RESEARCH ARTICLE

CLINICAL, HEMATOLOGICAL, BIOCHEMICAL AND RADIOLOGICAL PREDICTORS OF SEVERITY AND OUTCOME IN DENGUE INFECTION.

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Manuscript Info

Abstract

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Introduction:
Dengue infection, the most prevalent -borne viral illness in humans is caused by dengue virus which belongs to flaviviridae family and is one of the most important tropical infectious diseases of the world. Several outbreaks of dengue infection have been reported from India. In the past 50 years, the prevalence of dengue fever has increased 30 fold with increasing geographic expansion to new countries and, in the present decade, from urban to rural setting (1).

The 2009 World Health Organization (WHO) criteria classify (2) dengue according to levels of severity: dengue without warning signs; dengue with warning signs (abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, liver enlargement, increasing hematocrit with decreasing platelets); and severe dengue (dengue with severe plasma leakage, severe bleeding, or organ failure).

An estimated 50-100 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries. Case fatality rates vary from 1% to 5%, but can be < 1% with appropriate treatment (3,4). In its most severe form, it manifests itself clinically as dengue with warning signs and severe dengue. Unusual clinical manifestations of dengue fever have become more common in the last few years. Although the liver is not a major target organ, hepatic dysfunction is a well recognized feature, often characterized by acute hepatitis, with pain in the right hypochondrium, hepatomegaly, jaundice and raised aminotransferase levels (5-11). The degree of liver dysfunction varies from mild injury with elevation of transaminase activity to severe injury with liver cell failure. The severity of liver dysfunction varies according to the type of clinical presentation of dengue fever, and is more common in children with severe dengue fever. Liver dysfunction as a result of dengue infection can be a direct viral effect on liver cells or an adverse consequence of dysregulated host immune response against the virus (5,11).

Abdominal ultrasound can detect gall bladder thickening, ascites in addition to hepatomegaly, pleural effusion which usually occurs in severe dengue.

Heart involvement in the form of myocarditis can occur in severe dengue which can be assessed by measuring enzymes like creatine phosphokinase-MB (CPK-MB) and echocardiography.

Since our hospital is a tertiary care hospital, we do see a lot of children with dengue infection including those with atypical manifestations and at present there are very few studies done in children to predict the severity and outcome of dengue infection. Hence the present study is intended to predict the severity and outcome of dengue infection based on clinical parameters, liver enzymes like AST, ALT, CPK-MB, and abdominal ultrasound.

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Materials and methods:

Source of data:
Children with dengue infection admitted in pediatric ward and/or pediatric intensive care unit, fulfilling the inclusion and exclusion criteria.

Period of study –
18 months (October 2016-march 2018)

Method of collection of Data (including sampling procedures if any)
After obtaining ethical clearance from institutional ethical committee the study was started. The written informed consent is taken from the parents of patients fulfilling inclusion and exclusion criteria and then the patients are included in the study. In this prospective observational analytical study, a sample of 35 patients proven to be dengue positive [NS1 or IgM or IgG positive (card test or ELISA)] admitted in pediatric ward and pediatric intensive care unit will be included. For these patients, specific investigations like complete hemogram which includes even platelet count and hematocrit, liver function tests(bilirubin, serum protein, AST, ALT, ALP), coagulation profile(PT,APTT), CPK-MB, chest x ray, ultrasound abdomen and pelvis were between day 1 and day 3 of admission. At the time of admission blood was collected in different vacutainers for these investigations and sent to the laboratory. Following which, the results of these investigations are analysed in order to interpret the severity of dengue infection in the subjects.

Determination of sample size (n):
With 90% proportion of hepatic derangement among patients with dengue infection \(^ {\text{90}}\) at 95% significance level and at ±15% allowable error sample size is 65, with finite population correction.
Statistical formula:
\[
n = \frac{Z^2 P(100-P)}{d^2}
\]
1. Z=level of significance
2. P=expected proportion/prevalence=90%
3. d=expected margin of error

Statistical Analysis:-
All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. Chi-square (\( \chi^2 \)) test was used for association between two categorical variables. The formula for the chi-square statistic used in the chi square test is:
\[
\chi^2 = \sum \frac{(O_i - E_i)^2}{E_i}
\]
The subscript “c” are the degrees of freedom. “O” is observed value and E is expected value.
C= (number of rows-1)* (number of columns-1)

In cases of more than 30% cell frequency <5, Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables between two independent groups was tested by unpaired t test.

The t statistic to test whether the means are different can be calculated as follows:
\[
t = \frac{(\bar{x}_1-\bar{x}_2)-(\mu_1-\mu_2)}{\sqrt{s_1^2/n_1 + s_2^2/n_2}}
\]
where \( \bar{x}_1 \) = mean of sample 1  
\( \bar{x}_2 \) = mean of sample 2  
\( n_1 \) = number of subjects in sample 1  
\( n_2 \) = number of subjects in sample 2  
\( s_1^2 \) = variance of sample 1  
\( s_2^2 \) = variance of sample 2  

The difference of the means of analysis variables between more than two independent groups was tested by ANOVA and F test of testing of equality of Variance.

\[
\text{ANOVA}
\]

| Source          | d.f.  | SS            | MS            | F                  |
|-----------------|-------|---------------|---------------|-------------------|
| Treatment       | \( a - 1 \) | SS_{treat}   | \( \frac{SS_{treat}}{a-1} \) | \( \frac{MS_{treat}}{MS_{error(a)}} \) |
| Error (a)       | \( N-a \) | SS_{error(a)} | \( \frac{SS_{error(a)}}{N-a} \) |                      |
| Time            | \( t-1 \) | SS_{time}     | \( \frac{SS_{time}}{t-1} \) | \( \frac{MS_{time}}{MS_{error(b)}} \) |
| Treat x Time    | \((a-1)(t-1)\) | SS_{treat x time} | \( \frac{SS_{treat x time}}{(a-1)(t-1)} \) | \( \frac{MS_{treat x time}}{MS_{error(b)}} \) |
| Error (b)       | \((N-a)(t-1)\) | SS_{error(b)} | \( \frac{SS_{error(b)}}{(N-a)(t-1)} \) |                      |
| Total           | \( Nt-1 \) | SS_{total}    | MS_{total}    |                    |

The sources of the variation include treatment; Error (a); the effect of Time; the interaction between time and treatment; and Error (b). Error (a) is the effect of subjects within treatments and Error (b) is the individual error in the model. All these add up to the total.

Degrees of Freedom: \( a-1 \), the number of treatments minus 1, .. \( N-a \), the total number of all experimental units minus the number of treatments, .. \( t-1 \), for time, .. Total df is the total number of subjects times the number of times minus 1. The degrees of freedom for error(b) is obtained by subtraction.

Tukey's post-hoc test was used for multiple comparison.

The formula for Tukey's test is:

\[
\frac{M_i - M_j}{\sqrt{MS_{w} \left( \frac{1}{n} \right)}}
\]

\( M \) = treatment/group mean  
\( n \) = number per treatment/group  
ROC analysis for Sensitivity- specificity was done to check relative efficiency.
If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office 2007.

Selection criteria

Inclusion criteria:
All patients aged 1month-14years with dengue NS1 positive or IgM positive or IgG positive (card test or ELISA) at Shri B.M.Patil Medical College Hospital & Research Center.

