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ORIGINAL ARTICLE

Abnormalities in Serum Electrolytes in DF, DHF and DSS as Prognostic Indicators for Dengue Severity: A Comparative Model

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ABSTRACT

About 250 positive patients were included in the study for diagnosis, of whom 146 were Male and 104 were Female. The M±SD of severity level in DF and DHF patients was 120.5±53.3, Variance=2841.18, Cl95% 1.960, and P=value was calculated as 0.001. The Comparative Analysis of DF and DHF symptoms between group SS (576), df (1), MS (576), F (0.52978) and p=value was calculated p=.478. Whereas within groups SS (15221.5), df (14), MS (1087.25), F (0.52978) and p=value was calculated as p=.478. The M±SD of severity level in DF and DSS patients was 118.4±59.5, Variance=3551.96, Cl95% 1.960, and P=value was calculated as 0.001. The M±SD of dengue serological markers such as 20±9.26, Variance=85.824, and Cl95% 1.960. The M±SD of Na+ in DF 132.4±3.8, DHF 129.5±2.5, DSS 119.5±2.5. K+ in DF 3.38±0.32, DHF 2.97±1.01, DSS 2.4±0.93. Ca+ in DF 8.81±0.53, DHF 7.82±1.2, DSS 6.36±0.57. Mg+ in DF 1.39±0.71, DHF 1.39±0.41, DSS 1.62±0.31. Po4 in DF 3.47±0.53, DHF 2.21±0.62, and DSS 2.34±0.31. It was concluded that dengue shock syndrome patients were found highly affected by serum electrolytes, so we need to focus on the replacement and treatment of serum electrolytes.

Keywords: Dengue virus, Civil Hospital, Serological Markers, Abnormal Serum Electrolytes**,** Clinical manifestation

INTRODUCTION

The source of dengue infection is the dengue virus (Ross, 2010). It consists of a single positive-stranded RNA virus, or Flavivirus can transmit to mosquitoes (Halstead, 2008). There are 4 different types of serotypes of the dengue virus has been discovered, found variation based on the genetic makeup (Konongoi et al., 2016). 47 subspecies of dengue have been verified by researchers based on the immunological grouping (Dash et al., 2006). For the last 2 decades, the dengue virus has grown significantly, making it one of the worst human diseases spread by mosquitoes in tropical countries (Rueda, 2004).

The symptom of the dengue virus infection may appear within 2-6 days (Chan & Johansson, 2012) of the initial infection and can progress towards a quite serious phase. In dengue, fever can fall but it doesn't mean the patient is getting normal (Pal, Dutta, Mandal, Saha, & Tripathi, 2014). Dengue infection is classified based on the infection type such as dengue fever (DF) (Wiwanitkit, 2010), dengue shock syndrome (DSS) (Richardson-Boedler, 2022), and dengue hemorrhagic fever (DHF) (Wang et al., 2020).

The dengue infection acute stage includes (high temperature, headaches, nausea, muscle aches, musculoskeletal pain, and, in rare cases, some brief macular rashes) (Hunsberger et al., 2020), (Kien et al., 2020), (Shams et al., 2018). Respiratory problems may be caused by the dengue virus such as anorexia, nausea, vomiting, constipation, stomach discomfort, hemorrhagic signs, conjunctival injection, pharyngeal erythema, lymphadenopathy, hepatomegaly, facial oedema, petechial are discovered during the evaluation (Khetarpal & Khanna, 2016), (Balasubramanian, Ramachandran, & Amperayani, 2012).

Leucopenia is frequently observed with dengue fever in the parameters of blood tests (Pal et al., 2014). A possible indicator of dengue hemorrhagic fever is thrombocytopenia (Hottz, Tolley, Zimmerman, Weyrich, & Bozza, 2011). Due to the concentration of plasma fluid leakage, which results in an increase in the haemoglobin weight in a unit volume of blood and hemoconcentration might be another frequent indication (Riswari et al., 2022).

In the dengue viral infection, the serum electrolytes have been shown as altered and affected by the dengue virus. The affection of serum electrolytes might be the source of mortality in patients infected with the dengue virus.

Abnormalities in the blood/serum parameters such as sodium, potassium, magnesium, calcium and phosphorus may cause hyponatremia and hypokalemia, also accumulate the blood urea nitrogen and reduce the volume of creatinine by clearance (Lumpaopong et al., 2010). Dengue viral infection requires excessive fluid therapy to maintain the serum electrolytes and other blood components in patients infected with dengue (Bhagyamma, Sreenivasulu, Shyam Prasad, Anuradha, & Durga, 2015). Whereas there are no proper antiviral drugs for the dengue virus, so supportive treatments like a fluid replacement, pain killer, and antipyretic are recommended to overcome the infection severity (Syed et al., 2014).

