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CLINICAL CHARACTERISTICS AND LABORATORY PARAMETERS IN DENGUE HEMORRHAGIC FEVER

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ABSTRACT

Introduction: Dengue is an infection caused by Dengue virus which transmitted by the bite of an infected mosquito.

Objectives: The main objective of the study is to find the clinical characteristics and laboratory parameters in Dengue hemorrhagic fever among local population of Pakistan**.**

Material and methods: This cross sectional study was conducted in RYK Teaching Hospital Rahim Yar Khan Pakistan. The data was collected from 200 patients of both genders. Clinical data was collected from medical records and compared between the dengue and control groups included demographic data, clinical presentations and all parameters from the CBC.

Results: The results indicate a significant reduction in T-SOD activity in the serum of infected patients (220.15 ± 34.50 U/ml.mg) compared to controls (310.45 ± 39.20 U/ml.mg) ($p<0.05$), suggesting increased oxidative stress during dengue infection. Additionally, MDA levels, a marker of lipid peroxidation, were significantly elevated in infected patients (6.12 ± 1.35 nmol/ml.mg) compared to controls (3.98 ± 0.40 nmol/ml.mg) ($p<0.05$), further highlighting oxidative damage.

Conclusion: It is concluded that dengue infection significantly alters oxidative stress markers and hematological parameters, leading to reduced SOD and CAT activity, elevated MDA levels, and a decreased GSSG/GSH ratio in both serum and liver. These changes reflect the oxidative damage and systemic stress associated with the disease, emphasizing the need for early intervention to mitigate these effects.

Keywords: CBC, Dengue, Antioxidants, Patients

Introduction

Dengue is an infection caused by Dengue virus which transmitted by the bite of an infected mosquito. The disease is detected in about 50 million people across the world every year and 2. At least US $ 5 billion in dengue endemic countries [1]. From the population of Thailand from 1 January 2016 to 20

November 2016 the number of cases recorded is 34677 and the mortality rate is 0. 01/100,000 population [2].

Dengue comes in a spectrum from"; mild disease to stated dengue shock syndrome. Dengue patients normally present with acute febrile illness without localizing sign or symptoms that may depict other infections. Hence there is the necessity to use other additional tests such as the complete blood count (CBC), serological test or blood culture to differentiate between and confirm the diagnosis. The CBC in dengue patients changes by day of fever; Days 3 to 8 show progressive leukopenia, thrombocytopenia and hemoconcentration because of plasma leakage [3]. The results from Brazil showed that mean white blood cell count (WBC) of dengue infected patients were 4. 6 with counts of 0 at the lowest and this guarantees the ability to handle one's bacterial count desired by any patient. The WBC count was reported to be between 7 n 109 /L and the mean platelet count was 26. It was established that the median of platelet count in the patients was approximately 4×109/L while the minimum platelet count in the included patients was below 1×109/L [4].

Dengue fever is usually a mild disease and in most instances it is not fatal and is thus referred to as nonsymptomatic. However, one may progress to DHF or dengue shock syndrome which is a more severe form of the disease. DHF is a serious febrile disease which is associated with damage to the coagulation system and increased vascular permeability; severe progression of the disease leads to DSS [5]. The clinical manifestation of DSS is Manifest as a type of hypovolemic shock; characterized by hemoconcentration and if left untreated this can end up in death. Despite the fact that DF is classified separately from DHF/DSS by standard criteria, the clinical symptoms that occur after a dengue virus infection range from mild to severe reactions as in many other viral illnesses [6].There is still no definite knowledge on how exactly DHF is developed. Many of epidemiologic investigations show that secondary infection with a different dengue serotype is the leading cause of this severe disease. Even though this hypothesis is well accepted there is controversy as to how high viremia levels leads to the pathology and symptoms associated with DHF3. High concentration of different cytokines elaborated by both dengue virus-infected monocytes and activated specific T lymphocytes could perhaps account for the main feature of DHF: plasma leakage [7].