Exclusion criteria:
1. Known case of liver disease.
2. Known case of heart disease
3. Patients on ATT, anticonvulsants and long term steroid therapy
4. Patients who are on regular blood transfusions for thalassemia
5. Denial of consent

Results And Analysis:--

Table 01:-Age Wise Distribution Among Types Of Dengue Illness:

| Age (Yrs) | Total cases | Dengue fever | Dengue fever with warning signs | Severe dengue | P value |
|-----------|-------------|--------------|---------------------------------|---------------|---------|
| n         | %           | n            | %                               | n             | %       |
| 0-5       | 16          | 24.6         | 6                               | 24.0          | 19.4    | 4       | 44.4    | 0.012*   |
| 6-10      | 26          | 40.0         | 11                              | 44.0          | 12      | 38.7    | 3       | 33.3     |
| 11-14     | 23          | 35.4         | 8                               | 32.0          | 13      | 41.9    | 2       | 22.2     |
| Total     | 65          | 100.0        | 25                              | 100.0         | 31      | 100.0   | 9       | 100.0    |

![Graph showing age-wise distribution among types of dengue illness](image)
1. Out of 65 cases majority of the cases were under age group 6-10 years (n=26) accounting to 40%.
2. In Dengue fever (DF) cases, out of 25 maximum cases (n=11) are from 6-10 years accounting to 44%.
3. In Dengue fever with warning signs (DFWS) cases, out of 31 maximum cases (n=13) are from 10-14 years accounting to 41.9%.
4. In Severe Dengue (SD) cases, out of 9 maximum cases (n=4) are from 0-5 years accounting to 44.4%.
5. ‘p value’ = 0.012 suggests that there is statistically significant difference among age wise distribution of different types of dengue illness.

Table 02:-Sex distribution among types of dengue illness:

| Sex   | Total cases | Dengue fever | Dengue fever with warning signs | Severe dengue | P value |
|-------|-------------|--------------|--------------------------------|---------------|---------|
|       | n | % | n | % | n | % | n | % |       |
| Male  | 41 | 63 | 15 | 60.0 | 20 | 64.5 | 6 | 66.7 | 0.914 |
| Female | 24 | 37 | 10 | 40.0 | 11 | 35.5 | 3 | 33.3 |       |
| Total | 65 | 100.0 | 25 | 100.0 | 31 | 100.0 | 9 | 100.0 |       |

Out of 25 cases of DF majority of patients are males (n=15) accounting to 60%.
Out of 31 cases of DFWS majority of patients are males (n=20) accounting to 64.5%.
Out of 9 cases of SD majority of patients are males (n=6) accounting to 66.7%.
‘p value’ = 0.914 suggests no statistical significance in gender distribution among various types of dengue illness i.e no gender is specific to any group.

Table 03:-Distribution of cases according to diagnosis:

| Type Of Illness          | No. Of Cases (n) | Percentage (%) |
|--------------------------|------------------|----------------|
| Dengue Fever (DF)        | 25               | 38.5           |
| DF With Warning Signs    | 31               | 47.7           |
| Severe Dengue            | 9                | 13.8           |
| Total                    | 65               | 100            |
Out of 65 cases maximum cases (n=31) are of DFWS accounting to 47.7% followed by DF (n=25) accounting to 38.5% and SD (n=9) accounting to 13.8%.

### Table 04a: Distribution of clinical symptoms according to types of dengue illness:

| SYMPTOMS          | Total | DF     | DFWS  | SD    |
|-------------------|-------|--------|-------|-------|
|                   | n     | %      | n     | %     | n     | %  |
| FEVER             | 65    | 100    | 25    | 100   | 31    | 100 |
| VOMITING          | 31    | 47.6   | 8     | 32    | 19    | 61.29032 | 4    | 44.44 |
| PAIN ABDOMEN      | 23    | 35.4   | 2     | 8     | 19    | 61.29032 | 2    | 22.22 |
| HEPATOMEGALY      | 16    | 24.6   | 0     | 0     | 13    | 41.94   | 3    | 33.3  |
| MYALGIA           | 9     | 13.85  | 6     | 24    | 3     | 9.677419 | 0    | 0     |
| HEADACHE          | 10.77 | 2      | 8     | 3     | 9.677419 | 2    | 22.22 |
| LOOSE STOOLS      | 6     | 9.23   | 2     | 8     | 2     | 6.451613 | 2    | 22.22 |
| ARTHRALTIA        | 5     | 7.7    | 3     | 12    | 2     | 6.451613 | 0    | 0     |
| COUGH             | 3     | 4.6    | 0     | 0     | 1     | 3.225806 | 2    | 22.22 |
| COLD              | 3     | 4.6    | 1     | 4     | 0     | 0       | 2    | 22.22 |
| NAUSEA            | 2     | 3.08   | 2     | 8     | 0     | 0       | 0    | 0     |
| GIDDINESS         | 2     | 3.08   | 1     | 4     | 1     | 3.225806 | 0    | 0     |
| LOSS OF APPETITE  | 2     | 3.08   | 1     | 4     | 1     | 3.225806 | 0    | 0     |
| RASHES            | 2     | 3.08   | 0     | 0     | 2     | 6.451613 | 0    | 0     |
| HURRIED BREATHING | 2     | 3.08   | 0     | 0     | 0     | 0       | 2    | 22.22 |
| ITCHING           | 1     | 1.84   | 1     | 4     | 0     | 0       | 0    | 0     |
| IRRITABILITY      | 1     | 1.84   | 1     | 4     | 0     | 0       | 0    | 0     |
| PERI ORBITAL PAIN | 1     | 1.84   | 1     | 4     | 0     | 0       | 0    | 0     |
| ICTERUS           | 1     | 1.84   | 0     | 0     | 1     | 3.225806 | 0    | 0     |
| BLEEDING PER NOSE | 1     | 1.84   | 0     | 0     | 1     | 3.225806 | 0    | 0     |
| LETHARGY          | 1     | 1.84   | 0     | 0     | 0     | 0       | 1    | 11.11 |
| DROWSINESS        | 1     | 1.84   | 0     | 0     | 0     | 0       | 1    | 11.11 |
| EDEMA             | 1     | 1.84   | 0     | 0     | 0     | 0       | 1    | 11.11 |
| CONVULSION        | 1     | 1.84   | 0     | 0     | 0     | 0       | 1    | 11.11 |

1. Fever was found to be the most common symptom and is present in all cases (n=65) i.e 100%.
2. Vomiting is present in 8 of 25 cases of DF (32%), 19 of 31 cases in DFWS (61.2%) & 4 of 9 cases in SD (44.4%).
3. Next most common is Myalgia (n=6) in DF accounting to 24% and pain abdomen(n=19) in DFWS (61.2%)
This table shows distribution of cases according to the day of presentation to the hospital after the onset of fever. In present study of 65 cases there is no statistical difference between the three groups of dengue illness according to day of presentation to the hospital (p value = 0.872).

**Most common symptoms in dengue illness:**

Above figure shows the most common symptoms in dengue, in descending order it is as follows: fever, vomiting, abdominal pain, myalgia, headache, loose stools, arthralgia, cough, cold, rashes, nausea etc.

**Most common warning signs in dengue illness:**
Above figure shows the most common warning signs in dengue, in descending order abdominal pain (30.7%), hepatomegaly (24.6%), abdomen tenderness (23%), raised hematocrit with reduced platelet count (6%), 3% each in ascites & tender right hypochondrium.