MATERIALS AND METHOD

Study Area: The study was designed at the Department of Microbiology, University of Haripur and conducted at the Department of Pathology, Civil Hospital Laboratory in New Darband Township.

Selection of patients: We selected 250 patients based on clinical manifestation, active symptoms and diagnostic tests.

Specimen collection and processing: We used purple tops containing EDTA tubes (K3) for blood serology and yellow top (clothing tubes) for the serum electrolytes. The dengue serological markers such as IgG/IgM and NS1 antigen was detected by CTK Biotech® rapid cassette, whereas serum electrolytes were performed Microlab-400 automated instrument used for the analysis of the biochemical parameters.

Medical record: We used the patient's previous history, previous dengue exposure, and risk factors associated with dengue. All patients were registered in the outdoor patient department under the specific registration number.

Ethical approvals: The study approved by the Department of Microbiology, The University of Haripur under registration number F20-2013 and the Research Ethical Review Committee of a Civic Hospital in New Darband gave the Ethical Approval Enlisting #MIC-UOH002.

Statistical significance: The isolated Data such as data (Age, sex, Areas, Medical history, and dengue-related questions were

interpreted through IBM SPSS 2.0 by applying specific tests such as One-way ANOVA, Mean, and Std. deviation.

Methods in Study Serological Detection: Blood samples of 250 patients were tested in the Department of Pathology, Civil hospital New Darband for the aetiology of the dengue virus. We used CTK biotech® rapid cassettes for the detection of serological markers such as IgM, IgG, and NS1. One of CTK biotech®'s great missions is to improve the lives and well-being of people around the globe. Through the spreading out of in vitro diagnostic tools and technology, they have successfully commercialized high-quality products to fight malaria, dengue, Corona, and other serious diseases.

Antibodies test: IgM/IgG and NS1 rapid test kit: We used CTK biotech® a rapid vital diagnostic cassette labelled with artificial antibodies such as IgG and IgM and NS1 Antigen tests for the dengue virus. The vital diagnostic cassette detected different classes of antibodies (IgM, IgG), which are produced by the body against dengue fever infection. Tests were performed after 5-8 days of the initial infection for the detection of IgM antibodies.

NS1 Antigen test: We used the CTK biotech® NS1 vital diagnostic cassette to detect the non-structural proteins NS1 for the presence of dengue virus antigen. We used the serum for the analysis of the NS1 antigen due to the dengue virus secretes the NS1 in the infected person and is found in the portion of body serum.

RESULTS

The Rural Health Center (Civil hospital), New Darband, served as the study's site. The only healthcare facility serving a large number of populated towns and villages (more than 20). Since the questionnaire was completed and we moved through with further diagnostic testing to find the particular antigen and antibodies against DEN-Virus by CTK Biotech®. About 250 positive patients were included in the study for diagnosis, of whom 146 were Male and 104 were Female.

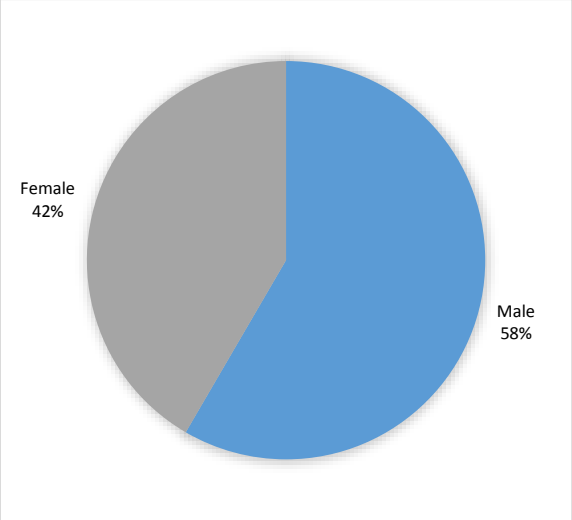

Fig. 1: Dengue affected genders

Symptomology: The sig and symptoms were recorded in the patients infected with the dengue virus.

The M±SD of severity level in DF and DHF patients was 120.5±53.3, Variance=2841.18, Cl95% 1.960, and P=value was calculated as 0.001. The Comparative Analysis of DF and DHF symptoms between group SS (576), df (1), MS (576), F (0.52978) and p=value was calculated p=.478. Whereas within groups SS (15221.5), df (14), MS (1087.25), F (0.52978) and p=value was calculated as p=.478.

