e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(8); 1681-1687

Original Research Article

Hepatic Involvement in Children with Dengue Infection between 6 Months to 14 Years of Age

S. Bharathi[1], Nusrat Shameem[2], Anil Vuppala[3]

[1]Professor, Department of Paediatrics, Deccan College of Medical Sciences, Hyderabad city, Telangana, India

[2,3]Senior Resident, Department of Paediatrics, Deccan College of Medical Sciences, Hyderabad City, Telangana, India

Received: 01-05-2026 / Revised: 15-06-2026 / Accepted: 21-07-2026

Corresponding author: Dr. S. Bharathi

Conflict of interest: Nil

Abstract

Background: Dengue is one of the most important mosquito-borne viral infections affecting children in tropical and subtropical countries. Hepatic involvement is a common but often under-recognized manifestation of dengue infection, ranging from asymptomatic elevation of liver enzymes to severe hepatitis and hepatic failure. Early identification of hepatic dysfunction is essential for appropriate management and prevention of complications.

Objectives: To study the hepatic involvement in children with dengue infection between 6 months and 14 years of age.

Materials and Methods: This hospital-based prospective observational study was conducted in the Department of Paediatrics, DCMS, Hyderabad, from 1st November 2019 to 30th April 2021. A total of 104 serologically confirmed dengue cases (NS1 antigen and/or IgM ELISA positive) aged 6 months to 14 years were included. Detailed clinical evaluation and liver function assessment, including serum bilirubin, AST, ALT, alkaline phosphatase, serum proteins, serum albumin, and PT/INR, were performed. Hepatic dysfunction was defined as elevation of AST/ALT to more than twice the upper limit of normal, hepatomegaly, jaundice, or PT/ INR ≥1.5. Statistical analysis was performed using SPSS version 20.0, and associations were assessed using the Chi-square test.

Results: Among the 104 children, 68 (65.38%) were males and 36 (34.61%) were females, with a mean age of 6.36 ± 3.9 years. Fever was present in all children (100%), followed by vomiting (61.53%) and abdominal pain (34.61%). Flushing (50.00%) and hepatomegaly (40.38%) were the most common clinical signs. Elevated liver enzymes (>2 times the upper limit of normal) were observed in 64 (61.53%) children, hepatomegaly in 42 (40.38%), PT/INR >1.5 in 16 (15.38%), and jaundice in 2 (1.92%). Hepatic dysfunction was present in 70 (67.31%) children. Although hepatic dysfunction was more frequent among infants (85.71%) and children with severe dengue (83.33%), no statistically significant association was found with age, sex, or disease severity (P > 0.05).

Conclusion: Hepatic involvement is a common manifestation of dengue infection in children and is characterized predominantly by biochemical abnormalities rather than clinically evident liver disease. Elevated liver enzymes are the most frequent indicator of hepatic dysfunction, whereas jaundice is uncommon. Routine monitoring of liver function tests and coagulation parameters in children with dengue facilitates early recognition of hepatic involvement, timely intervention, and improved clinical outcomes.

Keywords: Dengue; Hepatic Involvement; Children; Liver Function Tests; Hepatomegaly; Transaminases.

DOI: 10.25258/ijcpr.18.8.250

Introduction

Dengue is one of the most important mosquito-borne viral infections affecting populations in tropical and subtropical regions worldwide. Over the past five decades, the global incidence of dengue has increased nearly 30-fold, making it a significant public health challenge. Despite difficulties in accurately estimating its worldwide burden, the disease continues to have substantial health and economic consequences. Approximately 75% of the global population at risk of dengue resides in the Asia-Pacific region, where the disease remains highly endemic. It is estimated that nearly 50 million dengue infections occur annually, placing around 2.5 billion people at risk of infection. [1-3] In Southeast Asia, dengue is a leading cause of illness and death among children. Paediatric patients are

particularly vulnerable, as the risk of mortality during a secondary dengue infection is considerably higher than that observed in adults. The transmission and distribution of dengue are influenced by several environmental and demographic factors, including rainfall, temperature, humidity, rapid urbanization, and inadequate vector control measures. The disease is caused by four antigenically distinct serotypes of the dengue virus (DENV-1 to DENV-4), all of which may circulate simultaneously in endemic regions, resulting in hyperendemic transmission in many countries. [3]