Table 05a: Distribution of serological tests

| TEST | TOTAL | DF | DFWS | SD | CHI SQUARE |
|------|-------|----|------|----|------------|
|      | Positiv e cases | % | Positive cases | % | Positive cases | % | Positive cases | % | TEST |
| CARD TEST NS1 | 58 | 89.2 | 25 | 100.0 | 28 | 9.0 | 5 | 5 | 6 | 0.001* |
| CARD TEST IgM | 10 | 15.4 | 2 | 8.0 | 7 | 2.3 | 1 | 1 | 1 | 0.300 |
| CARD TEST IgG | 15 | 23.1 | 5 | 20.0 | 8 | 2.6 | 2 | 2 | 2 | 0.875 |

1. Card test NS1 was positive in 100% cases of DF, 90% of DFWS & 56% of SD.
2. Card test IgM was positive in 8% cases of DF, 23% of DFWS & 11% of SD.
3. Card test IgG was positive in 20% cases of DF, 26% of DFWS & 22% of SD.

Table 05b: Distribution Of Serological Tests

| RAPID CARD TEST | DF no of cases | DFWS no of cases | SD no of cases | TOTAL no of cases |
|-----------------|----------------|------------------|----------------|------------------|
| NS1             | 19             | 20               | 5              | 44               |
| IgM             | 0              | 1                | 1              | 2                |
| IgG             | 0              | 1                | 2              | 3                |
| NS1, IgM        | 1              | 2                | 0              | 3                |
| NS1, IgG        | 4              | 3                | 0              | 7                |
| IgM, IgG        | 0              | 1                | 0              | 1                |
| NS1, IgM, IgG   | 1              | 3                | 0              | 4                |

Out of 65 cases of dengue illness
DF constitutes 25 cases of which 19(76%) were only NS1 positive, 1(4%) was NS1 & IgM positive, 4(16%) were NS1 & IgG positive & 1(4%) was NS1, IgM, IgG positive.
DFWS constitutes 31 cases of which 20 (64.51%) were only NS1 positive, 1 (3.22%) was only IgM positive, 1 (3.22%) was only IgG positive, 2 (6.45%) were NS1 & IgM positive, 3 (9.68%) were NS1 & IgG positive, 1 (3.22%) was IgM & IgG positive & 3 (9.68%) were NS1, IgM, IgG positive.

SD constitutes 9 cases of which 5 (55.56%) were only NS1 positive, 1 (11.1%) was only IgM positive, 2 (22.22%) were only IgG positive.

Table 05c & 05d:- Diagnostic Efficacy Of Card Test To Detect IgM Positive Compared To Elisa Test

| DENGUE | CARD TEST IG M   | ELISA   | p value |
|--------|------------------|---------|---------|
|        | POSITIVE         | NEGATIVE|         |
|        | n   | %  | n   | %  |
| DF     | POSITIVE | 0   | 0.0 | 1   | 20.0 | 0.198 |
|        | NEGATIVE | 11  | 100.0 | 4   | 80.0 |
|        | TOTAL    | 11  | 100.0 | 5   | 100.0 |
| DFWS   | POSITIVE | 1   | 12.5 | 0   | 0.0  | 0.589 |
|        | NEGATIVE | 7   | 87.5 | 5   | 100.0 |
|        | TOTAL    | 8   | 100.0 | 5   | 100.0 |
| SD     | POSITIVE | 0   | 0.0 | 0   | 0.0  | 1     |
|        | NEGATIVE | 3   | 100.0 | 1   | 100.0 |
|        | TOTAL    | 3   | 100.0 | 1   | 100.0 |
| OVERALL| POSITIVE | 1   | 4.5 | 1   | 9.1  | 0.606 |
|        | NEGATIVE | 21  | 95.5 | 10  | 90.9 |
|        | TOTAL    | 22  | 100.0 | 11  | 100.0 |

| CARD TEST | ELISA          |
|-----------|----------------|
| DF        |                |
| Sensitivity | 0.00%          |
| Specificity | 80.00%        |
| PPV        | 0.00%          |
| NPV        | 26.67%         |
| Accuracy   | 25.00%         |

| DFWS |                |
|      | 12.50%          |
|      | 100.00%         |
|      | 0.00%           |
|      | 4.55%           |
|      | 100.00%         |

| SD   |                |
|      | 0.00%           |
|      | 100.00%         |
|      | 100.00%         |
|      | 100.00%         |

| OVERALL |                |
|         | 4.55%           |
|         | 100.00%         |

In present study ELISA IgM was done in 33 cases and is compared to rapid card test IgM of the same cases. ELISA is more efficacious in detecting dengue IgM with a 100% sensitivity and 100% specificity than rapid card test whose sensitivity and specificity are 4.55% and 90.91% respectively.

Table 06:- Haematological & biochemical parameters:

| Parameter                           | n(65) | Percentage |
|-------------------------------------|-------|------------|
| TLC<4000 cells/mm³                  | 27    | 41.5       |
| PCV ≥ 35%                           | 41    | 63.07      |
| PLT < 50,000/mm³                    | 17    | 26.1       |
| PLT: 50,000 – 1 lakh/mm³            | 11    | 16.9       |
| PLT > 1 lakh/mm²-1.5lakhs           | 17    | 26.1       |
| PT > 13.5 sec.                      | 54    | 83         |
| APTT > 34 sec.                      | 47    | 72.3       |
| AST> 41 U/L-100U/L                  | 25    | 38.46      |
| > 101 U/L-200U/L                    | 15    | 23.07      |
| > 200U/L                            | 16    | 24.61      |
| ALT > 41 U/L-100U/L                 | 15    | 23.07      |
| > 101 U/L-200U/L                    | 7     | 10.76      |
| > 200U/L                            | 8     | 12.3       |
In our study of 65 cases, TLC <4000 cells/mm³ was seen in 27 cases (41.5%), PCV ≥ 35% in 41 cases, PLT <50,000/mm³ in 17 cases, PLT: 50,000 – 1 lakh/ mm³ in 11 cases, PLT >1 -1.5 lakhs/ mm³ in 17 cases, PT >13.5 sec. in 54 cases and APTT > 34 sec. in 47 cases, AST > 41U/L in 56 cases, ALT > 41U/L in 30 cases, CPK-MB > 26 U/L in 54 cases & albumin < 3.5g/dl in 34 cases.

Table 07: Comparison of various parameters between different types of dengue:

| Variable | TOTAL | DF | DFWS | SEVERE DENGUE | ANOV A test |
|----------|-------|----|------|---------------|-------------|
|          | Mean  | STD | Mean | STD | Mean | STD | Mean | STD | Mean | STD | p value |
| Total count at admission | 6578.3 | 3456.3 | 4490.4 | 2447.51 | 5700.32 | 3241.056 | 9544.44 | 4680.804 | 0.001* |
| Platelet at admission | 108699.6 | 79663.5 | 138160.0 | 66021.89 | 110161.3 | 82991.56 | 77777.78 | 89977.46 | 0.121 |
| PCV at admission | 36.7 | 5.45 | 36.80 | 4.717 | 36.16 | 5.962 | 37.44 | 5.703 | 0.801 |
| PT | 18.03 | 4.23 | 15.5 | 3.5 | 16.0 | 3.4 | 22.6 | 5.8 | <0.001* |
| APTT | 50.1 | 20.6 | 47.9 | 14.2 | 51.4 | 22.6 | 51.0 | 25.1 | 0.801 |
| AST | 316.4 | 253.7 | 82.9 | 61.1 | 140.5 | 99.7 | 725.9 | 600.5 | <0.001* |
| ALT | 233.6 | 278.1 | 31.7 | 18.9 | 80.7 | 87.1 | 588.4 | 728.3 | <0.001* |
| BIL | 0.8 | 1.03 | 0.4 | 0.1 | 0.7 | 1.2 | 1.3 | 1.8 | 0.108 |
| Albumin | 3.36 | 0.63 | 3.6 | 0.3 | 3.2 | 0.6 | 3.3 | 1.0 | 0.044* |
| ALP | 179 | 62.3 | 148.1 | 43.3 | 171.7 | 76.8 | 217.2 | 66.9 | 0.026* |
| CPKMB | 64.5 | 46.03 | 51.3 | 28.7 | 41.4 | 20.8 | 100.8 | 88.6 | 0.001* |

Note: * significant at 5% level of significance (p<0.05)

1. The mean of total count at admission is 6578.3 ± 3456.3, Platelet at admission is 108699.6±79663.5, PCV at admission is 36.7±5.45, PT is 18.03±4.23, APTT is 50.1±20.6, SGOT is 316.4±253.7, SGPT is 233.6±278.1, BIL is 0.8±1.03, Albumin is 3.36±0.63, ALP is 179±62.3 and CPKMB is 64.5±46.03.

