|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| , | **Total**  **(n=170)** | **Dengue with renal involvement**  **(n=51)** | **Dengue without renal involvement**  **(n=119)** | **2-tail sig**  **or**  **p-value** |
| Age in years | 36 (23-46) | 39 (28-50) | 34 (22-43) | 0.30 |
| Male | 101 (59) | 32 (62.7) | 69 (58) | 0.56 |
| **Address** |  |  |  |  |
| Urban | 85 (50) | 19 (37.3) | 66 (55.5) | **0.03** |
| **Comorbidities** |  |  |  |  |
| Diabetes | 15 (8.8) | 4 (7.8) | 11 (9.2) | 0.76 |
| Hypertension | 11 (6.5) | 4 (7.8) | 7 (5.9) | 0.63 |
| CAD | 2 (1.2) | 1 (2) | 1 (0.8) | 0.53 |
| CVA | 2 (1.2) | 1 (2) | 1 (0.8) | 0.53 |
| Hypothyroidism | 2 (1.2) | 0 | 2 (1.7) | 0.35 |
| Charlson comorbidity index | 0 (0-0) | 0 (0-0.5) | 0 (0-0) | 0.61 |
| **Presentation** |  |  |  |  |
| Fever | 169 (99.4) | 51 (100) | 118 (99.2) | 0.51 |
| Chills | 93 (54.7) | 32 (62.7) | 61 (51.3) | 0.16 |
| Myalgia | 96 (56.5) | 30 (58.8) | 66 (55.5) | 0.68 |
| Joint pain | 23 (13.5) | 8 (15.7) | 15 (12.6) | 0.59 |
| Rashes | 9 (5.3) | 2 (3.9) | 7 (5.9) | 0.60 |
| Headache | 51 (30) | 15 (29.4) | 36 (30.3) | 0.91 |
| Retro orbital pain | 7 (4.1) | 2 (3.9) | 5 (4.2) | 0.93 |
| Nausea/Vomiting | 89 (52.4) | 23 (45.1) | 66 (55.5) | 0.21 |
| Bleeding manifestations | 43 (25.3) | 10 (19.6) | 33 (27.7) | 0.26 |
| Hematuria | 5 (2.9) | 5 (9.8) | 0 | **0.001** |
| Oliguria | 12 (7.1) | 9 (17.6) | 3 (2.5) | **0.000** |
| Altered sensorium | 29 (17.1) | 17 (33.3) | 12(10.1) | **0.000** |
| Abdominal pain | 66 (38.8) | 13 (25.5) | 53 (44.5) | **0.02** |
| **Physical Examination** |  |  |  |  |
| Heart rate, per minute | 98 (86-110) | 102 (86-112) | 96 (86-110) | 0.06 |
| Systolic blood pressure, mm of Hg | 110 (100-122) | 108 (90-128) | 111 (100-122) | 0.30 |
| Diastolic blood pressure, mm of Hg | 71 (60-80) | 69 (60-84) | 71 (60-80) | 0.49 |
| Respiratory Rate per minute | 22 (20-24) | 22 (20-24) | 22 (20-22) | 0.83 |
| Pallor | 20 (11.8) | 8 (15.7) | 12 (10.1) | 0.29 |
| Icterus | 10 (5.9) | 6 (11.8) | 4 (3.4) | **0.03** |
| Edema | 33 (19.4) | 19 (37.3) | 14 (11.8) | **0.000** |
| Lymphadenopathy | 1 (0.6) | 0 | 1 (0.8) | 0.51 |