The clinical manifestations of dengue vary widely, ranging from asymptomatic infection and mild febrile illness to severe forms of the disease characterized by plasma leakage, severe hemorrhage, and multi-organ dysfunction. Besides the classical features, atypical involvement of various organs, including the liver, heart, kidneys, and central nervous system, has increasingly been recognized. Hepatic involvement is among the most frequently reported systemic complications, especially in children. The severity of liver injury may range from transient elevation of liver enzymes to acute hepatitis, jaundice, and, in rare cases, acute liver failure. The underlying mechanisms are believed to involve direct viral cytopathic effects, immune-mediated hepatocellular injury, circulatory impairment, metabolic acidosis, and hypoxic damage resulting from hypotension or hepatic microvascular leakage. [4,5]

Hepatic dysfunction is observed more commonly in patients with severe dengue, particularly those with dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Elevation of serum aminotransferases occurs early during the acute phase of illness and has been reported as a useful biochemical marker for dengue infection. Increased aminotransferase levels have also been associated with a higher risk of hepatic dysfunction, spontaneous bleeding, and severe clinical outcomes. Several studies from India and Thailand have identified dengue infection as one of the leading causes of acute liver failure in children, accounting for approximately 18.5% and 34.3% of paediatric acute hepatic failure cases, respectively. [6,7,8]

Our institution is a tertiary care referral hospital that receives a large number of paediatric patients with dengue infection presenting with diverse clinical manifestations. Considering the increasing burden of dengue and the clinical significance of hepatic involvement, the present study was undertaken to evaluate the extent and pattern of liver dysfunction among children diagnosed with dengue fever.

Objective: To study the hepatic involvement in children with dengue infection between 6 months to 14 years of age.

Materials and Methods

Source of Data: Children between 6 months and 14 years of age, admitted to Department of Paediatrics in DCMS Hyderabad from 1st November 2019 to 30th April 2021 with Dengue NS1 ELISA or IgM MAC ELISA positive.

Sample Size: Time bound study

Type of the Study: Hospital based prospective observational study.

Inclusion Criteria: Children between 6 months to 14 years, admitted in Department of paediatrics, DCMS, Hyderabad who are confirmed (positive NS1 Ag and IgM ELISA) case of dengue fever.

Exclusion Criteria

1. Children with associated infections known to cause hepatic involvement like Malaria, typhoid, Acute viral hepatitis, Leptospira, Viral exanthematous fevers.
2. IGM negative dengue like illnesses.
3. Children 14 years of age.

Method of Study: This is a time bound prospective observational study conducted between 1st November 2019 to 30th April 2021 in Department of Paediatrics, DCMS, and Hyderabad. Ethical approval was obtained from the Ethical Committee of DCMS, Hyderabad. All the serologically confirmed cases by dengue NS1 antigen detection or dengue IGM Mac ELISA aged from 6 months to 14 years as per the WHO guidelines were included in this study. The purpose of the study was explained to the parents or guardians of the child and an informed consent was taken from them enrolling a child in study group.

Drug induced hepatitis and other infective hepatitis like Malaria, enteric fever, hepatitis A and hepatitis B were excluded by history, examination and investigations.

Details were entered in a predesigned proforma which included details of clinical features and examination.

Children were treated according to recent WHO protocol. [9]

Methods

Children who met inclusion criteria were enrolled in the study. Detailed history and clinical examination findings were entered in a predesigned proforma. All the cases were subjected to liver function tests including total serum bilirubin (TSB), direct serum bilirubin, indirect serum bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), total protein, serum albumin and prothrombin time (PT)/international normalized ratio (INR). Patients were classified into groups of dengue without warning signs, dengue with warning signs and severe dengue according to

recent WHO protocol. [9] Liver dysfunction was considered if any of following is present:

- AST and/or ALT levels more than twice the upper limit of normal (ULN) with or without hepatomegaly.
- Jaundice.
- PT/INR ≥ 1.5.
- Based on elevation of liver enzymes (AST and/or ALT) following terms are defined as:
- **Liver Function Impairment:** Defined as an increase in aspartate transaminase (AST) and/or alanine transaminase (ALT) level of at least twice than the upper limit of normal. [9]
- **Hepatitis** – defined as an AST and/or ALT level at least four times higher than the upper limit of normal. [9]
- **Severe Hepatitis** – defined as an AST and/or ALT level of at least 10 times higher than the upper limit of normal. [9]

Liver Function Test: Liver function test was done using Trans Asian Biochemicals ERBA XL-300 fully computerised auto analyser. Parameters like total serum bilirubin (TSB), direct serum bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), total protein, serum albumin were measured by advanced calorimetric methods. [9]

Normal values of different parameters of liver function tests are taken as described in Annexure III.