2. The mean of total count at admission in DF is 4490.4 ± 2447.5, in DFWS is 5700.32 ±3241.056 and in SD is 9544.44 ±4680.804 with statistically significant p value (0.001).

3. The mean of platelet count at admission in DF is 138160 ±66021.8, in DFWS is 110161.3 ±82991.5 and in SD is 77777.7 ±89977.4 without statistically significant p value.

4. The mean PCV value at admission in DF is 36.8 ± 4.7, in DFWS is 36.16 ±5.96 and in SD is 37.4 ±5.7 without statistically significant p value.

5. The mean PT value at admission in DF is 15.5 ± 3.5, in DFWS is 16 ±3.4 and in SD is 22.6 ±5.8 with statistically significant p value (<0.001).

6. The mean APTT value at admission in DF is 47.9 ±14.2, in DFWS is 51.4 ± 22.6 and in SD is 51 ± 25.1 without statistically significant p value.

7. The mean AST value at admission in DF is 82.9 ± 61.1, in DFWS is 140.5 ± 99.7 and in SD is 725.9 ±600.5 with statistically significant p value (<0.001).

8. The mean ALT value at admission in DF is 31.7 ± 18.9, in DFWS is 80.7 ± 87.1 and in SD is 588.4 ± 728.3 with statistically significant p value (<0.001).

9. The mean Bilirubin value at admission in DF is 0.4 ± 0.1, in DFWS is 0.7 ± 1.2 and in SD is 1.3 ± 1.8 without statistically significant p value.

10. The mean Albumin value at admission in DF is 3.6 ± 0.3, in DFWS is 3.2 ± 0.6 and in SD is 3.3 ± 1 with statistically significant p value (=0.044).

11. The mean ALP value at admission in DF is 148.1 ± 43.3, in DFWS is 177.7 ± 76.8 and in SD is 217.2 ± 66.9 with statistically significant p value (=0.026).
12. The mean CPKMB value at admission in DF is 51.3 ± 28.7, in DFWS is 41.4 ± 20.8 and in SD is 100.8 ± 88.6 with statistically significant p value (=0.001).

### Table 07: ‘P value’ comparison of Laboratory parameters among DF, DFWS & SD.

| Multiple Comparisons (Post hoc test) | P Value |
|--------------------------------------|---------|
| Total count at admission             |         |
| Dengue Fever with Dengue fever with warning signs | 0.377   |
| Dengue Fever with Severe Dengue      | 0.001*  |
| Dengue fever with warning signs with Severe Dengue | 0.009* |
| PT                                  |         |
| Dengue Fever with Dengue fever with warning signs | 0.590   |
| Dengue Fever with Severe Dengue      | <0.001* |
| Dengue fever with warning signs with Severe Dengue | <0.001* |
| APTT                                |         |
| Dengue Fever with Dengue fever with warning signs | 0.501   |
| Dengue Fever with Severe Dengue      | 0.654   |
| Dengue fever with warning signs with Severe Dengue | 0.961   |
| AST                                 |         |
| Dengue Fever with Dengue fever with warning signs | 0.014*  |
| Dengue Fever with Severe Dengue      | <0.001* |
| Dengue fever with warning signs with Severe Dengue | <0.001* |
| ALT                                 |         |
| Dengue Fever with Dengue fever with warning signs | 0.008*  |
| Dengue Fever with Severe Dengue      | <0.001* |
| Dengue fever with warning signs with Severe Dengue | <0.001* |
| BIL                                 |         |
| Dengue Fever with Dengue fever with warning signs | 0.249   |
| Dengue Fever with Severe Dengue      | 0.018*  |
| Dengue fever with warning signs with Severe Dengue | 0.248   |
| Albumin                             |         |
| Dengue Fever with Dengue fever with warning signs | 0.003*  |
| Dengue Fever with Severe Dengue      | 0.163   |
| Dengue fever with warning signs with Severe Dengue | 0.819   |
| ALP                                 |         |
| Dengue Fever with Dengue fever with warning signs | 0.176   |
| Dengue Fever with Severe Dengue      | 0.001*  |
| Dengue fever with warning signs with Severe Dengue | 0.117   |
| CPK-MB                              |         |
| Dengue Fever with Dengue fever with warning signs | 0.138   |
| Dengue Fever with Severe Dengue      | 0.132   |
| Dengue fever with warning signs with Severe Dengue | 0.001*  |

Note: * significant at 5% level of significance (p<0.05)

### Table 08:- Distribution of chest xray findings among types of dengue illness:

| CXR                        | TOTAL   | Dengue Fever | D.F With warning sign | Sever Dengue | Chi square test |
|----------------------------|---------|--------------|-----------------------|--------------|-----------------|
|                            | n       | %            | n         | %            | n         | %            |               |
| NORMAL                     | 59      | 90.7         | 25        | 100          | 29        | 93.5         | 5             | 55.6          | <0.001*        |
| LUNG CONSOLIDATION         | 6       | 9.23         | 0         | 0            | 2         | 6.5           | 4             | 44.4          |               |
| Total                      | 65      | 100          | 25        | 100.0        | 31        | 100.0         | 9             | 100.0         |               |
Chest X-ray findings was mainly consolidation and is seen in 44.4% of severe dengue cases and 6.5% of DFWS cases.

X-ray was normal in 100% cases of DF, 93.5% of DFWS and 55.6% of SD.

Chi square test p<0.001 suggests consolidation is more common & specific in severe dengue over DFWS & DF.

**Table 09:** Distribution of ultrasound findings among types of dengue illness:

| USG Abdom & pelvis | Total        | Dengue fever | Dengue fever with warning signs | Severe dengue | p value |
|-------------------|--------------|--------------|---------------------------------|---------------|---------|
|                   | n | % | n | % | n | % | n | % |                  |
| CHOLECYSTITIS     | 2 | 5 | 38.4 | 20.0 | 16 | 51.6 | 4 | 44.4 | 0.049 * |
| ASCITES           | 3 | 2 | 27.0 | 32.0 | 19 | 61.3 | 5 | 55.6 | 0.086 |
| HEPATOMEGALY      | 6 | 9.23 | 1 | 4.0 | 5 | 16.1 | 0 | 0.0 | 0.174 |
| SPLENOMEGALY      | 3 | 4.61 | 0 | 0.0 | 3 | 9.7 | 0 | 0.0 | 0.178 |
| GB WALL EDEMA     | 8 | 12.3 | 3 | 12.0 | 4 | 12.9 | 1 | 11.1 | 0.988 |
| PLEURAL EFFUSION  | 1 | 16.9 | 0 | 0.0 | 8 | 25.8 | 3 | 33.3 | 0.014 * |
1. Out of 65 cases maximum cases (n=32) showed ascites accounting to 49.2% followed by cholecystitis (n=25) accounting to 38.4% and pleural effusion (n=11) accounting to 17%.
2. Ascites constituted about 32%, 61.3% & 55.6% in DF, DFWS & SD respectively.
3. Cholecystitis constituted about 20%, 51.6% & 44.4% in DF, DFWS & SD respectively which shows statistical significant difference with p=0.049 stating it is more specific for DFWS & SD.
4. Pleural effusion constituted about 0%, 25.8% & 33.3% in DF, DFWS & SD respectively which shows statistical significant difference with p=0.014 stating it is specific for DFWS & SD.