The mechanisms by which DHF/DSS causes liver injury are still unknown. The replication of DV requires many host cellular factors that regulate other cellular activities relevant in cellular physiology and also play a role in the pathogenesis of DV infection. In more recent times, there has been the intracellular redox state implicated in viral infections as well as the development of viral diseases [8]. One of the major causes of cellular damage in virus infected cells is increased ROS levels and ROS can be scavenged by antioxidant molecules, such as GSH SOD, Trx and CAT and these enzymes and molecules make up the cellular system which works against oxidation and are involved in modulating intracellular redox balance. It is a cysteine-containing tripeptide which is the best known and the most widely distributed antioxidant produced in the human organs. GSH is involved more so in the liver where it exists as the major NPS thiol protective constituent in the cellular antioxidant system [10].

The main objective of the study is to find the clinical characteristics and laboratory parameters in Dengue hemorrhagic fever among local population of Pakistan**.**

Material and Methods

This cross sectional study was conducted in RYK Teaching Hospital Rahim Yar Khan Pakistan. The data was collected from 200 patients of both genders.

Biochemical analysis

Clinical data was collected from medical records and compared between the dengue and control groups included demographic data, clinical presentations and all parameters from the CBC. Leukopenia was defined as total white blood cell count of <4000 per cu. Thrombocytopenia was defined as platelet count less than 100 000 per mm. ; /Thrombocytopenia was defined as a total platelet count of less than 100 000 per. cu. mm; monocytosis was determined by the presence of monocyte count of above 10%; eosinophilia was determined where the eosinophils count was above 3% and basophilia where the basophils was above 2% of the total WBC. The CBC parameters were obtained

each time blood test was taken in relation to days of fever up to recovery from the disease at the 10th day or any time the blood component was transfused because the post transfused CBC would not be required.

Measurement of antioxidants

Antioxidants levels in the blood were measured by getting blood samples of patients. The sample of 5cc blood sample was taken and then it was centrifuged at 4000 rpm for the purpose of separate the serum. The extent of lipid peroxidation in the serum as well as in tissue homogenates was assessed using Thiobarbituric Acid (TBA) which reacts with MDA to produce a coloured compound with an absorbance maximum at 532 nm. The total SOD activity in the serum and tissues was assessed depending on the xanthine oxidase method. Serum and tissue homogenate CAT activity was estimated using CAT colorimetric kit purchased from Sigma-Aldrich Chemicals as per manufacturer's instruction. Similarly the concentration of GSSG/GSH in the liver was also measured using the colorimetric kit following the instructions provided by the manufacturer.

Statistical Analysis

Statistical analysis was performed with SPSS 16.0 software. Data from separate experiments are expressed as the arithmetic mean ± standard deviation.

Results

The data was collected from 200 patients of both male and female patients. The results indicate a significant reduction in T-SOD activity in the serum of infected patients (220.15 ± 34.50 U/ml.mg) compared to controls (310.45 ± 39.20 U/ml.mg) ($p<0.05$), suggesting increased oxidative stress during dengue infection. Additionally, MDA levels, a marker of lipid peroxidation, were significantly elevated in infected patients (6.12 ± 1.35 nmol/ml.mg) compared to controls (3.98 ± 0.40 nmol/ml.mg) ($p<0.05$), further highlighting oxidative damage.

Table 01: Alterations of SOD, MDA, and CAT in the Serum

Parameter	Group	Mean ± SD	p-value
T-SOD (U/ml.mg)	Infectious	220.15 ± 34.50	<0.05
	Control	310.45 ± 39.20	
MDA (nmol/ml.mg)	Infectious	6.12 ± 1.35	<0.05
	Control	3.98 ± 0.40	
CAT (U/ml.mg)	Infectious	2.10 ± 0.60	NS (Not Significant)
	Control	2.50 ± 1.05	