Statistical Analysis: The data collected by a predesigned proforma from the patients was tabulated. Graphs and tables were generated for better understanding using Microsoft Word and Excel. Categorical data are presented as frequency and percentage (%).

Continuous data are presented as mean and standard deviation (SD) or median and interquartile range. Categorical variables between the groups were compared using chi-square test.

Continuous variables between the groups were compared using ANOVA. The contribution of different variables or attributes are depicted using bar diagrams, pie charts, etc. All analyses were performed using Statistical Package for the Social Sciences (SPSS) software, version 20.0.

Results

Table 1: Distribution according to age and gender

Variable	Category	Number of children	Percentage (%)
SEX	Male	68	65.38
	Female	36	34.61
AGE	6–12 months	14	13.46
	1–5 yrs	32	30.77
	6–10 yrs	32	30.77
	>11 yrs	26	25

Table 1 shows the distribution of the study participants according to sex and age. A total of 104 children were included in the study. Of these, 68 (65.38%) were males and 36 (34.61%) were females, indicating a male predominance. With regard to age distribution, the highest proportion of children belonged to the 1–5 years and 6–10 years age groups, with 32 (30.77%) children in each category. This was followed by the >11 years age group comprising 26 (25.00%) children, while the 6–12 months age group had the lowest representation with 14 (13.46%) children. Overall, the study population was predominantly male, with most participants aged between 1 and 10 years.

Table 2: Distribution according to clinical symptoms

Clinical symptoms	Total (n = 104)	Percentage (%)
Fever	104	100
Vomiting	64	61.53
Abdominal pain	36	34.61
Myalgia	24	23.07
Skin rash	18	17.3
Facial puffiness	18	17.3
Abdominal distension	12	11.53
Bleeding manifestations		
Malena	24	23.07
Haematemesis	2	1.92
Epistaxis	6	5.76
Convulsions	8	7.69
Altered sensorium	8	7.69
Limb swelling	4	3.84
Jaundice	2	1.92

Table 2 shows the distribution of clinical symptoms among the 104 children with dengue. Fever was the most common presenting symptom, observed in all children (104, 100%).

Vomiting was the second most frequent symptom, affecting 64 (61.53%) children, followed by abdominal pain in 36 (34.61%). Myalgia and malena were each reported in 24 (23.07%) children. Skin rash and facial puffiness were present in 18 (17.30%) children each, while abdominal distension was observed in 12 (11.53%) children. Convulsions and altered sensorium were noted in 8 (7.69%) children each, epistaxis in 6 (5.76%), and limb swelling in 4 (3.84%).

Hematemesis and jaundice were the least common manifestations, each occurring in 2 (1.92%) children. Overall, fever and gastrointestinal symptoms predominated, while bleeding manifestations and neurological symptoms were relatively less frequent.

Table 3: Distribution of Clinical Signs among the Study Participants (n = 104)

Clinical signs	Total (n = 104)	Percentage (%)
Flushing	52	50
Hepatomegaly	42	40.38
Pallor	24	23.07
Rashes/Petechiae	22	21.15
Ascites	16	15.38
Hepatosplenomegaly	14	13.46
Pedal edema	6	5.77
Icterus	2	1.92

Table 3 shows the distribution of clinical signs among the 104 children with dengue. Flushing was the most common clinical sign, observed in 52 (50.00%) children, followed by hepatomegaly in 42 (40.38%). Pallor was present in 24 (23.07%) children, while rashes/petechiae were noted in 22 (21.15%). Ascites and hepatosplenomegaly were observed in 16 (15.38%) and 14 (13.46%) children, respectively. Pedal edema was present in 6 (5.77%) children, whereas icterus was the least common clinical sign, occurring in only 2 (1.92%) children. Overall, flushing and hepatomegaly were the predominant clinical findings, while signs suggestive of severe systemic involvement, such as pedal edema and icterus, were relatively uncommon.

Table 4: Hepatic Dysfunction among the Study Participants (n = 104)

Hepatic dysfunction	Number (n = 104)	Percentage (%)
Elevated liver enzymes (>2 times)	64	61.53
Hepatomegaly	42	40.38
INR >1.5	16	15.38
Jaundice	2	1.92

Table 4 shows the hepatic dysfunction observed among the 104 children with dengue. Elevated liver enzymes (>2 times the upper limit of normal) were the most common hepatic abnormality, seen in 64 (61.53%) children. Hepatomegaly was present in 42 (40.38%) children, while an elevated international normalized ratio (INR >1.5), suggestive of impaired liver synthetic function, was observed in 16 (15.38%) children. Jaundice was the least common manifestation, occurring in only 2 (1.92%) children. Overall, biochemical evidence of hepatic involvement was more frequent than clinically apparent liver dysfunction in children with dengue.

