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SERUM ELECTROLYTE IMBALANCE IN DENGUE AND THE CORRELATION OF SODIUM WITH THE SEVERITY OF DENGUE INFECTION.

Paediatrics

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ABSTRACT

Background: The viral illness dengue, which is spread by mosquitoes, has recently spread quickly throughout the WHO's geographical regions. For the accurate early identification of dengue infection, careful monitoring of electrolytes, acid-base balance, and renal function is required. **Aim:** The aim of the present study was to study the serum electrolyte imbalance in dengue and the correlation of sodium with the severity of dengue infection. **Materials And Method:** This prospective study present study was carried out in the Department of Peadiatrics, Vydehi Institute of Medical Sciences and Research Center, Whitefield, Bangalore. The study was carried out for a period of 18 months from February'2021 to July'2022. **Results:** The clinical presentations observed in our study were fever (93.10 %); abdominal pain (51.23 %); vomiting (50 %); petechiae (2.46 %); epistaxis (1.85 %); melena (3.08 %) and organomegaly (57.40 %). There was a statistical difference in terms of the distribution of subjects based on the fluid leakage (p: 0.02). The majority of subjects had fluid leakage (79.88 %). There was a highly significant statistical difference in terms of mean serum sodium levels of study subjects based on their severity of dengue(p: 0.001). There was a decrease in the mean serum sodium levels with the severity of the disease. **Conclusion:** Hyponatremia is the most common electrolyte disturbance in dengue fever as well as dengue-associated complications. Thus, serum sodium plays a most important role in the prognosis of dengue fever and associated complications.

KEYWORDS

dengue, clinical presentation, sodium levels in dengue, hyponatremia.

INTRODUCTION

The mosquito-transmitted illness dengue is most prevalent in tropical and subtropical regions of the world. Transmission has been worse recently, mostly in urban and semi-urban areas, and is now a major global public health concern. Worldwide, the number of dengue cases has dramatically increased in recent decades. Since many dengue episodes are mild, asymptomatic, and self-managed, there is an underreporting of dengue cases. Frequently, other febrile infections are given the wrong diagnosis [1]. Dengue is viewed as a reemerging disease in India, and not enough epidemiological data have been generated. Numerous factors contribute to the nation's rising prevalence. According to the National Vector Borne Disease Control Programme (NVBDCP), the states with the most cases in 2022 were Uttar Pradesh, Punjab, Rajasthan, Madhya Pradesh, Delhi, Maharashtra, Haryana, Gujarat, West Bengal, Odisha, Karnataka, Telangana, Tamil Nadu, Andhra Pradesh, Kerala, J & K, Puducherry, Chandigarh, Chhattisgarh, and others. (4). According to the most recent statistics from the National Vector Borne Disease Control Program 2017–2022, more dengue-related deaths were reported in Maharashtra than in Karnataka(4). 7829 cases and 65 fatalities occurred in Maharashtra in 2017, 11011 cases and 55 fatalities occurred in 2018, 14907 cases and 29 fatalities occurred in 2019, 3356 cases and 10 fatalities occurred in 2020, 12720 cases and 42 fatalities occurred in 2021, and 6330 cases and 5 fatalities occurred in 2022. As opposed to this, Karnataka saw 17844 cases and 10 fatalities in 2017, 4427 cases and 4 deaths in 2018, 16986 cases and 13 fatalities in 2019, 3823 cases and 0 deaths in 2020, 7393 cases and 7 deaths in 2021, and 7317 cases and 4 fatalities in 2022. In India, it has expanded relatively widely over the past 20 years. Anyone can contract dengue, regardless of their age or gender. However, child mortality are frequent during a DHF outbreak. The burden of dengue is expected to increase in the future due to factors including climate change, globalisation, trade, urbanisation, socioeconomics, viral evolution, and others. So that the proper supportive treatment can be provided, it is imperative to work rapidly to develop better diagnostic and prognostic methods to identify severe dengue cases. To establish biomarker panels as prognostic indicators of severe dengue, it is ideal that one day particular treatments, CBC, Liver function tests, and other common laboratory markers would be examined. [6].

Rapid complement system activation during the early acute stage of secondary dengue infection causes decreased C1q, C3, C4, C5, C6, C7, C8, and C3 proactivators as well as high C3 catabolic rates, which harm endothelial cells and circulatory viral nonstructural protein 1 (NS1) levels. This viral toxin destroys capillaries and causes fluid, electrolytes, protein, and occasionally RBCs to leak into intravascular regions by binding to toll receptors 4, which also drive myeloid cells to release cytokines and raise vascular permeability. This fluid redistribution causes hemoconcentration, hypovolemia, increased cardiac effort, tissue hypoxia, metabolic acidosis, and hyponatremia[3] along with the deficit brought on by fasting, vomiting, and thirst. Given the wide range of serum sodium levels in dengue patients and the high frequency of dengue in India, it is important to be somewhat suspicious of sodium levels in dengue patients and treat them accordingly.