Table 10:-Roc analysis of selected parameters to detect severe dengue

Table 10a:-

| Test Variables | Area Under the Curve | Std. Error | p value | 95% Confidence Interval |
|----------------|----------------------|------------|---------|------------------------|
|                |                      |            |         | Lower Bound | Upper Bound  |
| PCV            | 0.528                | 0.105      | 0.79    | 0.322       | 0.734       |
| AST            | 0.824                | 0.102      | 0.002*  | 0.625       | 1.000       |
| ALT            | 0.824                | 0.081      | 0.002*  | 0.665       | 0.984       |
| BIL            | 0.81                 | 0.082      | 0.003*  | 0.649       | 0.97        |
| ALP            | 0.756                | 0.107      | 0.014*  | 0.545       | 0.967       |
| PT             | 0.890                | 0.047      | <0.001* | 0.798       | 0.983       |
| APTT           | 0.495                | 0.128      | 0.697   | 0.208       | 0.710       |
| CPK-MB         | 0.691                | 0.114      | 0.067   | 0.467       | 0.916       |
| AST*/ALT       | 0.813                | 0.101      | 0.003*  | 0.615       | 1.000       |

Note: * significant at 5% level of significance (p<0.05)

Table 10b:-

| Test Variables | Positive if Greater Than or Equal To | Sensitivity | Specificity |
|----------------|-------------------------------------|-------------|-------------|
| PCV            | 35.95                               | 44.4%       | 41.1%       |
| AST            | 156.0                               | 77.8%       | 76.8%       |
| ALT            | 44.00                               | 66.7%       | 62.5%       |
| BIL            | 0.45                                | 88.9%       | 53.6%       |
| ALP            | 191.5                               | 77.8%       | 75.0%       |
| PT             | 17.35                               | 77.8%       | 75.0%       |
| APTT           | 45.85                               | 55.6%       | 50.0%       |
| CPK-MB         | 45.5                                | 66.7%       | 66.1%       |
Table 10c:-

| Test Variables | Area Under the Curve | Std. Error | p value | 95% Confidence Interval |
|----------------|----------------------|------------|---------|-------------------------|
| TOTAL COUNT    | 0.163                | 0.060      | 0.001*  | 0.044 - 0.281           |
| PLATELET       | 0.739                | 0.102      | 0.022   | 0.540 - 0.939           |
| ALBUMIN        | 0.643                | 0.123      | 0.171   | 0.402 - 0.884           |

Note: * significant at 5% level of significance (p<0.05)

Table 10d:-

| Test Variables | Positive if Less Than or Equal To | Sensitivity | Specificity |
|----------------|-----------------------------------|-------------|-------------|
| TOTAL COUNT    | 6220                              | 33.3%       | 25.0%       |
| PLATELET       | 80500                             | 66.7%       | 66.1%       |
| ALBUMIN        | 3.25                              | 66.7%       | 66.1%       |
Table 11: Blood component usage in management.

| Blood     | DF       | DFWS     | SD       | Pooled Chi square test |
|-----------|----------|----------|----------|------------------------|
|           | No. of cases | %        | No. of cases | %        | No. of cases | %        |           |
| FFP       | 0         | 0        | 2        | 6.5       | 1           | 11.1     | P=0.0067* |
| PLATELET  | 0         | 0        | 6        | 19.4      | 3           | 33.3     |           |
| WHOLE BLOOD | 0       | 0        | 1        | 3.2       | 2           | 22.2     |           |

1. FFP was administered to 2 (6.5%) of 31 DFWS cases, 1(11.1%) out of 9 cases of SD and none of the cases with DF received FFP.
2. Platelets was administered to 6(19.4%) of 31 DFWS cases, 3(33.3%) out of 9 cases of SD and none of the cases with DF received platelets.
3. Whole blood was administered to 1(3.2%) of 31 DFWS cases, 2(22.2%) out of 9 cases of SD and none of the cases with DF received whole blood.
4. There is a statistically significant difference in transfusion of blood components between different types of dengue with p value of 0.0067.

Table 12: Distribution of cases according to duration of stay:

| Variable      | Dengue Fever | Dengue Fever with warning signs | Severe Dengue | ANOVA test |
|---------------|--------------|---------------------------------|---------------|------------|
|               | Mean         | STD                             | Mean          | STD        | Mean       | STD        | 0.002*     |
| Duration of Stay | 4.92         | 1.470                           | 6.00          | 1.732      | 7.78       | 3.701      |            |

ANOVA test shows ‘p value’ of 0.002 suggesting it is statistically significant and states that prolonged duration of stay is specific for severe dengue.

Table 13: Distribution of cases according to outcome:

| Outcome     | Dengue Fever | D.F With warning sign | Severe Dengue | Chi square test |
|-------------|--------------|-----------------------|---------------|----------------|
|             | No of cases  | %                     | No of cases   | %              |              |
| IMPROVED    | 25           | 100.0                 | 31            | 100.0          | 7            | 77.8       | 0.001*     |
| EXPIRED     | 0            | 0                     | 00            | 0              | 2            | 22.2       |            |
| Total       | 25           | 100.0                 | 31            | 100.0          | 9            | 100        |            |
Out of 65 cases 2 cases of SD (22.2%) expired with chi square test of ‘p value =0.001’ stating it is specific for SD.

**Discussion:**

A total of 65 proven cases of dengue enrolled during the study period from November 2016 to September 2018 were studied & classified based on 2009 WHO classification into dengue fever without warning signs (DF), dengue fever with warning signs (DFWS) and severe dengue (SD). The cases are proven to be dengue positive by card test (NS1, IgM & IgG) or ELISA IgM.

The levels of haematological, biochemical parameters were evaluated in each case to assess the severity of Dengue infection. Imaging findings involving Chest x-ray and Ultrasound abdomen and pelvis were assessed in each case.

**Age:**

Age group and mean age of patients at presentation in this study were comparable to studies by K.S.Sahana et al\(^{(61)}\) & Chacko B et al\(^{(56)}\).

| STUDY SERIES     | AGE IN YEARS | MEAN AGE |
|------------------|--------------|----------|
| Present study    | 0-14         | 7.6      |
| K.S.Sahana et al\(^{(31)}\) | 0-15         | 8        |
| Chacko B et al\(^{(45)}\) | 0-14         | 7.87     |

The mean age of presentation of children with Dengue fever without warning signs, with warning signs and severe dengue in the present study were 8.91 yrs, 9 yrs and 4.88 yrs respectively with p value of 0.012 suggesting there is age wise significant difference.