Table 5: Association of age and sex with Hepatic Dysfunction among the Study Participants (n = 104)

Age group	Hepatic Dysfunction Present	Hepatic Dysfunction Absent	Total	P-value
6–12 months	12 (85.71%)	2 (14.29%)	14	0.264
1–5 years	20 (62.50%)	12 (37.50%)	32	0.622
6–10 years	18 (56.25%)	14 (43.75%)	32	0.257
>11 years	20 (76.92%)	6 (23.08%)	26	0.393
Total	**70**	**34**	**104**	
Sex	**Hepatic Dysfunction Present**	**Hepatic Dysfunction Absent**	**Total**	**P-value**
Male	44 (64.70%)	24 (35.30%)	68	0.43
Female	26 (72.22%)	10 (27.78%)	36	
Total	**70**	**34**	**104**	

Table 6 shows the association between age group and hepatic dysfunction among the 104 children with dengue. Hepatic dysfunction was most frequently observed in children aged 6–12 months, where 12 (85.71%) of the 14 children were affected. Among children aged 1–5 years, hepatic dysfunction was present in 20 (62.50%) of 32 children, while 18 (56.25%) of the 32 children in the 6–10 years age group had hepatic dysfunction. In the >11 years age group, 20 (76.92%) of the 26 children had hepatic dysfunction. Although the proportion of hepatic dysfunction varied across different age groups, the association was not statistically significant (Chi-square = 2.6812, P = 0.4431). Thus, age was not found to be significantly associated with hepatic dysfunction in the study population. Table 6 shows the association between sex and hepatic dysfunction among the 104 children with dengue. Hepatic dysfunction was present in 44 (64.70%) of the 68 male children and in 26 (72.22%) of the 36 female children. The remaining 24 (35.30%) males and 10 (27.78%) females did not have hepatic dysfunction. Although the proportion of hepatic dysfunction was slightly higher among females than males, the difference was not statistically significant (Chi-square = 0.3022, P = 0.5831). This indicates that the occurrence of hepatic dysfunction was not significantly associated with sex in the study population.

Table 7: Association between Disease Type and Hepatic Dysfunction among the Study Participants (n = 104)

Disease type	Hepatic Dysfunction Present	Hepatic Dysfunction Absent	Total
Dengue without warning signs	28 (53.84%)	24 (46.15%)	52
Dengue with warning signs	32 (80.00%)	8 (20.00%)	40
Severe dengue	10 (83.33%)	2 (16.67%)	12

Overall comparison (3 groups): Chi-square = 1.1592, P = 0.5601

Pairwise comparisons:

- Dengue without warning signs vs. Dengue with warning signs: Chi-square = 0.3572, P = 0.5501
- Dengue without warning signs vs. Severe dengue (Yates' correction): Chi-square = 0.0152, P = 0.9041
- Dengue with warning signs vs. Severe dengue (Yates' correction): Chi-square = 0.288, P = 0.592

Table 7 shows the association between disease type and hepatic dysfunction among the 104 children with dengue. Hepatic dysfunction was present in 28 (53.84%) of the 52 children with dengue without warning signs, 32 (80.00%) of the 40 children with dengue with warning signs, and 10 (83.33%) of the 12 children with severe dengue.

The proportion of hepatic dysfunction increased with disease severity, being lowest in children with dengue without warning signs and highest among those with severe dengue. However, the overall association between disease type and hepatic dysfunction was not statistically significant (Chi-square = 1.1592, P = 0.5601). Similarly, pairwise comparisons between the disease categories did not demonstrate statistically significant differences (all P > 0.05). Thus, although hepatic dysfunction appeared to be more frequent in children with warning signs and severe dengue, this trend did not reach statistical significance in the present study.

Discussion

Our study was conducted to study hepatic involvement in children with dengue infection aged 6 months to 14 years. During the study period, 104 confirmed cases of dengue were admitted. Of these, 50 were Dengue NS1 ELISA positive, 34 were Dengue MAC ELISA IgM positive, and 20 were positive for both NS1 antigen and IgM antibody.