The mean platelet count at discharge was 105.4×10^9/L, with a significant drop to a lowest mean of 30.1×10^9/L, indicating severe thrombocytopenia, a hallmark of dengue. Leucocyte counts also decreased, with the lowest mean value recorded at 5.2×10^9/L, reflecting leukopenia. Additionally, liver enzymes showed marked elevation, with AST levels averaging 320.5 IU/L and ALT at 170.9 IU/L

Table 02: CBC Parameters of Selected Patients

Parameter	Mean	SD	Median	95% CI
Platelets (×10^9/L)				
At discharge	105.4	85.3	90.5	95.6-115.2
Lowest	30.1	19.5	25.3	27.8-32.4
Leucocytes (×10^9/L)				
Lowest count	5.2	4.5	3.9	4.3-6.1
Transaminases				
AST (IU/L)	320.5	800.3	185	150.4-490.6
ALT (IU/L)	170.9	290.8	100	110.7-232.4

In the serum, the mean GSSG/GSH ratio for the infectious group was 0.45 ± 0.10, significantly lower than the control group's 0.65 ± 0.12 ($p<0.05$). Similarly, in the liver, the ratio decreased to 0.50 ± 0.08 in infected patients compared to 0.70 ± 0.10 in controls ($p<0.05$).

Table 03: GSSG/GSH Ratio in Serum and Liver

Parameter	Group	Mean ± SD	p-value
GSSG/GSH Ratio (Serum)	Infectious	0.45 ± 0.10	<0.05
	Control	0.65 ± 0.12	
GSSG/GSH Ratio (Liver)	Infectious	0.50 ± 0.08	<0.05
	Control	0.70 ± 0.10	

Discussion

DV infection is a rapidly growing health problem, with an estimated 2.5 billion people at risk and an estimated 50 million annual dengue infections worldwide [10]. But in human it is still unclear that how actual dengue virus infects the human body and till now there is no proper vaccine for dengue. Some reports have postulated that ROS-mediated oxidative stress, which is a reaction of host cells to viral infections, can be implicated in the development of a number of viral diseases including DV [11].

Oxidative stress is a situation characterized by the inability of antioxidant defense system of the cellular to manage and detoxify ROS. Excessive production of ROS is minimized by different techniques; GPx has been determined to be a more sensitive antioxidant enzyme in dengue infected [12]. It is possible that changes in redox markers begin to occur prior to manifestations that signal clinical disease, thereby indicating early pertubation of oxidant/ antioxidant balance [13].

Dengue is an endemic viral illness with frequent transmissions worldwide particularly in the developing countries. However, the economic progress achieved in the past few years, it has not been able to achieve control in this disease and dengue has come from cyclical epidemic phase to non-seasonal phase due to the emergence of new and repeated cases [14]. All these factors have been seen to attribute to increased frequency of complications and development of severe disease forms. Finally, the absence of the technical support and the scientific basis to provide an adequate management of cases with hemorrhagic signs, in particular referring to the transfusions' procedures can possibly have an impact on the death of children in potentially preventable situations [15].

This study showed that females were more affected than male with 57 % cases as compared to Indoensian report of 48%. The obtained results show that mean patient age in our study was 38. 2 years (95% CI: 35. 3-41. 2 years), greater than what was found by Brito in 2007 for a 13-year period in Brazil and a 25-year period in India. These variations may be explained by the case selection criteria and kinds of prior coverage in the hospitals in which the studies occurred [16].

Conclusion

It is concluded that dengue infection significantly alters oxidative stress markers and hematological parameters, leading to reduced SOD and CAT activity, elevated MDA levels, and a decreased GSSG/GSH ratio in both serum and liver. These changes reflect the oxidative damage and systemic stress associated with the disease, emphasizing the need for early intervention to mitigate these effects.

