Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

EVALUATION OF SERIAL LACTATE LEVEL IN THE SEVERELY AFFECTED PATIENT'S WITH DENGUE INFECTION AND ITS CORRELATION WITH RENAL DYSFUNCTION: A PROSPECTIVE STUDY

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ABSTRACT

Background- Dengue infection has been associated with a variety of renal disorders. Acute renal failure is a potential complication of severe dengue infection and is typically associated with hypotension, rhabdomyolysis, or hemolysis. Acute renal failure occasionally complicates severe dengue infection and carries a high mortality rate. The main aim of this study to identify the correlation between the serum lactate level and renal profile as diagnostic and predictive markers of mortality in the affected patient's with dengue infection.

Methods - The study enrolled confirmed 132 severe dengue patients that were hospitalized in Index Hospital, Indore (M.P). They were classified into two groups; survivors and non – survivors. Serum lactate was estimated in the interval of 0 hour (on admission) and 24 hours to MICU. The data analysis is expressed as mean and standard deviation (S.D). Statistical comparisons were performed by student t-test using the SPSS 20.0 software. The P value < 0.05 was considered to be statistically significant.

Results: The mean level of serum lactate (5.6 ± 3.69) were significantly higher in the non- survivor group as compare to survivor group. In renal profile, the mean level of urea (68.2 ± 12.8), creatinine (4.2 ± 0.46) were significantly higher in the non- survivors group as compare to survivors group while sodium (128.5 ± 6.75) and potassium (3.21 ± 0.92) levels were found significantly lower in among the groups.

Conclusions: Patients with RF and dengue viral infections have significantly higher risks for DHF / DSS and mortality. Serum lactate level is important predictor of mortality in severely ill dengue patients. The biochemical parameter such as Urea, Creatinine and Uric acid was associated with severity of dengue infection with mortality. Mild hyponatremia and hypokalemia were more common amongst patients of DF as compared to DHF and DSS.

Keywords: Serum lactate, dengue infection, renal disorders, mortality

1. INTRODUCTION

Dengue fever is a mosquito borne viral infection that constitutes a major health problem in tropical and sub-tropical regions of the world. Over 2.5 billion people of the world's population are now at risk for Dengue. The consequence of Dengue virus (DENV) infection ranges from the asymptomatic condition (Dengue fever (DF), to more severe forms, such as Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS). Severe Dengue is

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

characterized either by plasma leakage, fluid accumulation, respiratory distress, severe bleeding, or organ impairment. Clinical manifestations offer the earliest markers in predicting severe Dengue Disease [1].

Acute kidney injury (AKI) is one of the least studied complications of dengue, but it carries high mortality rates and prolonged hospital stay. Due to the severity of this complication, the risk of developing chronic kidney disease (CKD) and the increasing number of dengue cases reported worldwide, particularly in the tropical and subtropical regions of Africa, Southeast Asia and South America, including Brazil, we embarked on this narrative review, aimed to update the epidemiology of AKI associated with dengue, elucidate the main patho-physiological mechanisms of AKI caused by the dengue virus infection, as well as discuss useful information on the prevention and management of AKI in patients with dengue. [2]

Acute kidney injury (AKI) is a condition where kidneys suddenly stop working properly. It can range from minor loss of kidney function to complete kidney failure. AKI normally happens as a complication of another serious illness. [3] [4]

Patients with Dengue fever are clustered into two groups: one with warning signs including abdominal pain, mucosal bleeding and hepatomegaly that warrant ICU admission and the other without those signs. Early prediction of severe Dengue infection in patients without any warning signs who may later develop severe DHF is very important to give the best supportive care since approved vaccines for immunization are yet to be commercialized. [5]This study is designed to incorporate the prediction of acute renal injury as a routine check in approaching Dengue fever patients.

