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ORIGINAL RESEARCH

Correlation between diabetics and non diabetics recovery in hospitalised dengue positive patients

[1]Dr. Kanika Munish, [2]Dr. Gunjan Singhal, [3]Dr. Abhishek Gupta

[1-3]Assistant Professor, Department of Pathology, GBCM DRKKBM Hospital, Dehradun, Uttarakhand, India

Corresponding Author
Dr. Abhishek Gupta
Assistant Professor, Department of Pathology, GBCM DRKKBM Hospital, Dehradun, Uttarakhand, India

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ABSTRACT

Introduction – Dengue fever is a highly prevalent infectious disease that is rapidly increasing worldwide. There is a connection between Diabetes Mellitus and long-term inflammation.The aim of present study was to find out the correlation between diabetics and non diabetics recovery in hospitalised dengue positive patients. **Material and methods –** The prospective observational study was conducted at a tertiary care centre among 100 admitted dengue patients [50 were diabetic (Group A) and 50 were not diabetic (Group B)] during the study period of one year. Clinical and demographic data was recorded and results were analyzed using SPSS version 25.0. **Results –** The levels of all three inflammatory mediators were higher in patients with both dengue and diabetes compared to those with dengue alone. These differences were also found to be statistically significant ($p < 0.05$). Mortality rate (4/50) was higher in those having diabetes with dengue. **Conclusion –** Patients with dengue and diabetes mellitus are more susceptible to bleeding disorders, which can lead to illness and death. This is due to the activation of inflammatory processes that cause high blood sugar levels and poor control of blood sugar.

Keywords – diabetes mellitus, dengue, fever, hyperglycemia, inflammation

INTRODUCTION

Dengue is a widely recognised viral illness that is prevalent in tropical and subtropical regions of the world and has a significant impact on both illness rates and death rates. The transmission occurs through the female Aedes mosquito vector [1]. In the past, dengue was a leading cause of death among children in many nations where the disease is prevalent. Currently, there is a rising trend in the number of dengue infection cases among adults. The expansion of infection to previously unaffected regions in temperate portions of the world results in noticeable alterations in the epidemiological pattern and significant economic consequences of dengue [2].

Dengue infection is the result of being infected by any of the four distinct serotypes of the dengue virus. The symptoms experienced by patients can vary greatly, ranging from mild infection to a severe and potentially fatal condition known as dengue shock syndrome [1].

The infectivity and clinical characteristics vary significantly based on age, immunological status, and underlying medical conditions.

Dengue is pathologically marked by elevated levels of inflammatory markers such as CRP, endocan, and IL-8. Therefore, individuals with co-morbid diseases of inflammation, such as diabetes, may have a more severe and life-threatening form of dengue fever [3]. Multiple studies over the years have consistently shown a strong correlation between diabetes and inflammation.

Hyperglycaemia disrupts the structure and function of the endothelium, causing a long-lasting inflammatory condition triggered by the activation of T-lymphocytes and the release of proinflammatory cytokines such gamma interferon (IFN) and TNF [4,5]. These cytokines have a significant impact on one of the main symptoms of complicated dengue fever. In addition, it has been found that DM has detrimental effects on the immune system, including decreased chemotaxis, leukocyte adhesion, and infection phagocytosis, which increases an individual's vulnerability to infections [6-10].

Dengue patients with preexisting diabetes mellitus may experience severe impairment of glucose metabolism, leading to both hyperglycemia and hypoglycemia. [11] The primary consequences

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observed are diabetic ketoacidosis and hyperosmolar hyperglycemia.These individuals mostly have symptoms such as nausea, vomiting, and abdominal discomfort, which are common to both diabetic ketoacidosis and severe dengue. Likewise, individuals taking oral hypoglycemic medications may have hypoglycemia as a result of inadequate oral consumption or vomiting during dengue infection. [11] In diabetic patients, electrolyte imbalance can complicate the treatment of dengue. [11] Therefore, this study is aimed to gain the better picture for understanding the correlation between diabetics and non diabetics recovery in hospitalised dengue positive patients

MATERIAL AND METHODS

The prospective observational study was conducted at a tertiary care centre among admitted dengue patients during the study period of one year. Ethical permission was taken from institutional ethics committee before commencement of study. Patients were asked to sign an informed consent form before participating in the study.

Through consecutive sampling a total of 100 dengue patients were selected among which 50 were diabetic (Group A) and 50 were not diabetic (Group B). Patients were selected on the basis of inclusion and exclusion criteria.