Table 1: Comparison of severity level in DF and DHF patients

Symptoms	Dengue fever n=178	DHF n=53	Total	M±SD	Variance, σ^2	Cl95%	P=value
Bleeding	5	92	97	120.5±53.3	2841.18	1.960	0.001*
Abdominal pain	37	12	49				
Skin rash	11	23	34				
Vomiting	63	83	146				
Lethargy	71	70	141				
Joint Pain	67	59	126				
Headache	87.5	94	181.5				
Fever	92.5	97	189.5				

*Significant at <0.005

Table 2: Comparative analysis of DF and DHF symptoms by One-Way ANOVA

Study Variables	SS	df	MS	F=ratio	P=value
Between DF, DHF	576	1	576	F = 0.52978	.478
Within DF, DHF	15221.5	14	1087.25		
Total	15797.5	15			

SS (sum of squares deviation of data), df (Difference), MS (the mean sum of squares of data), and F (the F-statistic).

The M±SD of severity level in DF and DSS patients was 118.4±59.5, Variance=3551.96, Cl95% 1.960, and P=value was calculated as 0.001.

Table 3: Comparison of severity level in DF and DSS patients

symptoms	Dengue fever n=178	DSS n=19	Total	M±SD	Variance, σ^2	Cl95%	P=value
Bleeding	5	7	12	118.4±59.5	3551.96	1.960	0.001*
Abdominal pain	37	9	46				
Skin rashes	11	92	103				
Vomiting	63	87	150				
Lethargy	71	41	112				
Joint Pain	67	82	149				
Headache	87.5	97	184.5				
Fever	92.5	98.5	191				

*Significant at <0.005

Table 4: Comparative analysis of DF and DSS symptoms by One-Way ANOVA

Study Variables	SS	df	MS	F=ratio	P=value
Between DF, DSS	395.0156	1	395.0156	F = 0.30054	592
Within DF, DSS	18400.9688	14	1314.3549		
Total	18795.9844	15			

SS (sum of squares deviation of data), df (Difference), MS (the mean sum of squares of data), and F (the F-statistic).

Dengue Serological markers: We confirmed dengue serological markers such as IgG, IgM and NS1 antigen in dengue-infected patients by CTK Biotech®. The M±SD of dengue serological markers such as 20±9.26, Variance=85.824, and Cl95% 1.960.

Table 5: Distribution of dengue serological markers based on genders

Dengue markers	Male n=146	Female n=104	Total	%	M±SD	Variance	Cl95%
IgM	43	51	94	37.6	20±9.26	85.824	1.960
IgG	36	14	50	20			
IgG/IgM	21	13	34	13.6			
IgM/NS1	12	17	29	11.6			
NS1	34	9	43	17.2			

Electrolytes panel in dengue infection: The serum electrolytes level was analyzed by the Microlab-400 machine. The M±SD of Na+ in DF 132.4±3.8, DHF 129.5±2.5, DSS 119.5±2.5. K+ in DF 3.38±0.32, DHF 2.97±1.01, DSS 2.4±0.93. Ca+ in DF 8.81±0.53, DHF 7.82±1.2, DSS 6.36±0.57. Mg+ in DF 1.39±0.71, DHF 1.39±0.41, DSS 1.62±0.31. Po4 in DF 3.47±0.53, DHF 2.21±0.62, DSS 2.34±0.31.

Table 6: Comparison of serum electrolytes in the patients infected with dengue virus

Blood parameters	Dengue fever n=178	DHF n=53	DSS n=19
Na+	132.4±3.8	129.5±2.5	119.5±2.5
K+	3.38±0.32	2.97±1.01	2.4±0.93
Ca+	8.81±0.53	7.82±1.2	6.36±0.57
Mg+	1.39±0.71	1.39±0.41	1.62±0.31
Po4	3.47±0.53	2.21±0.62	2.34±0.31

Na+ (sodium), K+ (potassium), Ca+ (calcium), Mg+ (magnesium), Po4 (phosphorus)

Table 7: Effect of dengue virus on serum sodium based on the systematic complication