**Table no 1 Baseline Characteristics of the study participants with and without Renal involvement**

Abbreviation: CAD, Coronary Artery Disease

CVA, Cerebrovascular Accident

The values are presented as mean (95% confidence interval) or numbers (percentage).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Total**  **(n=170)** | **Dengue with renal involvement**  **(n=51)** | **Dengue without renal involvement**  **(n=119)** | **2-tail sig**  **or**  **p-value** |
| Haemoglobin (g/L) | 12.19 (11.72-12.65) | 11.78 (10.81-12.75) | 12.4 (11.8-12.9) | 0.25 |
| Total Leucocyte Count x 103 (cells/)\* | 6.9 (4.75-11.02) | 9.6 (6.3-13.5) | 6.1 (4.3-9.5) | **0.005** |
| Platelet count x 103 cells/\* | 34 (16-65) | 47 (18-78) | 29 (14-58) | **0.043** |
| Hematocrit | 38 (36-39) | 37 (34-39.9) | 38 (37-40) | 0.489 |
| Sodium (meq/l) | 136.70 (135.95-137.46) | 135.92 (134.33-137.51) | 137.03 (136.19-137.89) | 0.182 |
| Potassium (meq/l) | 4.26 (4.14-4.38) | 4.51 (4.22-4.80) | 4.15 (4.03-4.26) | **0.006** |
| Chloride (meq/l) | 101.33 (99.06-103.6) | 103.26 (101.6-104.93) | 100.5 (97.33-103.67) | 0.272 |
| Calcium (mg/dl) | 8.27 (8.1-8.4) | 8.0 (7.7-8.4) | 8.3 (8.2-8.4) | 0.058 |
| Phosphorous (mg/dl)\* | 2.96 (2.41-3.5) | 3.4 (2.4-4) | 2.84 (2.41-3.26) | **0.000** |
| Magnesium (mg/dl) | 2.84 (1.22-4.74) | 2.16 (2.0-2.31) | 3.12 (0.88-5.41) | 0.599 |
| Urea (mg/dl)\* | 25 (17-48) | 65 (25-89) | 21 (15-32) | **0.00** |
| Creatinine (mg/dl)\* | 0.8 (0.63-1) | 1.7 (0.96-2.47) | 0.73 (0.57-0.9) | **0.00** |
| Total Bilirubin (mg/dl)\* | 0.7 (0.5-1.6) | 1.3 (0.7-2.67) | 0.7 (0.43-1.3) | 0.117 |
| Total Protein (mg/dl) | 5.9 (5.7-6.0) | 5.7 (5.35-6.04) | 5.96 (5.81-6.12) | 0.103 |
| Albumin (mg/dl) | 4.5 (1.7-7.3) | 2.88 (2.68-3.08) | 5.2 (1.19-9.21) | 0.456 |
| Aspartate Transaminase (IU/L)\* | 181 (97-450) | 224 (133-1279) | 160 (92-342) | 0.015 |
| Alanine Transaminase (IU/L)\* | 96 (54-277) | 126 (74-755) | 91 (49-198) | 0.008 |
| Alkaline phosphatase (IU/L)\* | 123 (91-187) | 133 (93-333) | 120 (90-165) | **0.000** |
| pH | 7.39 (7.38-7.48) | 7.35 (7.32-7.40) | 7.41 (7.40-7.42) | **0.001** |
| Bicarbonate | 21.0 (20.23-21.77) | 17.7 (16.19-19.280) | 22.41 (21.64-23.17) | **0.000** |
| Lactate\* | 1.5 (1.0-2.39) | 1.95 (1.2-4.7) | 1.4 (1-2) | **0.000** |
| NS1 Ag Positive | 81 (47.6) | 22 (43.1) | 59 (49.6) | 0.13 |
| Anti-Dengue IgM Positive | 111 (65.3) | 36 (70.6) | 75 (63) |  |
| ECG Abnormality | 46 (27.1) | 13 (25.5) | 33 (27.7) | 0.76 |
| Chest Xray Abnormality | 78 (45.9) | 35 (68.6) | 43 (36.1) | **0.00** |
| * Pleural Effusion | 50 (29.4) | 17 (33.3) | 33 (27.7) | **0.01** |
| * Pulmonary Edema | 28 (16.5) | 18 (35.3) | 10 (8.4) | **<0.001** |
| Ultrasound Abnormal | 117 (68.8) | 40 (78.4) | 77 (64.7) | 0.07 |
| **Outcome** |  |  |  |  |
| Death | 17 (10) | 14 (27.5) | 3 (2.5) | **0.00** |
| Duration of hospital stay in  Days\* | 4 (2-6) | 4 (2-8) | 4 (2-5) | 0.102 |

**Table 2 Baseline investigations and outcomes of the study participants with and without renal involvement**

\*Represents variables where data is skewed and hence median is used. In such cases, Parenthesis indicates interquartile range.

In all other variables, wherever applicable, values have been represented as mean (95% confidence limits) and numbers (percentage).

**Table 3 Urine microscopic abnormalities in patients with renal involvement**

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
| Urinary microscopic abnormality | Total Patients | With AKI | Without AKI |
|  |  |  |  |
| Proteinuria\* | 21 | 12 | 9 |
| Moderately increased proteinuria | 6 | 1 | 2 |
| Severely Increased proteinuria | 14 | 9 | 5 |
| Nephrotic range proteinuria | 1 | 1 | 0 |
| Haematuria | 13 | 7 | 6 |
| Granular casts | 9 | 9 | 0 |
| Pyuria | 4 | 3 | 1 |

Abbreviation: AKI, Acute Kidney Injury

\*included epithelial cell casts and granular casts in our patients

The values are presented as numbers (percentage)