**Gender:**

Gender distribution in present study was comparable to studies by Mulay S et al\(^{(65)}\), Chacko B et al\(^{(56)}\) & Jain H et al\(^{(63)}\).

| STUDY SERIES      | MALE (no of cases) | FEMALE (no of cases) | M:F     |
|-------------------|--------------------|----------------------|---------|
| Present Study     | 41                 | 24                   | 1.70:1  |
| Mulay S et al\(^{(4)}\) | 56                 | 32                   | 1.75:1  |
| Chacko B et al\(^{(45)}\) | 44                 | 29                   | 1.52:1  |
| Jain H et al\(^{(2)}\) | 35                 | 30                   | 1.16:1  |

**Incidence:**

Incidence in our study was comparable to studies by Mulay S et al\(^{(65)}\) & Jain H et al\(^{(63)}\) where there is predominance of DFWS and opposed to study by Kumar AMK et al\(^{(64)}\) where there is predominance of DF cases.
**Clinical features:**

Dengue virus infections may be classified into dengue fever without warning signs, dengue fever with warning signs and severe dengue based on symptoms and signs in 2009 WHO classification. Infants and young children usually develop an undifferentiated febrile disease that can be accompanied by a maculopapular rash. Older children and adults may develop either a mild febrile syndrome or the classical dengue fever, characterized by fever, headache, myalgia, arthralgia and rash.

Most of the cases (n=40) in present study came to the hospital with in first 4 days of onset of illness accounting to 61.5%. Maximum cases of DF, DFWS presented during 3-4 days of onset of illness where as SD presented during 5-7 days. This is comparable to study by Mishra S et al (62).

In our study most common symptom was found to be fever which is noted in all cases(100%) followed by vomitings(47.6%), pain abdomen (35.4%) which was considered as a warning sign only when it was persistent(30.77%), hepatomegaly (24.6%), myalgia (13.85%), headache (10.7%), loose stools (9.23%), arthralgia (7.7%), cough & cold (4.6% each), hurried breathing (3.08%) and other fewer symptoms like nausea, giddiness, rashes, icterus, convulsions. This was comparable to studies by Narayanan et al (51) & Mulay S et al (65) where fever and vomiting are the most common symptoms with variations in other symptoms and opposed to study by Jain H et al (63) where most common symptoms were fever, bleeding, headache, nausea & vomiting.

| Symptoms and Signs | Present Study (N=65) (%) | Narayanan et al (n=89) (%) | Mulay S et al(n=88) (%) | Jain H et al (n=65) (%) |
|--------------------|--------------------------|---------------------------|-------------------------|------------------------|
| Fever              | 100                      | 97                        | 100                     | 100                    |
| Vomiting           | 47.7                     | 83                        | 64.8                    | 46.1                   |
| Pain Abdomen       | 35.4                     | 23.7                      | 62.5                    | 36.9                   |
| Hepatomegaly       | 24.6                     | 54                        | 39.8                    | 90.7                   |
| Myalgia            | 13.85                    | 54.2                      | 53.4                    | 63                     |
| Headache           | 10.77                    | 28.8                      | 48.9                    | 64.6                   |
| Splenomegaly       | 4.6                      | 10                        | 20.5                    | 26.1                   |
| Bleeding Manifestations | 1.5   | 66                        | -                       | 58.4                   |
| Icterus            | 1.5                      | 10                        | -                       | -                      |

**Warning signs:**

In our study most common warning signs were persistent abdominal pain (30.77%), hepatomegaly (24.6%), abdominal tenderness (23.07%), increase in hematocrit with decrease in platelet count (7.69%) and persistent vomiting (6.15%) and other fewer signs included bleeding tendencies, ascites, pleural effusion etc. This is comparable to warning signs in study by Jain H et al (63).

**Serology Tests**

Of 65 cases NS1 was noted positive in DF (100%), DFWS (90%) & SD (56%).

IgM in DF (8%), DFWS (23%) & SD (11%). IgG in DF (20%), DFWS (26%) & SD (22%). These findings are comparable to Kumar AMK et al (64). To enrol in the study, positive result in any of the above serological tests is considered.
In present study most of the cases (n=44) are only NS1 positive accounting to 67.7% followed by positivity in NS1+IgG in 7(10.76%) cases, NS1+IgM+IgG in 4(6.15%) cases, NS1+IgM in 3(4.61%) cases, only IgG in 3(4.61%) and only IgM in 2(3.07%) cases. These NS1 findings are comparable to study by Mishra S et al\(^62\). ELISA IgM was done in 33 cases out of which 22 were positive and 11 were negative. Rapid card test IgM was positive only in 2 out of these 33 cases in which ELISA was done. Both ELISA and Rapid card test were positive in only one case suggesting that ELISA is superior to rapid card test in detecting Dengue.

**Laboratory investigations:**

**Haematological findings:**
Platelets and haematocrit values are commonly measured during the acute stages of dengue infection. A drop of the platelet count below 100 000 per µL may be observed in dengue fever but it is a constant feature of severe dengue. Thrombocytopenia is usually observed in the period between day 3 and day 8 following the onset of illness. Haemoconcentration, as estimated by an increase in haematocrit of 20% or more compared with convalescent values, is suggestive of hypovolaemia due to vascular permeability and plasma leakage.

1. Of 65 cases, thrombocytopenia was noted in 69.23% of cases, among these Platelet count (PLC) of 1-1.5 lakh/mm\(^3\) is seen in 26.1%, 50000-1 lakh/mm\(^3\) in 16.9% and <50000/mm\(^3\) in 26.1% of cases.
2. Mean values of PLC at admission when compared among DF, DFWS & SD showed a decreasing pattern with least value in SD & highest in DF suggesting worsening from DF to SD.
3. Raised hematocrit of ≥35% is seen in 63.07% cases.
4. Mean values at admission when compared among DF, DFWS & SD showed a drop from DF To DFWS but increased to SD with highest value in SD & least in DFWS with no statistical significance (p=0.801).
5. Total leukocyte count <4000cells/mm\(^3\) i.e Leukopenia is seen in 41.5% of cases.
6. Mean values of TC at admission when compared among DF, DFWS & SD showed an increasing pattern with highest value in SD & least in DF with statistical significance (p=0.001) suggesting worsening from DF to SD.
7. APTT of more than 34 seconds is seen in 72.3% of cases. Mean values of APTT when compared among DF, DFWS & SD showed an increasing pattern with similar values in DFWS & SD with least value in DF with no statistical significance was noted.
8. PT of more than 13.5 seconds is seen in 83% cases. Mean values of PT when compared among DF, DFWS & SD showed an increasing pattern with highest value in SD & least in DFWS with statistical significance (p=0.001) suggesting worsening from DFWS to SD.
9. This findings are comparable to study by Pothapregada S et al\(^89\) & few variables of study by Jain H et al\(^63\).

| Variable          | Present Study (%) | Pothapregada S et al\(^89\)(%) | Jain H et al\(^63\)(%) |
|-------------------|-------------------|---------------------------------|------------------------|
| TLC <4000cells/mm\(^3\) | 41.5              | 19.1                            | 44                     |
| Raised Hematocrit | 63.07             | 46.4                            | 84                     |
| PLC <1.5lakh/mm\(^3\) | 69.23             | 82.4                            | -                      |
| PLC <1 lakh/mm\(^3\) | 43.07             | -                               | 80                     |
| PLC<50000/mm\(^3\) | 26.1              | 16.5                            | -                      |
| PT (>13.5sec)     | 83                | 3.4                             | -                      |
| APTT (>34sec)     | 72.3              | 1.5                             | -                      |