Inclusion criteria- Patient ages between 15 and 65 years, patient with confirmed dengue diagnosis and patient with or without diabetes since 5 years.

Exclusion criteria- Pregnant females, patients with autoimmune or chronic infectious disease and patients with haematological disorders and neoplasia .

Details like age, gender, medical history (specifically diabetes and duration), height, and weight for each patient was noted. On the initial day, blood samples were collected from these patients. The haematological biochemical analysis comprises the assessment of various parameters, including the count of white blood cells (WBC), hematocrit levels, platelet count, blood glucose levels, serum creatinine levels, liver function tests (specifically SGOT and SGPT), serum albumin levels, total protein levels, and glycated haemoglobin (HbA1c, applicable exclusively to diabetic patients). The blood pressure of all the patients was measured and included in the study.

Blood samples were collected and processed using an ELISA test kit and laboratory research. The samples were centrifuged to get serum, which was then used to analyse inflammatory biomarkers including C-reactive protein, Serum Endocan, Interleukin 8, and Perfusion Index.

The data was presented as the mean value together with the standard error of the mean (SEM). The data gathered in the study were analysed using SPSS version 25.0. A comparison was made between the variables of diabetes and non-diabetic patients using the student t-test. The Mann-Whitney U test was utilised to compare the disparities in endocan, CRP, and perfusion index between the two groups. The association between inflammatory indicators and HbA1c data was evaluated using the Pearson correlation coefficient test. A p-value less than 0.05 was deemed statistically significant.

RESULTS

Table 1 shows the socio-demographics, symptoms, bleeding type, and laboratory characteristics of the study population. The mean age of patients diagnosed with both dengue and diabetes was 56.75 ± 1.92, while the mean age of patients diagnosed with only dengue was 58.78 ± 2.80. The number of males affected by dengue was higher than the number of females, both among those with diabetes and those without diabetes. The study evaluated bleeding sites in individuals with dengue, comparing those with diabetes to those without diabetes. It was found that individuals with diabetes had a higher incidence of skin damage (petechiae) compared to the other study group. On the other hand, patients without diabetes had a higher incidence of bleeding in the gastrointestinal system (melena) and mucous membranes (epistaxis), and this difference was statistically significant ($p \leq 0.05$).The clinical features, including blood glucose (HbA1C), SGPT, SGOT, and serum creatinine, serum albumin and platelet count, were found to have a significant statistical association with individuals who have both dengue and diabetes ($p \leq 0.05$).

Table 1 Baseline characteristics of patients

Variable		Group A	Group B	P value
Mean age (years)		56.75 ± 1.92	58.78 ± 2.80	0.612
Gender	Male	30 (60)	35 (70)	0.456
	Female	20 (40)	15 (30)	
Symptoms	Fever	30 (60)	20 (40)	0.349
	Arthralgia	20 (40)	25 (50)	0.456
	Myalgia	25 (50)	23 (46)	0.368
Site of bleeding	Petechiae	35 (70)	28 (56)	0.384
	Malena	10 (60)	20 (40)	0.453
	Epistaxis	5 (10)	2 (4)	0.328
Laboratory results	HbA1c	6.87±1.90	5.03±1.03	0.01
	SGPT	138.23±13.1	106.78±8.34	0.03
	SGOT	181.28±12.4	150.39±7.09	0.02

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	S.creatinine	1.04±0.35	1.29±0.16	0.01
	S.albumin	0.70±0.04	1.27±0.89	0.02
	Platelet count	48.76±3.2	59.21±1.8	0.02

The levels of inflammatory markers (C-reactive protein, Endocan, Interleukin-8, and Perfusion Index) were measured in both groups: patients with dengue and diabetes, and patients with dengue but without diabetes. The levels of all three inflammatory mediators were higher in patients with both dengue and diabetes compared to those with dengue alone. These differences were also found to be statistically significant ($p < 0.05$).

Table 2 Comparison of inflammatory factors

Inflammatory variable	Group A	Group B	P value
CRP	37.09±1.23	18.79±0.67	0.023
Endocan	43.21±1.90	33.45±0.34	0.015
IL-8	143.78±1.08	103.34±0.24	0.017
Perfusion index	3.89±0.13	1.90±0.05	0.014

In this study, treatment outcomes showedstatistically difference (p=0.042) in both groups and patients with diabetes mellitus had more complications but results were non significant (0.321) as shown in table 3.