**Table 4 Multivariable analysis in Renal v/s No Renal Involvement**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | Renal Involvement | No Renal Involvement | Odd’s Ratio (95% Confidence Intervals) | p-value |
| Address (Urban and Rural) | 19/51 (37.3) | 66/119 (55.5) | 1.48 (0.03-0.2) | 0.140 |
| Altered sensorium | 17/51 (33.3) | 12/119 (10.1) | 3.19 (0.1-0.4) | 0.002 |
| Platelet Count x 103 cells/ | 47 (18-78) | 29 (14-58) | 1.025 (0.001-0.002) | 0.307 |
| Lactate | 1.95 (1.2-4.7) | 1.4 (1-2) | 4.16 (0.03-0.1) | 0.000 |

**Table 5 Baseline characteristics of the study participants among survivors versus non-survivors**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Total  N=170 | Survivors  N=153 | Non-Survivors  N=17 | P value/sig |
| Age | 36 (23-46) | 34 (32-37) | 35 (17-75) | 0.925 |
| Male | 101 (59) | 71 (60.2) | 9 (52.9) | 0.567 |
| **Presentation** |  |  |  |  |
| Oliguria | 12 (7.1) | 8 (5.2) | 4 (23.5) | 0.005 |
| Altered sensorium | 29 (17.1) | 17 (11.1) | 12 (70.6) | 0.000 |
| Oxygen requirement | 37 (21.8) | 25 (16.3) | 12 (70.6) | 0.000 |
| Pallor | 20 (11.8) | 13 (8.5) | 7 (41.2) | 0.000 |
| Edema | 33 (19.4) | 26 (17) | 7 (41.2) | 0.017 |
| Inotropic Requirement | 20 (11.76) | 15 (9.8) | 5 (29.4) | 0.03 |
| Hemodialysis requirement | 7 (4.1) | 2 (1.3) | 5 (29.4) | 0.000 |
| Chest Xray Abnormality | 78 (45.9) | 66 (43.1) | 12 (70.6) | 0.033 |
| Pottasium (meq/l) | 4.26 (4.14-4.38) | 4.19 (4.0-4.3) | 4.88 (4.35-5.42) | 0.000 |
| Phosphorous (mg/dl)\* | 2.96 (2.41-3.5) | 2.8 (2.3-3.4) | 3.65 (3.27-6.75) | 0.00 |
| Magnesium (mg/dl) | 2.84 (1.22-4.74) | 2.89 (1.12-4.66) | 2.33 (1.93-2.73) | 0.856 |
| Urea (mg/dl)\* | 25 (17-48) | 24 (17-43) | 81 (20-118) | 0.00 |
| Creatinine (mg/dl)\* | 0.8 (0.63-1) | 0.79 (0.61-1) | 2.03 (0.91-2.82) | 0.00 |
| Total Bilirubin (mg/dl)\* | 0.7 (0.5-1.6) | 0.7 (0.4-1.4) | 2.3 (0.74-4.95) | 0.00 |
| Aspartate Transaminase (IU/L)\* | 181 (97-450) | 174 (95-377) | 445 (147-2241) | 0.00 |
| Alanine Transaminase (IU/L)\* | 96 (54-277) | 94 (52-246) | 169 (85-2240) | 0.10 |
| Alkaline Phoshatase(IU/L)\* | 123 (91-187) | 122 (91-187) | 133 (82-280) | 0.150 |
| pH | 7.39 (7.38-7.48) | 7.41 (7.39-7.42) | 7.28 (7.20-7.36) | 0.00 |
| Bicarbonate | 21.0 (20.23-21.77) | 21.7 (21.01-22.46) | 14.4 (11.73-17.13) | 0.00 |
| Lactate\* | 1.5 (1.0-2.39) | 1.46 (1-2.1) | 4.24 (1.75-6.5) | 0.00 |
| Renal involvement | 51 (30) | 37 (24.2) | 14 (82.4) | 0.00 |
| with AKI | 36 (21.17) | 23 (15.03) | 13 (76.47) | 0.00 |
| Asymptomatic urinary  abnormalities | 15 (8.8) | 14 (9.2) | 1 (5.9) | 0.00 |

Abbreviation: AKI, Acute Kidney Injury

Age is represented as Mean (Range)

\*Represents variables where data is skewed and hence median is used. In such cases, Parenthesis indicates interquartile range.

In all other variables, wherever applicable, values have been represented as mean (95% confidence limits) and numbers (percentage).