2. Material and Methods

The observational retrospective study was carried out in patients hospitalized from 15th march 2022 to 22nd October 2023 at Index Medical College, Hospital and Research Center, Indore (M.P). Study was approved by the ethical committee of the institute. Informed consent was obtained according to institutional guidelines. This study was included 132 patients age of 18 to 60 years, hospitalized with probable diagnosed with DF, DHF/DSS and having positive NS-1 antigen or dengue serology. Patients taking anti-platelet medications, having platelet disorder, hemolytic anemia or co morbidities (like IHD, hepatitis due to non-dengue cause, pancreatitis, and chronic renal or liver disease) and infections other than dengue were excluded. Informed consent was signed by each patient before enrolment in the study.

2.1 Blood sampling

5ml of blood sample was collected from each participant in SST or EDTA tube under aseptic conditions. The tube was centrifuged at 3000 to 4000 rpm for 15-20 minutes. Serum or plasma collected carefully and stored in sterile aliquots and freeze at -20^{0}C to -80^{0}C until ready for assay.

2.2 Assay Methods

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Dengue patients was admitted (either directly from the emergency department or transferred from the other wards) to our medical intensive care unit (MICU) for various critical illnesses (presence of warning signs according to WHO criteria for dengue) were screened for their eligibility as study participant[6]. The analysis of serum lactate and renal function test such as Urea, Creatinine, Uric acid, sodium and potassium of all patients included in the study was evaluate by the standard operating procedure on automated analyzer.

3. STATISTICAL ANALYSIS

Result can be expressed as Mean ± SD with 95% confidence interval. Statistical analysis is done by Student's t-test using SPSS 20.0 software. Significant value considered as P value <0.05.

4. RESULTS

Table no. 1: The demographic clinical characteristics of severe dengue in the survivors and non- survivors groups:

Clinical characteristics	Total patients (n= 132)	Survivors (n=108)	Non- survivors (n=24)	P value <0.05
Age (years)	38.6 ± 8.92	29.6 ± 8.16	40.7 ± 10.5	**<0.0001**
Gender				
Male	88 (66.6%)	74 (68.5%)	14 (58.3%)	
Female	44 (33.3%)	38 (35.1%)	06 (25%)	
NS-1	112 (84.8%)	96 (88.8 %)	16 (66.6%)	
IgG	98 (74.2%)	86 (79.6%)	12 (50.0%)	
IgM	108 (81.8%)	94 (87.0%)	14 (58.3%)	
Type of dengue infection				
Dengue fever (DF)	96 (72.7%)	92 (85.1%)	04 (16.6%)	
Dengue hemorrhagic fever (DHF)/ dengue shock syndrome (DSS)	36 (27.2%)	18 (16.6%)	18 (75.0%)	
ARF	59 (44.6%)	40 (37.0%)	19 (79.1%)	
Without ARF	73 (55.3%)	68 (62.9%)	05 (20.8%)	

The demographic representation in table no.1 shows the clinical characteristics of patients with severe dengue in both group (survivors and non-survivors). This results show significant difference of age in survivors group (29.6 ± 8.16) as compare to non-survivors group (40.7±10.5) in severe dengue patients (P <0.0001). We found that males (66.6%) are more likely to develop severe form of disease compare to female (33.3%) in both groups (survivor and non-survivors). 96 Patients with DF (72.7%), 36 patients with DHF/DSS (27.2%) were relatively affects with higher mortality. Out of 108 confirmed dengue patients, 59 (44.6%) had ARF with severe dengue.

Table No. 2: Comparison of serum lactate level at different intervals in the survivors and non-survivors group:-

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PARAMETER	SURVIVORS (n = 108)		NON-SURVIVORS (n = 24)		P-VALUE (P <0.05)
	On admission (0-hours)	After 24-hours	On Admission (0- hours)	After 24- hours	
Lactate (< 2mmol/L)	1.8 ± 0.64	2.2 ± 0.81	3.8 ± 1.42	5.6 ± 3.69	**<0.0001**

The demographic data in table no.2 shows the comparison of serum lactate level of dengue patients in the survivors and non survivors group on the basis of two (0 hours and 24 hours) intervals after admitted to the MICU wards. Comparison between survivor and non- survivor groups, serum lactate level were significantly higher in the non-survivor group after 24 hours of admission in MICU.

