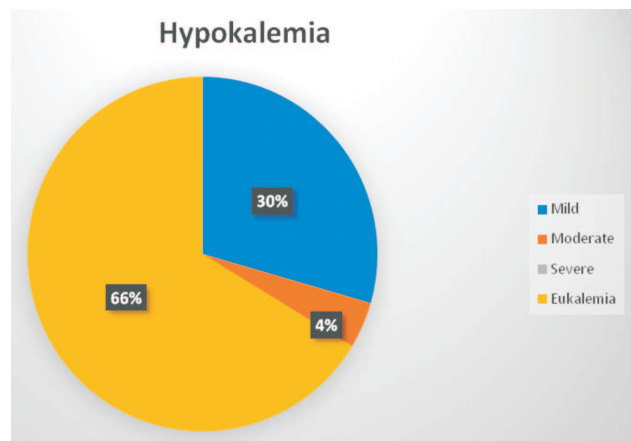


Fig. 2: Proportion of patients with hypokalaemia.

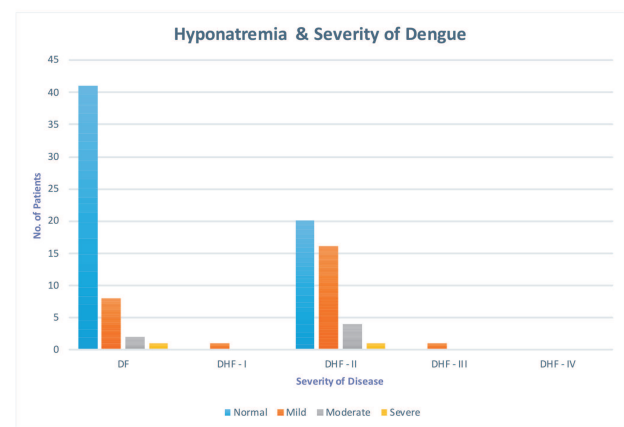


Fig. 3: Hyponatraemia and severity of dengue.

moderate hypokalaemia (2.5 - 2.9 mEq/l). No patient had severe hypokalaemia (< 2.5 mEq/l).

Table IV (i) categorises study subjects according to the severity of illness and serum sodium levels. Fig. 3 compares these two parameters. Out of the 52 patients who had DF, 41 (78.8%) patients had normal serum sodium levels, 8 (15.38%) had mild hyponatraemia, 2 (3.85%) had moderate and 1 (1.92%) had severe hyponatraemia. The patient who had DHF I had mild hyponatraemia. 41 patients had DHF II, out of which 20 (48.8%) had eunatraemia, 16 (57.1%) had mild, 4 (9.75%) had moderate and 1 (2.44%) had severe hyponatraemia. Only one patient had DHF III, who showed mild hyponatraemia.

Table IV (ii) categorises patients according to the severity of illness and serum potassium levels. Fig. 4 is the graphical representation. It is clear from the graph that serum potassium levels show a significant correlation with the severity of illness. All 52 patients who had DF had eukalaemia. Only one patient had DHF I, who showed mild

hypokalaemia. Of the 41 patients who had DHF II, 10 had eukalaemia, 28 had mild hypokalaemia (68.3%) and 3 had moderate hypokalaemia. Only one patient had DHF III, who showed moderate hypokalaemia. No patient had severe hypokalaemia.

Table IV: Correlation of electrolyte imbalance with severity of illness.

Severity of illness	Eunatraemia		Hyponatraemia		
		Mild	Moderate	Severe	
DF	41	8	2	1	
DHF I	0	1	0	0	
DHF II	20	16	4	1	
DHF III	0	1	0	0	
DHF IV	0	0	0	0	

Table IV (ii)

Severity of illness	Eukalaemia		Hypokalaemia		
		Mild	Moderate	Severe	
DF	52	0	0	0	
DHF I	1	0	0	0	
DHF II	10	28	3	0	
DHF III	0	0	1	0	
DHF IV	0	0	0	0	

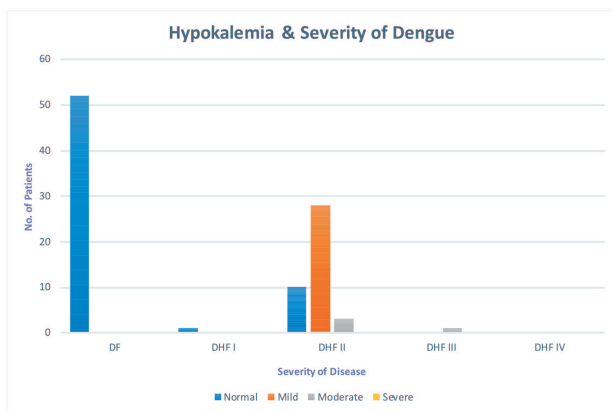


Fig. 4: Hypokalaemia and severity of dengue.