**Table 6 Multivariable Analysis for factors among Survivor and Non survivor groups:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variables | Non-Survivors | Survivors | Odd’s Ratio (95% Confidence Intervals) | p-value |
| Renal Involvement | 14/17 (82.4) | 37/153 (24.2) | 3.85 (0.084-0.271) | 0.00 |
| Oxygen Requirement | 12/17 (70.6) | 25/153 (16.3) | 4.13 (0.10-0.31) | 0.00 |
| Inotropic Requirement | 5/17 (9.8) | 15/153 (29.4) | 1.50 (0.03-0.224) | 0.13 |

**Table 7 Comparison of AKI, mortality, and risk factors for AKI in DVI across various studies in the last ten years**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.No. | Study | Year | Study Population | Study location and size | Severity of Cases | Incidence of AKI | Risk factors for AKI identified | Mortality  AKI v/s Non-AKI |
| 1. | Mehra et al.17 | 2012 | Age not defined | Chennai, 223 | All | 10.8% | High ALT, ALP, Hypoalbuminemia, Metabolic acidosis, Hypoxia, Shock | All-cause mortality 9% |
| 2. | Khalil et al.9 | 2012 | >14 years | Karachi, 532 | All | 13.3% | Higher age group, Male gender, CNS involvement, Respiratory failure, prolonged aPTT | 11.3% v/s 0 |
| 3. | Mallhi et al.8 | 2015 | >12 years | Malaysia, 667 | All | 14.2% | Male gender, DHF, Rhabdomyolysis, MODS, DM, Use of nephrotoxic drugs | 1.2% v/s 0 |
| 4. | Diptyanusa et al.14 | 2018 | >18 years | Bangkok, 1484 | All | 4.8% | Lower age, Male gender, DM, Obesity, Severe Dengue, Severe thrombocytopenia, Hypoalbuminemia, Severe transaminitis, Coagulopathy, Shock, Metabolic acidosis, Rhabdomyolysis, Respiratory failure | 12.7% v/s 0 |
| 5. | Patel et al.18 | 2019 | >14 years | Lucknow, 620 | All | 14.51% | Lower Age, Male gender, Urban residence, Diabetes, 6.HTN, IHD, Severe Dengue, | 15.61% v/s 0 |
| 6. | Eswarappa et al.10 | 2019 | >15 years | Bengaluru, 2416 | All | 3.4% | Lower Age, Hypotension, MODS, Diabetes | 13.41% v/s 0.7% |
| 7. | Rajan et al.11 | 2020 | Children admitted to PICU | Chennai, 127 | Severe Dengue | 20.5% | Hypotension, Ventilatory requirement, Secondary HLH, Higher potassium levels, Higher AST and ALT, Coagulopathy | 11.53% v/s 0.9% |
| 8. | Surasombatpattana et al.19 | 2021 | >18 years | Songkla (Thailand), 120 | All | 14% | MODS, NSAID use | 12% v/s 1% |
| 9. | Bui Vu Huy et al.15 | 2021 | >18 years | Hanoi (Vietnam), 2417 | All | 2.7% | Male gender, HTN, Shock, MODS, Myocarditis | 12.5% v/s 0.9% |
| 10. | Wang C. et al.20 | 2023 | >18 years | Guangdong, China, 242 | Severe Dengue | 35.1% | HTN, Nephrotoxic drugs, Respiratory distress, Hematuria | 22.4% v/s 0 |
| 11. | Present Study (PGIMER, Chandigarh) | 2022-23 | >12 years | Chandigarh, 170 | All | 21.17% | Rural residence, Altered sensorium, Edema, Thrombocytopenia, Hyperkalaemia, Metabolic acidosis, Higher lactate levels | 7.64% v/s 0.005% |

\*Enrolled severe Dengue cases only. All other studies had cases of varying severity

Abbreviation: AKI, Acute Kidney Injury; DVI, Dengue Viral Infection; ALT, Alanine aminotransferase; ALP, Alkaline Phosphatase; DHF, Dengue Haemorrhagic Fever; MODS, Multi-Organ Dysfunction Syndrome; DM, Diabetes Mellitus; CNS, Central Nervous System; HTN, Hypertension; IHD, Ischemic Heart Disease; AST, Aspartate aminotransferase; HLH, Hemophagocytic Lymphohistiocytosis; NSAID, Non-Steroidal Anti-inflammatory Drug

|  |  |
| --- | --- |
| **A** | **B** |
| **C** | **D** |

**Figure 1 Renal Biopsy:** Imagesshow **A** low power view and **B** high power view ofkidney biopsy showing PAS stain showing 1 glomerulus with mesangial hypercellularity and tubules showing presence of pigment casts, that were further positive for hemoglobin immuno stain. Images **C** and **D** show low power view (20X) of kidney biopsy with PAS staining showing severe acute tubular injury with pigmented red cell casts in tubules with Glomerulus being unremarkable.