**Biochemical findings:**

Biochemical findings include Liver function tests (LFT) & CPK-MB levels. Upon injury to the liver, the enzymes, aspartate aminotransferase(AST) and alanine aminotransferase (ALT), are released into the bloodstream, and as a consequence these enzymes are believed to be sensitive indicators of liver damage. In the acute phase of the disease, an increase occurs in aminotransferases, the levels of which subsequently decrease as the liver recovers. AST may be found in high concentrations in the heart muscle, liver cells and skeletal muscle and, in lower concentrations, in the kidneys and pancreas. ALT is mainly found in the liver and in lower concentrations in the kidney. While majority of the patients have only mild or moderate elevation of these transaminases, some of them have levels elevated by 10-fold or greater. In dengue infections, the levels of serum AST are greater than serum ALT, which is in contrast to the normal finding with viral hepatitis. It has been suggested that this may be due to excess release of AST from damaged myocytes during dengue infection. The elevation of the AST level is usually higher than that of ALT in patients with dengue fever during the first week of infection, with a decrease to normal levels within three weeks. Some studies have suggested that the average levels of transaminases were significantly higher in SD patients than in DF patients.
1. Mean value of AST was 316.4 IU/L, it was raised (>40IU/L) in 56 cases (86%). On comparison of mean values among DF, DFWS & SD there is an increasing pattern with highest value in SD & least in DF with statistical significance (p<0.001) suggesting high values are specific for SD.

2. Mean value of ALT was 233.6 IU/L, it was raised (>40IU/L) in 30 cases (46%). On comparison of mean values among DF, DFWS & SD there is an increasing pattern with highest value in SD & least in DF with statistical significance (p<0.001) suggesting high values are specific for SD.

3. Mean value of ALP was 179 IU/L. On comparison of mean values among DF, DFWS & SD there is an increasing pattern with highest value in SD & least in DF with statistical significance (p<0.001) suggesting high values are specific for SD.

4. Mean value of CPK-MB was 64.5 IU/L. It was raised (>26IU/L) in 55 cases (84.6%). On comparison of mean values among DF, DFWS & SD there is a drop from DF to DFWS and increased in SD with highest value in SD & least in DFWS with statistical significance (p=0.001) suggesting high values are specific for SD.

5. These findings are comparable to study by Kulothungan R et al\textsuperscript{(94)}.

| Variable | Present study | Kulothungan R et al\textsuperscript{(94)} |
|----------|---------------|----------------------------------------|
| AST (Normal- < 40IU/L) | DF (%) | DFWS (%) | SD (%) | DF(%) | DFWS (%) | SD (%) |
| 41-100 | 6(24) | 2(6.45) | 1(11.1) | 42 (79.2) | 7 (23.7) | 0(0) |
| 101-200 | 5(20) | 9(29.03) | 2 (22.2) | 11 (20.8) | 23 (76.3) | 0 (0) |
| >200 | 1(4) | 8(25.8) | 6 (66.7) | 0 (0) | 0 (0) | 20 (100) |
| TOTAL | 25(100) | 31(100) | 9(100) | 53 (100) | 30 (100) | 20(100) |
| ALT (Normal- < 40IU/L) | 19(76) | 14(45.16) | 2(22.2) | 48 (90.6) | 23 (59) | 0 (0) |
| 41-100 | 6(24) | 8(25.8) | 1(11.1) | 5 (9.4) | 16 (41) | 0 (0) |
| 101-200 | 0(0) | 6(19.3) | 1(11.1) | 0 (0) | 0 (0) | 11 (100) |
| >200 | 0(0) | 3(9.6) | 5(55.5) | 0 (0) | 0 (0) | 11(100) |
| TOTAL | 25(100) | 31(100) | 9(100) | 53 (100) | 39 (100) | 11(100) |
| CPK-MB (Normal) | 4 (16) | 5(16.2) | 1 (11.1) | 51 (96.2) | 1 (6.67) | 0 (0) |
| CPK-MB (Abnormal) | 21 (84) | 26 (83.8) | 8 (88.9) | 2 (3.8) | 14 (93.3) | 35 (100) |
| TOTAL | 25(100) | 31(100) | 9(100) | 53 (100) | 15(100) | 35(100) |

**Serum Albumin & bilirubin:**

Of 65 cases in our study low serum albumin (<3.5g/dl) is noted in 34 cases (52.3%). Mean value was 3.36 g/dl. On comparison of mean values among DF, DFWS & SD there is a drop from DF to DFWS and increased in SD with highest value in DF & least in DFWS with statistical significance (p=0.044) suggesting low values are more common in DFWS & SD.

Mean value of total serum bilirubin (<1.3mg/dl) is 0.8mg/dl. On comparison of mean values among DF, DFWS & SD there is an increasing pattern with highest value in SD & least in DF with no statistical significance (p<0.108) suggesting no specific pattern in dengue.

**Comparison of ‘p values’ of laboratory findings among DF, DFWS & SD:**

Using Post Hoc test when p values of various laboratory parameters are compared among DF, DFWS & SD to assess the severity and pattern of disease progression following findings were noted:

1. In TLC evaluation on comparison of DF v/s DFWS no statistical significance was noted (0.377) where as DF v/s SD (0.001) & SD v/s DFWS (0.009) showed statistical significance suggesting no much difference between DF & DFWS but SD has high TLC values in dengue illness.

2. In PT evaluation on comparison of DF v/s DFWS no statistical significance was noted (0.590) where as DF v/s SD (<0.001) & SD v/s DFWS (<0.001) showed statistical significance suggesting no much difference between DF & DFWS but SD has high PT values in dengue illness.

3. In AST evaluation on comparison of DF v/s DFWS (0.014), DF v/s SD (<0.001) & SD v/s DFWS (<0.001) showed statistical significance among all three stages suggesting high values in dengue illness are more specific to SD.

4. In ALT evaluation on comparison of DF v/s DFWS (0.008), DF v/s SD (<0.001) & SD v/s DFWS (<0.001) showed statistical significance among all three stages suggesting high values in dengue illness are more specific to SD.
5. In CPK-MB evaluation on comparison of DF v/s DFWS (0.138) & DF v/s SD (0.132) no statistical significance was noted where as & SD v/s DFWS (0.001) showed statistical significance suggesting but SD has high values in dengue illness.
6. In Bilirubin evaluation on comparison of DF v/s DFWS (0.249) & SD v/s DFWS (0.248) no statistical significance was noted where as DF v/s SD (0.018) showed statistical significance suggesting SD has high values in dengue illness due to more liver damage.
7. In Albumin evaluation on comparison of DF v/s DFWS (0.003) showed statistical significance where as DF v/s SD (0.163) & SD v/s DFWS (0.819) showed no statistical significance suggesting DFWS has least values in dengue illness.

Imaging findings:

Chest x-ray:
In our study, among 65 cases with dengue infection, 6(9.23%) cases showed abnormal lung findings with lung infiltration, of which 2(6.5%) are of DFWS and 4(44.4%) are of SD. These findings are comparable to study by Kulothungan R et al.(94).

