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ACUTE KIDNEY INJURY IN DENGUE FEVER A ONE YEAR HOSPITAL BASED PROSPECTIVE STUDY

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ABSTRACT

Background: Dengue fever is amongst the most cardinal arthropod-borne infection among humans. Acute kidney injury is so far not a well-studied dengue complication. The renal abnormalities, though not common, are acute kidney injury, proteinuria, glomerulonephritis, and hemolytic uraemic syndrome, which are considered complications of the disease. This study was designed to evaluate the prevalence of acute kidney injury in dengue fever and find out the predictors of the development of acute kidney injury in patients with dengue.

Methods: This one-year hospital-based cross prospective study was performed in the Department of General Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala from March 2020 to April 2021. A total of 120 eligible patients with dengue were enrolled. These patients were evaluated for acute kidney injury based on acute kidney injury network criteria.

Result: The majority of the patients were males 57.5% and the male to female ratio was 1.35:1. Most of the patients were aged between 31 to 50 years 40.8% and mean age was 42.23±16.28 years. Majority of the patients 72.5% had dengue fever, 13.3% of the patients had dengue fever with warning signs and 14.2% of the patients had severe dengue. The prevalence of acute kidney injury was 27.5% in patients with dengue fever.

Conclusion: Based on the findings of this study it may be concluded that, there is a high prevalence of acute kidney injury (27.5%) in patients presenting with dengue fever in the study area hence it cannot be neglected.

KEYWORDS : Dengue, AKIN criteria

INTRODUCTION:

Arboviruses asseverate a pressing public wellbeing predicament. These are customarily accompanied by outbreaks that have huge moneymaking and social repercussions in tropical and subtropical areas around the world. [1] Dengue fever is amongst the most cardinal arthropod-borne infection among humans. Around the world, an estimated 2.5 billion individuals are at peril of infection. [2] It is thus appraised that approximately beyond the 50 million positive infections can be thought to occur each year, of which 500,000 inpatients are of dengue hemorrhagic fever, for the most part amid child, the case fatality rate of which outstanding 5% in some regions. [3] DF outbreaks have outstretched more or less in 120 nations and numerous of these countries, with high prevalence. [4] During the current decapod, DF has set off the second most widespread mosquito suffer infection after malaria. The total cases of DF have gotten to around 50 million in total. The spread of the virus in non-endemic regions with a high vector (Aedes aegypti and Ae. albopictus) population. [5] Despite this the prevention causes steps laid by the specific governments since that time, one by one outstretched have taken place, Though it was not proclaimed an epidemic in 2015, the number of cases documented was on the higher side. In India, the occurrence of dengue has been expanded year after year. Every monsoon season welcomes an outbreak of DF. New Delhi, from 1967-to 2003 has seen seven major outbreaks [6]. A substantiate case of dengue fever is a case which is confirmed by dealing with the given laboratory standards, that is, dengue virus isolation from serum or affirmation of tetra fold or greater change in reciprocal of IgG or IgM antibody numerations to other dengue dander in serum samples paired with cerebrospinal fluid (CSF) using techniques like enzyme-linked immunosorbent assay (ELISA). [7] Acute kidney injury (AKI) is so far not a well-studied dengue complication. The renal abnormalities, though not common, are AKI, proteinuria, glomerulonephritis, and hemolytic uraemic syndrome, which are considered complications of disease [8]. Furthermore, when given an insight there are only a few case reports and also in the literature, very few studies are done on AKI in dengue viral infection (DVI). [9-10] There are many timely epidemics of dengue infection and a limited database on the inclusion of the renal system in dengue infection. This study was planned to estimate the prevalence of acute kidney injury in dengue fever.