Table 3 Comparison of treatment outcomes and complications in two groups

Outcome		Group A	Group B	P value
Treatment	Complete recovery	46	48	0.042
	Death	4	2	
Complications	Yes	7	5	0.321
	No	43	45	

Table 4 shows the relationship between the inflammatory factors and both groups. The inflammatory markers (CRP, endocan, and perfusion index) showed a statistically significant ($p < 0.05$) positive relationship in those who had both dengue and diabetes. The serum levels of CRP and Endocan exhibited a significant correlation with the group of individuals who had both dengue and diabetes. Conversely, the association between the perfusion index and this group was sporadic and inconsistent. In addition, the study found that there was no significant link between inflammatory markers (CRP, Endocan, IL-8, and perfusion index) and dengue patients without diabetes.

Table 4 Correlation values of inflammatory variables of dengue patients with and without diabetes.

Inflammatory variables		Group A	Group B
CRP	r	0.987	0.134
	p value	0.014	0.569
Endocan	r	0.923	0.07
	p value	0.001	0.78
IL-8	r	0.788	0.08
	p value	0.004	0.897
Perfusion index	r	0.435	0.038
	p value	0.007	0.881

DISCUSSION

Diabetes and dengue are becoming more common and occurring more frequently worldwide. Nevertheless, it is crucial to establish the correlation between dengue and diabetes mellitus. Furthermore, if the severity of dengue continues to increase in people with uncontrolled or poorly controlled diabetes, it will lead to greater morbidity and death compared to both diabetic and non-diabetic individuals [12-14]. The current study found that diabetic patients had a higher percentage of elevated inflammatory markers and decreased platelet counts. This indicates that diabetes may contribute to a higher susceptibility to severe dengue infection. Although some investigations have demonstrated that diabetes mellitus can result in immunological and endothelial dysfunction, the specific mechanisms by which diabetes leads to Dengue Haemorrhagic Fever (DHF) remain unclear [15].

In our study maximum patients were in the age group of 50 to 60 years and female participants were affected more than males. The most common symptom was fever in both groups. Skin damagae was higher in diabetic group (petechiae). The glycelated haemoglobin was higher in diabetic group as compared to non diabetic group. Other inflammatory

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markers were also more worse in patients with diabetic group.

In a study done by George T et al it was found that the prevalence of dengue infection in our research group was predominantly detected in adult males under the age of 45 which was in contrast to our study in to age. [16] In theirstudy all patients had fever, accompanied by other typical symptoms such as headache and retroorbital pain, as documented in previous investigations.[17,18] Although there were not significant variations in the symptoms between deceased patients with and without diabetes, indicators such as pedal edoema, pleural effusion, and ascites were observed more frequently in deceased patients with diabetes. Both the diabetic dengue patients who survived and those who died were found to have high blood sugar levels, known as hyperglycemia, due to stress. The occurrence of stress-induced hyperglycemia is the result of an intricate interaction of counter-regulatory hormones, including catecholamines, growth hormone, cortisol, and cytokines.[19] The administration of corticosteroids was linked to a slightly increased likelihood of hyperglycemia, but did not result in any negative consequences or prolonging of viremia.

The levels of all three inflammatory mediators were higher in patients with both dengue and diabetes compared to those with dengue alone with significant relationship. The inflammatory markers (CRP, endocan, and perfusion index) showed a statistically significant ($p < 0.05$) positive relationship in those who had both dengue and diabetes in our study. Increased levels of CRP and Endocan trigger endothelial dysfunction which may be because of the biological mechanism that leads to the severity of dengue fever in diabetic subjects, by increasing the intrinsic permeability of the endothelial surface resulting with dengue complications in the diabetic population. In 2006, Chen et al., indicated diabetes can be a risk factor for mortality in adult DHF patients by demonstrating that serum levels of inflammatory markers(IL-6, IL-10 and CRP) was increased and positively correlated with the disease severity [12]

In our study the mortality rate was higher in diabetic group as compared to non diabetic group. In a study done by Latt KZ it was found that the overall mortality rate of dengue cases were 0.83%. Specifically, the fatality in diabetic group was 2.5% in comparison to 0% in non-diabetic group. Most of the patients were completely recovered similar to our study.[20]

CONCLUSION

The present study examined the relationship between inflammatory variables (CRP, Endocan, IL-8, and Perfusion Index) and glycated haemoglobin (HbA1C). The results showed a positive correlation between these variables in dengue patients with diabetes, while a linear correlation was observed in dengue patients without diabetes. Therefore, it is necessary to manage diabetes in patients to improve outcomes and effectively prevent the spread of dengue infection through a comprehensive national eradication campaign implemented by government authorities.

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