Methodology

Patients meeting the following criteria were enrolled in the study: Children admitted to the PICU, Peadiatric emergency, and Peadiatric wards with serologically positive dengue infection, Children diagnosed with Dengue NS1 or IgM Elisa, Children aged between 1 month to 15 years. Patients meeting the following criteria were excluded from the study: Children having deranged serum creatinine and blood urea nitrogen levels, Children with mixed infections, Children with known renal, hepatic, or cardiac disorders.

A suspected case of dengue was considered as per the WHO 2015 criteria (11). Based on the clinical examination, the severity of the illness was graded as dengue without warning signs, dengue with warning signs, and severe dengue. After taking informed consent from the patient's attenders, CBC, Serum electrolytes levels were sent within 24 hours of admission, preferably on the 4 th -day of fever, and the reports were recorded. Hyponatremia is defined as a serum Sodium level < 120 mEq/L)(64),(66). The socio-demographic data (age and gender), clinical presentation, and clinical diagnosis were obtained at admission, and a thorough clinical examination was performed. The serology of the patients was confirmed by dengue IgM and IgG enzymelinked immunosorbent assay (ELISA) test and NS1 antigen. The findings were recorded in a proforma. The demographical data of the patient and presenting complaints such as fever and its duration, presence of abdominal pain, vomiting, and any bleeding manifestations such as petechiae, epistaxis and melena, and organomegaly were recorded in the proforma. The clinical parameters recorded pertaining to the evidence of hemodynamic instability (pulse volume, blood pressure, and pulse pressure) and the evidence of fluid leakage (pleural effusion and ascites) were recorded and the patient was followed up throughout the course of the admission and serum sodium levels were compared to the severity of the disease. Children who had hyponatremia are adequately treated and serum sodium level was repeated after 24 hours after correction and monitored further.All the data was documented and analyzed by subjecting to statistical analysis.

RESULTS

162 subjects (93.10%) had fever; 83 subjects (51.23%) had abdominal pain; 81 subjects (50%) had vomiting; 4 subjects (2.46%) had petechiae: 3 subjects (1.85%) had epistaxis; 5 subjects (3.08%) had melena, and 93 subjects (57.40%) had organomegaly. Shown in table 1& figure 1.

The Majority of subjects had dengue without warning signs, i.e., 60 subjects (34.48%); followed by 59 subjects with warning signs (33.91%), and finally, 55 subjects (31.61%) had severe dengue. The p-value calculated was 0.05 indicating a statistical difference in terms of the dengue severity-wise distribution of subjects. Shown in table 2 & figure 2.

The mean serum sodium levels of subjects with dengue without warning signs disease was 130 ± 21mmol/L. The mean serum sodium levels of subjects with dengue with warning signs was 115 ± 11mmol/L. The mean serum sodium levels of subjects with severe disease were 101 ± 5mmol/L. The p-value calculated was 0.001 indicating a highly significant statistical difference in terms of mean serum sodium levels of study subjects based on their severity of dengue. There was a decrease in the mean serum sodium levels with the severity of the disease. Shown in table 3 & figure 3.

The co-relation value of serum sodium levels with the severity of the disease in subjects with dengue without warning signs was -1.135 indicating a decrease in the serum sodium values with an increase in the disease severity. The co-relation value of serum sodium levels with the severity of the disease in subjects with dengue with warning signs was -2.297 indicating a decrease in the serum sodium values with an increase in the disease severity. The co-relation value of serum sodium levels with the severity of the disease in subjects with severe dengue was -5.356 indicating a decrease in the serum sodium values with an increase in the disease severity. Shown in table 4 & figure 4.

DISCUSSION

100% of subjects had a fever; 51.23% of subjects had abdominal pain; 50% of subjects had vomiting; 2.46% of subjects had petechiae; 1.85% of subjects had epistaxis; 3.08% of subjects had melena and 57.50% of subjects had organomegaly. The results of our study were in co-relation with the past studies conducted by Wang SM et al (79) , T. Pang et al (80) , G. N. Malavige et al (81) .

Study by	Majority typical manifestations (Percentage)
Wang SM et al [79]	Fever (99%)
T. Pang et al [80]	Fever (95%)
G. N. Malavige et al [81]	Fever (93%)
Present study	Fever (93.10%)

The majority of subjects had dengue without warning signs, i.e., 34.48% of subjects; followed by 33.91% of subjects with severe disease, and finally 31.61% of subjects with dengue without warning signs. The p-value calculated was 0.05 indicating a statistical difference in terms of the dengue severity-wise distribution of subjects. The results of our study were in co-relation with the past studies conducted by Surangrat Pongpana et al (76) , Ho et al et al (77) , Guzman MG et al (78) .