Table no. 3: Biochemical findings of severe dengue in the survivors & non-survivors group:

Biochemical Parameters	Survivors (n = 108)	Non-survivors (n = 24)	P value (<0.05)
Urea (15-40 mg/dl)	28.6 ± 7.5	68.2 ± 12.8	**<0.0001**
Creatinine (0.6-1.4mg/dl)	1.4 ± 0.35	4.2 ± 0.46	**<0.0001**
Uric acid (3.5 – 7.0 mg/dl)	4.8 ± 2.17	3.2 ± 2.72	0.0023
Sodium (135-145 mEq/L)	132.4 ± 2.94	128.5 ± 6.75	**<0.0001**
Potassium (3.5-5.0 mEq/L)	3.54 ± 0.56	3.21 ± 0.92	0.0236

In the above data analysis, severe dengue infection patients with acute renal failure had the high significant levels of urea (68.2 ± 12.8), creatinine (4.2 ± 0.46) and sodium (128.5 ± 6.75) in the non-survivors group as compare to survivors group, while the level or uric acid was significantly low in the non-survivors as compare to survivors group. There is no significant difference in the potassium in among groups.

Table no. 4: Comparison between DF and DHF/DSS in the biochemical findings

Biochemical parameters	DF (n = 96)	DHF / DSS (n = 36)	P value (<0.05)
Urea (15-40 mg/dl)	24.3 ± 6.89	78.4 ± 25.26	**<0.0001**
Creatinine (0.6-1.4mg/dl)	1.2 ± 0.24	3.4 ± 1.20	**<0.0001**
Uric acid (3.5 – 7.0 mg/dl)	4.6 ± 2.74	3.8 ± 2.64	0.1338
Sodium (135-145 mEq/L)	134.6 ± 3.48	129.9 ± 4.25	**<0.0001**
Potassium (3.5-5.0 mEq/L)	3.54 ± 0.42	3.04 ± 1.26	0.750
Lactate (< 2.0 mmol/L)	2.9 ± 1.52	5.82 ± 3.69	**<0.0001**

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In contrast, table no.4 the demographic representation shows the significant difference in biochemical finding between Dengue fever (DF) and dengue hemorrhagic fever (DHF) / Dengue shock syndrome (DSS). Compare between DF and DHF / DSS, the levels of Urea (78.4 ± 25.26), Creatinine (3.4 ± 1.20), Sodium (129.9 ± 4.25) and serum Lactate (5.82 ± 3.69) shows a statistically significant (<0.0001) while levels of Uric acid (3.8 ± 2.64) and Potassium (3.04 ± 1.26) was non- significant in DHF /DSS compare to DF.

5. DISCUSSION

Acute renal failure occasionally complicates severe dengue infection and carries a high mortality rate. In this study we primarily focused on the biochemical indices of severity. At different interval of time period we found that the increased serum lactate level is to be associated with metabolic acidosis in the non-survivors group (5.6 ± 3.69) as compare to survivors (2.2 ± 0.81) as a predictor of mortality during intensive care stay. Several studies have suggested that blood lactate concentration has prognostic value in patients requiring critical care. [7-9] **Guzman MG. and Halsted SB et al (2010)** showed increased urea and creatinine levels in all categories of disease. [10] In our study the urea and creatinine levels was significantly increased in the DHF / DSS with high mortality as compared to DF. In this study, mild decreased uric acid level was observed in DHF patients compared to DF patients at the critical phase. Uric acid is an end product of purine catabolism, and numerous studies have shown that uric acid is a major antioxidant in the blood and can help to protect against free-radical oxidative damage. Several studies also show similar results with mild level of uric acid in the dengue infection. [11-12]