In both the studies most cases with positive findings are under severe dengue category. p value is <0.001 which shows statistical significance stating that positive chest x-ray findings are specific for severe dengue.

| Study Series     | DF (%) | DFWS (%) | SD (%) | Total (%) | P-value |
|------------------|--------|----------|--------|-----------|---------|
| Present Study    | 0      | 2 (6.5%) | 4 (44.4%) | 6 (9.23%) | 0.001   |
| Kulothungan R et al. | 4 (7.5%) | 0 (0%) | 15 (30%) | 19 (18.4%) | 0.003   |

USG abdomen and pelvis:
In our study of 65 cases with dengue infection, most common ultrasound finding was cholecystitis accounting to 38.4%, followed by ascites (27%), pleural effusion (17%), GB wall thickening (12.3%). This is comparable to studies by Mulay S et al (65) & Chacko B et al (56). Pleural effusion was better detected in ultrasound (17%) than in x-ray (0%).

| USG Finding           | Present Study (n=65) (%) | Mulay S et al\(^1\) (n=88) (%) | Chacko B et al\(^2\) (n=73) (%) |
|----------------------|--------------------------|-------------------------------|-------------------------------|
| Cholecystitis        | 38.4                     | 53.4                          | 21.91                         |
| GB Wall thickening   | 12.3                     | 27.07                         | 16.4                          |
| Ascites              | 27.07                    | 30.7                          | 16.4                          |
| Hepatomegaly         | 9.23                     | 39.8                          | 17.8                          |
| Splenomegaly         | 4.61                     | 20.5                          | 9.58                          |
| Pleural Effusion     | 16.92                    | 38.6                          | 30.13                         |

Out of 65 cases polyserositis manifestation in the form of ascites (27.07%) and pleural effusion (17%) was noted. These can be further subdivided under DF, DFWS & SD as follows. This is comparable to study by Kumar AMK et al (64).

| Polyserositis | DF (%) | DFWS (%) | SD (%) |
|--------------|--------|----------|--------|
| Present study | 32     | 87.1     | 89.9   |
| Kumar AMK et al\(^1\) | 20    | 47.4     | 57.1   |

Maximum percentage of polyserositis is noted in SD (89.9%) followed by DFWS (87.1%) and least in DF (32%) suggesting with increase in severity frequency of polyserositis increases.

Roc:
Among the 65 cases reviewed, about 9 cases (13.84%) had severe dengue.
1. AST, ALT, BIL, ALP, PT, SGOT\(^2\)/SGPT and total count were found to be good at identification of severe dengue.
2. AST (AUC 0.824; 95% CI 0.625-1.000) optimal cut off ≥156 U/L with sensitivity of 77.8% and specificity of 76.8%.
3. ALT (AUC 0.824; 95% CI 0.665-0.984) optimal cut off ≥44 U/L with a sensitivity of 66.7% and specificity of 62.5%.
4. Bilirubin (AUC 0.81; 95% CI 0.649-0.97) optimal cut off ≥0.45mg/dL with a sensitivity of 88.9% and specificity of 53.6%.
5. ALP (AUC 0.756; 95% CI 0.545-0.967) optimal cut off ≥191.5 U/L with a sensitivity of 77.8% and specificity of 75.0%.
6. PT (AUC 0.890; 95% CI 0.798-0.983) optimal cut off ≥17.35 sec with a sensitivity of 77.8% and specificity of 75.0%.
7. The composite index AST$^2$/ALT (AUC 0.813; 95% CI 0.615–1.000) optimal cut off ≥400.4 with a sensitivity of 88.9% and specificity of 76.8%.
8. Total count (AUC 0.163; 95% CI 0.044–0.281) optimal cut off ≤ 6220 cells/mm$^3$ with sensitivity of 33.3% and specificity of 25%.

In present study the composite index (AST$^2$/ALT) was the most accurate (AUC 0.813; 95% CI 0.615–1.000) when optimal cut off is ≥ 400.4 with highest sensitivity (88.9%) and specificity (76.8%) stating that it may be used as a marker for identification of severe dengue based on admission AST and ALT which is comparable to study done by Sani SS et al[95]. This is followed by AST, ALP, PT, ALT and BILIRUBIN which can be used to predict severity of dengue infection.

**Blood products usage in management:**

| Types of Dengue | Platelet transfusion | Kumar AMK et al |
|----------------|----------------------|----------------|
|                | YES | NO | YES | NO |
| DF             | 0%  | 100% | 6.7% | 93.3% |
| DFWS           | 19.4% | 81.6% | 26.3% | 73.7% |
| SD             | 33.3% | 66.7% | 14.3% | 85.7% |

Platelet transfusion was done in 19.4% of DFWS, 33.3% of SD which is comparable to study by Kumar AMK et al[64]. Out of 65 cases blood products were transfused in 13(20%) cases of which platelets were transfused in 9(13.8%) of 65 cases of which 3(33.3%) cases are from severe dengue group, FFP was transfused in 1(11.1%) of severe dengue group and three children required whole blood transfusion which is comparable to study by Sujatha R et al[66] in which out of 125(22%) children who received blood products, platelets were transfused in 80 children (14% of 568) out of which 64 (32.9%) were from SD group. Fresh frozen plasma (FFP) was used in 23 children (11.8%) of severe dengue group. Four children required whole blood transfusion.

**Mean duration of stay:**

Out of 65 cases mean stay of duration of DF, DFWS & SD are 4.92, 6 & 7.78 days respectively. The overall mean duration of stay of all the cases together is 6.2 days. The duration is categorised into 3 groups viz; 0-3 days, 4-6 days & >6 days. Under this non severe dengue (includes DF & DFWS) the number of cases registered are 5(8.93%), 32(57.14%) & 19(33.93%) respectively where as under SD the number of cases are 1(11.1%), 3(33.3%) & 5(55.6%) respectively. This is comparable to studies by Mishra S et al[62] & Natwar lal Sharma et al[67].

|                  | Non severe dengue | Severe dengue | Mean duration |
|------------------|-------------------|---------------|--------------|
|                  | Dengue fever without warning signs & Dengue fever with warning signs |                |              |
| Present study    |                    |               |              |
| 0-3 days         | 5(8.93%)           | 1(11.1%)      | 6.23 days    |
| 4-6 days         | 32(57.14%)         | 3(33.3%)      |              |
| >6 days          | 19(33.93%)         | 5(55.6%)      |              |
| Natwar lal Sharma et al |                |               |              |
| 0-3 days         | 45(25.42%)         | 0(0%)         | 4.61 days    |
| 4-6 days         | 128(72.32%)        | 2(8.7%)       |              |
| >6 days          | 4(2.26)            | 21(91.3%)     |              |
| Mishra S et al   | 0-3 days           | 27(32.1%)     | 1(7.7%)      | 3.8 days    |
|                  | 4-6 days           | 57(67.9%)     | 5(38.5%)     |              |
### Outcome:
Outcome in present study was comparable to studies by K.S. Sahana et al\(^{(61)}\), Sujatha R et al\(^{(66)}\) and Mulay S et al\(^{(65)}\).

| Types of Dengue | Present Study n (%) | K.S. Sahana et al n (%) | Sujatha R et al n (%) | Mulay S et al n (%) |
|-----------------|---------------------|-------------------------|-----------------------|---------------------|
|                 | Improved | Expired | Improved | Expired | Improved | Expired | Improved | Expired |
| DF              | 25(100)  | 0(0)    | 39(100)  | 0(0)    | 66(100)  | 0(0)    | 14(100)  | 0(0)    |
| DFWS            | 31(100)  | 0(0)    | 22(100)  | 0(0)    | 308(100) | 0(0)    | 49(100)  | 0(0)    |
| SD              | 7(77.8)  | 2(22.2) | 18(90)   | 2(10)   | 187(96.4)| 7(3.6)  | 23(92)   | 2(8)    |

### Limitations of my study:--
1. Patients present to the hospital on different days after the onset of illness which may alter the levels of various parameters at admission.
2. ELISA test for IgM could be done only in 33 cases as Bijapur was proven to be dengue positive region by the district surveillance officers and they didn’t collect samples further.
3. Sample size of the present study is small.