Study by	Majority (Percentage)
SurangratPongpana et al [76]	Dengue without warning signs (47 %)
Ho et al et al [77]	Dengue without warning signs (50 %)
Guzman MG et al[78]	Dengue without warning signs (51 %)
Present study	Dengue without warning signs (34.48 %)

The mean serum sodium levels of subjects with dengue without warning signs disease was 130 ± 21mmol/L. The mean serum sodium levels of subjects with dengue with warning signs was 115 ± 11mmol/L. The mean serum sodium levels of subjects with severe denguewere101 ± 5mmol/L. The p-value calculated was **0.001** indicating a highly significant statistical difference in terms of mean serum sodium levels of study subjects based on their severity of dengue. There was a decrease in the mean serum sodium levels with the severity of the disease.The results of our study were in co-relation with the past studies conducted by **T.Srichaikul**[88]**, E.Rueda**[89]**, L. H. Tan**[90]**.**

Study by	MEAN SERUM SODIUM LEVELS (mmol/l)		
	Dengue without warning signs	Dengue with warning signs	Severe Dengue
T.Srichaikul[88]	139 ± 12	118 ± 10	102 ± 7
E.Rueda [89]	136 ± 28	116 ± 12	101 ± 6
L. H. Tan [90]	131 ± 25	113 ± 15	103 ± 3
Present study	130 ± 21	115 ± 11	101 ± 5

The co-relation value of serum sodium levels with the severity of the disease in subjects with dengue without warning signs was **-1.135**indicating a decrease in the serum sodium values with an increase in the disease severity.

The co-relation value of serum sodium levels with the severity of the disease in subjects with dengue with warning signs was **-2.297**indicating a decrease in the serum sodium values with an increase in the disease severity.

The co-relation value of serum sodium levels with the severity of the disease in subjects with severe dengue was **-5.356**indicating a decrease in the serum sodium values with an increase in the disease severity.

The results of our study were in co-relation with the past studies conducted by **Olsen KM** [94]**, Gadkari DA** [95]**, Schoenfeld R** [96]

Study by	CO-RELATION VALUE		
	Dengue without warning signs	Dengue with warning signs	Severe Dengue
Olsen KM [94]	**-1.031**	**-2.312**	**-5.493**
Gadkari DA [95]	**-1.513**	**-2.814**	**-5.582**
Schoenfeld R[96]	**-1.391**	**-2.167**	**-5.915**
Present study	**-1.135**	**-2.297**	**-5.356**

CONCLUSION

Dengue has various presentations and features, but early diagnosis and management can decrease the case fatality rate significantly. Hyponatremia is the most common electrolyte disturbance in dengue fever as well as dengue-associated complications. The more the severity of the disease, the higher the incidence of complications associated with dengue fever. Thus, serum sodium plays a most important role in the prognosis of dengue fever and associated complications.

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Table 1: Distribution of subjects based on clinical presentation.

Clinical presentation	Number of subjects	Percentage
Fever	162	93.10
Abdominal pain	83	51.23
Vomiting	81	50
Bleeding manifestations		
• Petechiae	4	2.46
• Epistaxis	3	1.85
• Melena	5	3.08
Organomegaly	93	57.40

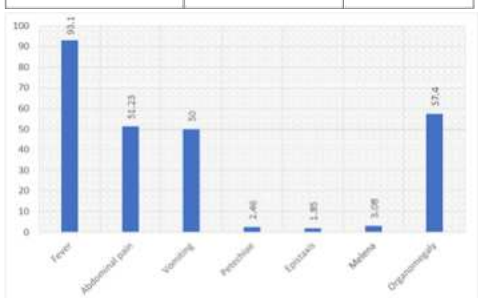

Figure-1: Distribution of subjects based on clinical presentation

Table 2: Distribution of subjects based on the severity of illness

Dengue severity	Number of subjects	Percentage	P value
Dengue without warning signs	60	34.48%	0.05
Dengue with warning signs	59	33.91%	
Severe dengue	55	31.61%	
Total	174	100%	

Table 3: Mean serum sodium levels of study subjects based on their severity of dengue.

Dengue severity	Mean serum sodium (mmol/L)	P value
Dengue without warning signs	130 ± 21	0.001
Dengue with warning signs	115 ± 11	
Severe dengue	101 ± 5	

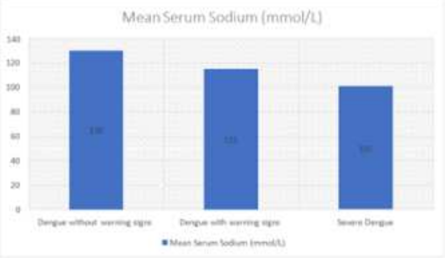

Figure-3: Mean serum sodium levels of study subjects based on their severity of dengue.

Table 4: Co-relation of serum sodium levels with the severity of the disease.

Dengue severity	Co-relation value
Dengue without warning signs	- 1.135
Dengue with warning signs	-2.297
Severe dengue	-5.356

Figure-4: Co-relation of serum sodium levels with the severity of the disease

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