METHODOLOGY:

This study was done in the Department of General Medicine, Maharishi Markandeshwar Institute of medical science and research, Mullana, Ambala from March 2020 to April 2021. The study is a hospital-based prospective study conducted in/ outpatients Department, Department of General Medicine with clinical suspicion of dengue fever confirmed on NS1/IgM from March 2020 to April 2021 on 120 patients. Patients fulfilling the inclusion criteria were enrolled based on convenient sampling. The patients with clinical suspicion of dengue fever confirmed on NS1/IgM are included in the study. Individuals with a known case of diabetic nephropathy, hypertensive nephropathy, known case of chronic kidney disease, infectious diseases like malaria, enteric fever. case of cirrhosis, liver dysfunction, and history of treatment with NSAIDs are excluded from our study. Those who were eligible were briefed about the nature of the study and written informed consent was obtained prior to the enrolment. Prior to the commencement, the study was approved by the Institutional Ethics Committee of Maharishi Markandeshwar Institute of Medical Science and Research, Mullana, Ambala. Patients were then interviewed and demographic data like gender and age were noted. Patients were also interviewed for the detailed clinical presentation, history of associated medical conditions like chronic kidney disease, diabetic nephropathy, hypertensive nephropathy. A thorough general physical examination was conducted to assess vital parameters, anthropometry, and clinical signs followed by a systemic examination. All these findings were noted on a predesigned and pretested Performa. Investigations underwent are-Complete blood count with Platelet count and total count, peripheral smear, Prothrombin time (PT), International normalized ratio (INR), Activated partial thromboplastin time (aPTT), Urine analysis-Routine &Microscopy (Proteins, casts, red blood cell, white blood cell), Urine output (per day measurement), Serum creatinine and blood urea, Serum glutamic oxaloacetic transaminase (SGOT), Serum glutamic pyruvic transaminase (SGPT), Serum electrolytes (Na, K, HCO_3), Random blood sugar, Ultrasound abdomen (Gall bladder wall thickness, pleural effusion, ascites), Special tests if required (Urine myoglobin, Kidney biopsy)

Based on the Acute Kidney Injury Network (AKIN) criteria, the patients were evaluated for the diagnosis of AKI based on the increase in serum creatinine of 0.3 mg/dL or > 50% developing in < 48 hours or urine output < 0.5 mL/Kg/hr for more than six hours.

The following predictors of AKI were evaluated;

- Sex
- Age
- Severity of dengue fever
- Other associated complications
- Serositis
- Thrombocytopenia at admission
- Blood urea at admission
- Creatinine at admission
- Laboratory parameters
- Imaging parameters

Statistical analysis

The data obtained were tabulated on a Microsoft Excel spreadsheet. The categorical data were expressed as ratios and percentages. The prevalence of acute kidney injury in dengue fever was expressed in terms of percentage. Chi-square test and/or Fisher's exact test were used to find the association between the predictors of the development of acute kidney injury. Continuous data were expressed as mean ± standard deviation (SD) and an independent sample-test was used to compare the data. At a 95% confidence interval (CI), a probability value ('p' value) of less than or equal to 0.050 was considered to be statistically significant.

RESULT:

This one-year hospital-based cross-sectional study was carried out in the Department of General Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala from March 2020 to April 2021. During the study period a total of 135 adults presented with dengue NS1/IgM tests. Of them, 120 were eligible and 15 were excluded. During the analysis, the majority of the patients were males 57.5% and 42.5% were females with most of the patients being aged between 31 to 50 years (40.8%) followed by < 30 years (30%). The mean age was 42.23 ± 16.28 years and the median age was 42 years with a range of 18 to 78 years. When considering the present complaints fever was manifested by 100% of patients, followed by myalgia, nausea, headache, vomiting, and retro-orbital pain. The detailed description of symptoms is explained in table 1. **T**he general condition of the patients was assessed on the basis of pallor, icterus, petechial hemorrhage, and rashes, and frequency also follows the same trend with numbers standing at 19,15,9,8 respectively. The haematuria (26) and proteinuria (25) was also observed with 34 patients showing the Total Leukocyte count <1000 /cumm. Hepatic function is asses on the basis of liver enzymes with ascites present in 36.7%. The majority of patients with 74.9% show normal X-ray findings with pleural effusion in 14.2%, ARDS in 8.3%, and ground glass appearance in 1.7% of the patients. Upon diagnosis of dengue without warning signs, dengue with warning signs and severe dengue was observed in 87 (72.5%), 16 (13.3%), and 17 (14.2%) respectively. The diagnosis of AKI with dengue was observed in 27.5% with 83.3% of the patient improved and discharged and mortality was noted in 16.7% of the patients. When AKI is associated with sex the applied statistics show that amongst the total 33 AKI-associated patients 9 were females and 24 were males. Similarly, the AKI is associated with age showing the majority of age groups lie between 31-50 years old (48%), dengue severity where the majority stands with dengue with no warning signs (16, 48.5%) and other complications (ARDS, CAD, MODS and sepsis) with chi-square value stands at 4.319, 10.029 and 19.564 respectively. The creatinine and urea values were also observed as the marker of deteriorating renal functions. Platelets values were also measured in our study and 14 patients were found to have the platelets in the range between 20-49 X1000/ cumm and 9 patients had plates less than 20 thousand per cumm

Table 1: Showing the present complaints of the patients

Present Complaints	No. of cases	Percentage
Fever	120	100.0%
Vomiting	52	43.3%
Headache	55	45.8%
Cough/Cold	12	10.0%
Rash	8	6.7%
Dyspnoea	28	23.3%
Nausea	57	47.5%
Myalgia	75	62.5%
Joint pain	30	25.0%
Retro orbital pain	23	19.2%
Abdominal pain	51	42.5%
Loose stools	8	6.7%
Oliguria	5	4.2%
Urine output	28	23.3%
Haemoptysis	2	1.7%
Epistaxis	3	2.5%
Malena	11	9.2%
Hematemesis	3	2.5%
Altered Mental Status	10	8.3%
Bleeding gums	10	8.3%
Visit to Endemic area	29	24.2%

Patients with numbers were having creatinine on the higher sides with >1.2 stands with 25 (75.8%) and the chi-square value stands at 54.2 whereas for urea the major numbers stand at 72.7% constituting the values range at 18-49 mg/dl, the chi-square value of which stands at 44.21 (see table 2 for more details). In the present study significant differences were noted in patients with and without AKI pertaining to age (49.94±15.15 vs 39.31±15.81 years; p<0.001), pulse rate (108.70±20.46 vs 90.15±14.59 per minute; p=0.000), respiratory rate (23.13±6.72 vs 18.18±2.17 per minute; p<0.001), total count (12480.67± 8776.09 vs 7348.39±5987.84per cumm; p=0.000), neutrophils (70.82±15.40vs 59.86±17.30percent; p<0.002), lymphocyte (22.15±14.00 vs 30.28±14.90percent; p=0.008), blood urea (88.64±57.37vs 29.17±20.19mg/dL; p<0.000), Serum creatinine on day one (2.36± 1.96 vs 0.86±0.51mg/dL; p<0.000), total bilirubin (1.60±2.31 vs 0.69±1.07mg/dL; p=0.004), direct bilirubin (0.97± 1.62 vs 0.31±0.59mg/dL; p=0.001), SGOT (1353.91±4351.35vs 202.69±442.53IU/L; p=0.016), SGPT (431.18±991.64vs 141.66±339.79IU/L; p=0.018), serum albumin (2.51±0.61vs 2.89±0.49mg/dL; p<0.001) and alkaline phosphatase (186.97±143.44 vs 120.78±58.06mg/dL; p=0.000).

DISCUSSION:

The incidence of dengue is equal in males and females. However, in the present study males (69, 57.5%) were more than females (51, 42.5%) with male to female ratio of 1.35:1. These findings were comparable with a study conducted by Sharma et al. (1998) who reported male to female ratio of 3:1. Laboratory parameters involves at admission platelet count of < 20000 was noted in 14.1%of the patients and 33% of the patients had platelet count between 20001 to 49999 /cumm that means nearly half of the patients (47.1%) had low platelet count.