Systems	Systematic obstacles	No hyponatremia %	Mild hyponatremia %	Moderate hyponatremia %	Severe hyponatremia %
Hematopoietic system	Epistaxis	0	14	12	9
	Bleeding from the IV site	9	14	8	10
	Malena	0	1	7	3
	Hematemesis	0	1	17	21
	petechial skin rash	8	11	9	13
	Gum bleeding	0	0	7	5
	Encephalopathy	0	6	11	13
Central nervous system	Hypokalemic paralysis	0	0	4	7
	Guillain barre syndrome	0	1	5	4
	Acute disseminating encephalo myelitis	0	0	3	4
Respiratory system	Acute respiratory distress syndrome	0	0	0	2
Hepato Biliary system	Acute acalculous cholecystitis	0	0	0	2

Table 8: Comparative analysis and effect of DF, DHF and DSS on blood serum electrolytes by One-Way ANOVA

Study Variables	SS	df	MS	F=ratio	P=value
Between DF, DHF, DSS	30.9317	2	15.4658	F = 0.00506	.994
Within DF, DHF, DSS	36710.02	12	3059.1683		
Total	36740.9	14			

SS (sum of squares deviation of data), df (Difference), MS (the mean sum of squares of data), F (the F-statistic)
Post Hoc Tukey Test

Table 9: Pairwise difference, comparison and effect of DF, DHF and DSS on blood serum electrolytes by Post Hoc Tukey HSD

Pairwise Mean	Difference in pairs	Q	P=value	Alpha (Top)	Alpha (Bottom)
DF=29.89 DHF=28.78	1.11	Q = 0.04	(p = .99944)	.05 = 3.7729	Q.01 = 5.0459
DF=29.89 DSS=26.44	3.45	Q = 0.14	(p = .99467)		
DHF=28.78 DSS=26.44	2.33	Q = 0.09	(p = .99755)		

The standardized range statistic (q), the critical values for q corresponding to alpha = .05 (top) and alpha =.01 (bottom).

DISCUSSION

The Rural Health Center (Civil hospital), New Darband, served as the study's site. The only healthcare facility serving a large number of populated towns and villages (more than 20). About 250 positive patients were included in the study for diagnosis, of whom 146 were Male and 104 were Female. We reported a high frequency of dengue in males due to working outdoors, as farmers, laborers, mechanics, and garage workers. Whereas females were seen less infected with dengue due to indoor working status. We isolated different concentrations of hyponatremia associated with systematic conditions based on the highly affected serum electrolyte. We observed serum electrolytes in dengue-infected patients and compare them within a group of DF, DHF, and DSS and between the group DF, DHF, and DSS by One-Way ANOVA. But we did not find a significant comparison (negative results). We analyzed the effect of the dengue virus on serum electrolytes by Post Hoc Tukey HSD. We compared the DF and DHF, DF and DSS, and DHF and DSS to find out the difference in different pairs. The standardized range statistic (q), the critical values for q corresponding to alpha = .05 (top) and alpha =.01 (bottom).

For the early identification and management of individuals at risk of developing severe dengue fever, epidemiological, behavioral, and biochemical characteristics of dengue incidence under study may be useful. Visceromegaly, increased hepatic enzymes, periorbital edema, dermatitis, vomiting, and stomach discomfort may all be indicators of the dengue virus. Policymakers, educators, and medical practitioners might concentrate their efforts to control dengue fever in the city in the regions identified in their analysis where dengue cases were identified most consistently. Co-morbidities associated with dengue infection were recognized to be strong predictors of the virus (Chacko & Subramanian, 2008).

In district Mardan, Khyber Pakhtunkhwa, the previous investigation provided data on the prevalence of dengue infection and proof of hematological abnormalities in individuals who tested positive for the dengue virus. Throughout the observational analyses of dengue infection, the evaluation and correlation of analytical biomarkers, clinical manifestations, and hematological features were crucial. A comprehensive study is crucial for the creation of effective, dependable, and precise screening techniques as well as for the establishment of well-known

prophylaxis approaches to reduce the effects of the dengue virus (Ali et al., 2019).

To distinguish dengue individuals from those diagnosed with diverse factors for rapid febrile infection, they highlighted crucial diagnostic manifestations and serum electrolytes. Relevant evidence can be gathered through serum electrolytes (Sarfraz, Rabbani, Manzoor, & Zahid, 2018).

CONCLUSION

We screened the low volume of serum electrolytes in the dengue shock syndrome, moderate in dengue hemorrhagic fever and normal in the dengue fever. It was concluded that dengue shock syndrome patients were found highly affected by serum electrolytes. We need to boost, replace and elevation of the serum electrolytes in dengue patients due to the dengue virus highly affected the blood parameters of serum electrolytes. We need to focus on the replacement and treatment of serum electrolytes.

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