Rathod N et al (2017) was found that there exists a positive and significant correlation between difference in sodium and potassium levels with dengue spectrums (DF, DHF, and DSS) which imply that as the difference between the levels increases, greater are chances of the Dengue spectrum towards DHF or DSS. Mild hyponatremia and hypokalemia were more common amongst patients of DF as compared to DHF and DSS. [13]

6. Conclusion

This study demonstrates that patients with RF and dengue viral infections have significantly higher risks for DHF / DSS and mortality. Serum lactate level is important predictor of mortality in severely ill dengue patients. The biochemical parameter such as Urea, Creatinine and Uric acid was associated with severity of dengue infection with mortality. Mild hyponatremia and hypokalemia were more common amongst patients of DF as compared to DHF and DSS. These parameters may be used as prognostic and predictor marker in severely ill dengue patients.

7. Conflicts of Interest

The authors have no conflicts of interest.

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8. References

1. John Wiley and Sons Ltd. Regulatory T-Cells in Acute Dengue Viral Infection. ***The Journal of Cells Molecules System and Technologies***. 2017:26; 162.
2. Paulo R. Bignardi, Gabriela R. Pinto, Maria Letícia N. Boscarioli, Raissa A. A. Lima, Vinícius D. A. Delfino. Acute kidney injury associated with dengue virus infection: a review. ***Braz. J. Nephrol. (J. Bras. Nefrol.)*** 2022; 44(2):232-237.
3. Doi K., Yuen, P.S Eisner, C Hu, X Leelahavanichkul, A Schnermann, J. and Star R.A. Reduced Production of Creatinine Limits Its Use as Marker of Kidney Injury in Sepsis. ***Journal of the American Society of Nephrology.*** 2019: 20; 1217-1221.
4. Ahmed M. and Akhanaizi. Acute Kidney Injury and Continuous Renal Replacement Therapy in Children; What Pediatricians Need to Know. ***Korean Journal of Pediatrics***. 2018; 61, 339.
5. John D.V., Lin Y.S. and Perng G.C.) Biomarker of Sever Dengue Disease: A Review. ***Journal of Biomedical Science***. 2015: 22; 83.
6. Raafat N, Loganathan S, Mukaka M, Blacksell SD, Maude RJ: Diagnostic accuracy the WHO clinical definitions for dengue and implications for surveillance: a systematic review and meta- analysis. ***PLos Negl Trop Dis.*** 2021.
7. Husain FA, Martin MJ, Mullenix PS, Steele SR, Elliott DC. Serum lactate and base deficit as predictors of mortality and morbidity ***Am J Surg***. 2003; 185: 485–491.
8. D'Abrantes R, Dunn L, McMillan T, Cornwell B, Bloom B, Harris T. Evaluation of the prognostic value of lactate and acid-base status in patients presenting to the emergency department. ***Cureus.*** 2021; 13:e15857.
9. Diagnostic accuracy of peripheral venous lactate and the 2009 WHO warning signs for identifying severe dengue in Thai adults: a prospective observational study. Thanachartwet V, Wattanathum A, Oer-areemitr N, et al. ***BMC Infect Dis***. 2016; 16:46.
10. Guzman, M., Halstead, S., Artsob, H., et al. (2010) Dengue: A Continuing Global Threat. ***Nature Reviews Microbiology.*** 11: 7-16.
11. Glantzounis GK, Tsimoyiannis EC, Kappas AM, Galaris DA. Uric acid and oxidative stress. ***Curr Pharm Des***. 2005; 11:4145–51.
12. Ames BN, Cathcart R, Schwiers E, Hochstein P. Uric acid provides an antioxidant defense in humans against oxidant- and radical-caused aging and cancer: a hypothesis. ***Proc Natl Acad Sci USA.*** 1981: 78:6858–62.
13. Rathod N. A study of Hematological& Radiological pro le of patients of Dengue fever in Paediatric Age group 2017; 440–4.