Table 2: Chi-square values and p- values of parameters

Sr. No	Parameter	Chi-Square value	P-value
1.	Sex	4.319	0.038
2.	Age	10.029	0.007
3.	Dengue severity	19.564	0.001
4.	Creatinine	54.213	0.001
5.	Urea	44.421	0.0001

The platelet count ranged between 4000 to 319,000 /cumm at admission and the mean was lower than the normal reference range (84.1±97.1 x 103 /cumm) which gradually increase over a period (111.85±91.08x 103 /cumm) suggestive of improvement. The total cell count was raised in (34 patients, 28.3%) and the mean total count was profoundly high (8759.76±7205.4/cumm) suggestive of infection. Also, the majority of the patients had higher SGOT (94 patients, 78.3%) and SGPT (101 patients, 84.2%) levels. Also, the mean SGOT (519.275±2345.11 IU/L) and SGPT (221.27±603.92IU/L) were very high. A study from Delhi by Sharma et al. (1998) showed that SGOT and SGPT were deranged in 88.4% and 76.7% of patients respectively. [11] Another study conducted by Agarwal et al (2010) also showed male preponderance that male to female ratio of 1.9:1. In the present study, the age ranged between 18 to 78 years. The common age group was 31 to 50 years (40.8%) followed by <30 years (30%). Dengue affects people of all ages. Our study suggests that DF was widely prevalent among the younger age group. [12] A retrospective study to review the changing epidemiology of dengue between the years 2002 and 2008 by Chakravarthy A et al(2012) reported the presence of dengue in all the age groups of the study population.[13] The mean age noted in the present study was similar to the study from AIIMS by S. Sharma et al (1998) who reported the median age as 26.3 years and also similar to the Mexico study by Navarette J (2005) that is, 26.9 years. These series indicate that the most commonly affected age group is between 20 to 40 years. [14] In this study serum, creatinine levels were estimated at the time of admission and serial measurement were obtained on a day-to-day basis in select cases. The creatinine levels at admission ranged between 0.1 to as high as 9.69 mg/dL but the mean serum creatinine levels were 1.27±1.29mg/dL and median levels were 0.87mg/dL suggestive of normal kidney function. However, based on AKIN criteria, 33 out of 120 patients developed AKI. Hence the prevalence of acute kidney injury in dengue fever was 27.5%. Looking at the raised serum creatinine level at admission, it may be hypothesized that, every one out of three patients with dengue fever is likely to present with raised serum creatinine as a consequence of dengue and accordingly is at high risk of developing AKI. In this study serum, creatinine levels were estimated at the time of admission and serial measurement were obtained on a day-to-day basis in select cases. The creatinine levels at admission ranged between 0.1 to as high as 9.69 mg/dL but the mean serum creatinine levels were 1.27±1.29mg/dL and median levels were 0.87mg/dL suggestive of normal kidney function. However, based on AKIN criteria, 33 out of

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Abbreviations:

DF: Dengue Fever, IgG: Immunoglobulin G, IgM: Immunoglobulin G, CSF: Cerebrospinal fluid, ELISA: Enzyme-linked immunosorbent assay, AKI: Acute kidney injury, DVI: Dengue viral infection, NSAIDs: Non-steroidal anti-inflammatory drugs, PT: Prothrombin time, INR: International normalized ratio, aPTT: Activated partial thromboplastin time, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, WHO: World Health Organization, DHF: Dengue Hemorrhagic fever, AKIN: Acute Kidney Injury Network, SD: Standard Deviation, CI: Confidence Interval, ARDS: Acute Respiratory Distress Syndrome, CAD: Coronary artery disease, MRD: Medical Records Department, AIIMS: All India Institute of Medical sciences and research.

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