One way ANOVA test was used for comparing serum electrolytes and the severity of dengue infection. Number of data sets present was 5. All tests were carried out at 5% level of significance and a p value < 0.05 was considered to be significant. For serum sodium, p value obtained was 0.8956, whereas for serum potassium, p value obtained

was 0.0278 (using Bonferroni method) which is significant, indicating that alterations in serum potassium is linked to the severity of illness.

Discussion

This was a prospective observational study to assess the serum electrolyte levels in patients admitted with DF and DHF and to correlate the electrolyte abnormalities with severity of the disease, if present.

All 95 patients were categorised according to the severity of their illness as dengue fever (DF) and dengue haemorrhagic fever (DHF) I, II, III, and IV according to the guidelines proposed by National Vector Borne Disease Control Programme (NVBDCP). For grading severity of the illness, parameters like platelet count, haematocrit, hydration status and bleeding diathesis were considered.

According to studies done previously, hyponatraemia was found to be more prevalent in patients with dengue fever. A study done in a paediatric population in Thailand showed the prevalence of hyponatraemia to be 61% in DF and 72% in DHF. The prevalence of hypokalaemia was only 14% in DF and 17% in DHF. Hyponatraemia was attributed to increased antidiuretic hormone levels, whereas hypokalaemia was due to increased renal excretion of potassium due to activation of renin-angiotensin-aldosterone mechanism secondary to volume depletion³.

A similar study done in a paediatric population with dengue fever in a tertiary care centre in Mumbai found the prevalence of hyponatraemia to be 40.3%⁴.

A study done in Salem, Tamil Nadu in 2014 among patients with dengue fever showed the prevalence of hyponatraemia to be 58%, but hypokalaemia was not found among the study patients⁵.

A study done in Karnataka in 2016 used serum sodium as a prognostic marker for dengue fever. Out of 99 subjects, 63 showed hyponatraemia. Among these, 33 patients showed mild hyponatraemia, 12 had moderate and 18 had severe hyponatraemia, and 2 patients developed complications⁷.

Thus, most of the previous studies suggest that hyponatraemia is the most common electrolyte abnormality in patients with dengue fever. This is in contrast to the present study, which found hypokalaemia to be more significant in accordance with the severity of illness. Even though the prevalence of hyponatraemia (36%) is more than that of hypokalaemia (34%), correlation of hypokalaemia with the severity of illness showed significance rather than hyponatraemia. Whether hypokalaemia is a cause or effect of the disease is not

known, but newer studies have showed increased incidence of hypokalaemic paralysis in patients with dengue fever⁸.

Conclusion

Hyponatraemia and hypokalaemia were found to be commonly present in patients with dengue fever. However, only hypokalaemia showed a significant correlation with the severity of illness among patients.

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INVITATION FOR NOMINATIONS FOR ORATION AWARDS FOR 2019

Suggestions are invited from Fellows/Members for the following Orations for the year 2019 so as to reach Dr.T.P.Singh, Hon. General Secretary, Indian Association of Clinical Medicine, on the official Address given below by **31th July, 2019**:

1. **Prof. B. C. Bansal – Mrs. Uma Bansal Oration**
2. **Dr. G. S. Sainani – Dr. Mrs. Pushpa G. Sainani Oration**
3. **Dr. G. B. Jain Oration**
4. **Founder-President Prof. M. C. Gupta Oration**

- The suggestions are to be made for above Orations to be awarded during IACMCON-2019 (Greater Noida). Nomination form is on page 74.
- The suggestions are to be made only by Fellows/Members of the Association, and must be accompanied with reasons for recommending the particular person showing the value of his/her research and accompanied with eight copies of three of his/her best publications. All the relevant papers in connection with suggestions such as Bio-data, list of publications, etc., should be submitted in **EIGHT SETS** by the proposer.
- The recipient of the above awards should deliver a lecture pertaining to his/her work at the Annual Conference of the Association in October 2017.

Members of the Governing Body of the Association are not eligible to receive the Orations.

Eligibility Criteria:

1. The Nominee should have a minimum of 3 years standing in the Association as a Fellow (Kindly mention the Fellowship number and date of award).
 - i. The member should have a standing of minimum three years in the Association.
 - ii. The member should have participated in the annual conferences, scientific programmes, contributed to the *Journal*, and actively engaged in the organisation of the annual conference of the IACM.
 - iii. For Founder-President Dr. M. C. Gupta Oration, the subject of Oration should be related to cardiology.

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