References

1. Palamara AT, Perno CF, Ciriolo MR, Dini L, Balestra E, et al. (1995) Evidence for antiviral activity of glutathione: in vitro inhibition of herpes simplex virus type 1 replication. Antiviral Res 27: 237–253.
2. Ciriolo MR, Palamara AT, Incerpi S, Lafavia E, Bue MC, et al. (1997) Loss of GSH, oxidative stress, and decrease of intracellular pH as sequential steps in viral infection. J Biol Chem 272: 2700–2708.
3. Droge W, Schulze-Osthoff K, Mihm S, Galter D, Schenk H, et al. (1994) Functions of glutathione and glutathione disulfide in immunology and immunopathology. FASEB J 8: 1131–1138.

4. Nencioni L, Iuvara A, Aquilano K, Ciriolo MR, Cozzolino F, et al. (2003) Influenza A virus replication is dependent on an antioxidant pathway that involves GSH and Bcl-2. FASEB J 17: 758–760.
5. Garaci E, Palamara AT, Ciriolo MR, D'Agostini C, Abdel-Latif MS, et al. (1997) Intracellular GSH content and HIV replication in human macrophages. J Leukoc Biol 62: 54–59.
6. Kalebic T, Kinter A, Poli G, Anderson ME, Meister A, et al. (1991) Suppression of human immunodeficiency virus expression in chronically infected monocytic cells by glutathione, glutathione ester, and N-acetylcysteine. Proc Natl Acad Sci U S A 88: 986–990.
7. Matthias LJ, Yam PT, Jiang XM, Vandegraaff N, Li P, et al. (2002) Disulfide exchange in domain 2 of CD4 is required for entry of HIV-1. Nat Immunol 3: 727–732.
8. Cai J, Chen Y, Seth S, Furukawa S, Compans RW, et al. (2003) Inhibition of influenza infection by glutathione. Free Radic Biol Med 34: 928–936.
9. Palamara AT, Garaci E, Rotilio G, Ciriolo MR, Casabianca A, et al. (1996) Inhibition of murine AIDS by reduced glutathione. AIDS Res Hum Retroviruses 12: 1373–1381.
10. Fraternale A, Paoletti MF, Casabianca A, Nencioni L, Garaci E, et al. (2009) GSH and analogs in antiviral therapy. Mol Aspects Med 30: 99–110.
11. Chaloemwong, J., Tantiworawit, A., Rattanathammethee, T. *et al.* Useful clinical features and hematological parameters for the diagnosis of dengue infection in patients with acute febrile illness: a retrospective study. *BMC Hematol* **18,** 20 (2018). https://doi.org/10.1186/s12878-018-0116-1
12. Ho, TS., Wang, SM., Lin, YS. *et al.* Clinical and laboratory predictive markers for acute dengue infection. *J Biomed Sci* **20,** 75 (2013). https://doi.org/10.1186/1423-0127-20-75
13. David A. Muller, Alexandra C. I. Depelsenaire, Paul R. Young, Clinical and Laboratory Diagnosis of Dengue Virus Infection, *The Journal of Infectious Diseases*, Volume 215, Issue suppl_2, 1 March 2017, Pages S89–S95, https://doi.org/10.1093/infdis/jiw649
14. Kabra SK, Jain Y, Singhal T, Ratageri VH. Dengue hemorrhagic fever: clinical manifestations and management. Indian J Pediatr. 1999 Jan-Feb;66(1):93-101. doi: 10.1007/BF02752362. PMID: 10798041.
15. Mallhi TH, Khan AH, Adnan AS, Sarriff A, Khan YH, Jummaat F. Clinico-laboratory spectrum of dengue viral infection and risk factors associated with dengue hemorrhagic fever: a retrospective study. BMC Infect Dis. 2015 Sep 30;15:399. doi: 10.1186/s12879-015-1141-3. PMID: 26423145; PMCID: PMC4590689.
16. Lee MS, Hwang KP, Chen TC, Lu PL, Chen TP. Clinical characteristics of dengue and dengue hemorrhagic fever in a medical center of southern Taiwan during the 2002 epidemic. J Microbiol Immunol Infect. 2006 Apr;39(2):121-9. PMID: 16604244.