In our study, the age of the patients ranged from 6 months to 14 years, with a mean age of 6.36 ± 3.9 years. The majority of cases belonged to the 1–5 years and 6–10 years age groups, each accounting for 30.77% of the study population. Children aged >11 years constituted 25.00%, while those aged 6–12 months comprised 13.46% of the cases. Overall, 61.54% of the children were between 1 and 10 years of age.

Although the majority of children with hepatic dysfunction belonged to the 1–5 years and 6–10 years age groups because these groups represented the largest proportion of the study population, the highest proportion of hepatic dysfunction was observed among infants aged 6–12 months (85.71%). This finding suggests that hepatic dysfunction may be proportionately more frequent among infants with dengue infection than in older children. In a study conducted by Pothapregada S. et al [10] at JIPMER, Puducherry, the mean age was 6.9 years, and the 6–12 years age group was the most commonly affected. Similarly, Setyoboedi B. et al [11] reported a mean age of 4.93 years, with the majority of children being older than 4 years.

Sex Distribution: Both sexes are susceptible to dengue infection. In the present study, males outnumbered females, with 68 (65.38%) males and 36 (34.62%) females, resulting in a male-to-female ratio of 1.9:1.

In a study by Prommalikit O. et al [13]., as well as in the study by Setyoboedi B. et al [11]., a female predominance was observed, with male-to-female ratios of 1:1.15 and 1:1.32, respectively.

The male predominance observed in the present study may be incidental or may reflect greater exposure of male children to mosquito bites due to increased outdoor activities and healthcare-seeking patterns. However, there is no conclusive evidence to suggest that biological sex independently influences susceptibility to dengue infection.

In the present study, elevated liver enzymes (>2 times the upper limit of normal) were the most common indicator of hepatic involvement, observed in 64 (61.53%) children. Hepatomegaly was present in 42 (40.38%) children, INR >1.5 was noted in 16 (15.38%), while jaundice was the least common manifestation, occurring in only 2 (1.92%) children.

Our findings are comparable with those of Jagadishkumar K. et al [13]., who reported elevated transaminases in nearly two-thirds of children with dengue, indicating that biochemical hepatic involvement is frequent even in the absence of overt clinical liver disease. They also observed hepatomegaly as one of the common clinical signs, whereas jaundice was uncommon.

Similarly, Fayyaz A. et al [6] reported raised liver enzymes in the majority of children with dengue infection, with hepatomegaly being the second most common manifestation. Clinical jaundice was rare, suggesting that hepatic involvement in dengue is predominantly biochemical rather than clinically apparent.

Yasmin A. et al [7] also demonstrated that liver involvement is common in pediatric dengue, with elevated serum transaminases being the earliest and most frequent abnormality. They observed that hepatomegaly occurred in a substantial proportion of patients, while jaundice was infrequent and usually associated with severe disease.

In the study by Setyoboedi B. et al [11]., liver enzyme elevation was documented in a majority of children with dengue infection, and hepatomegaly was commonly observed on clinical examination. Coagulopathy, reflected by prolonged coagulation parameters, was mainly seen in severe dengue cases, which is consistent with the 15.38% of children in our study who had an INR >1.5.

The WHO Dengue Guidelines state that hepatic involvement is a well-recognized feature of dengue infection, ranging from asymptomatic elevation of liver enzymes to severe hepatitis and hepatic failure in a small proportion of patients. Hepatomegaly is considered one of the warning signs of severe disease, whereas jaundice is relatively uncommon and generally indicates severe hepatic injury or multiorgan dysfunction. [8]

Overall, the findings of the present study are in agreement with previous studies, demonstrating that elevated liver enzymes constitute the most frequent manifestation of hepatic involvement, followed by hepatomegaly, whereas coagulopathy (INR >1.5) occurs in a smaller proportion of patients and jaundice remains a rare clinical finding in children with dengue infection.

Conclusion

The present hospital-based prospective observational study evaluated hepatic involvement in 104 children aged 6 months to 14 years with confirmed dengue infection. The findings demonstrate that hepatic involvement is a common manifestation of paediatric dengue.

Elevated liver enzymes were the most frequent evidence of hepatic dysfunction, observed in 61.53% of children, followed by hepatomegaly (40.38%), INR >1.5 (15.38%), and jaundice (1.92%). Fever was the universal presenting symptom, while vomiting and abdominal pain were the most common associated complaints. Flushing and hepatomegaly were the predominant clinical signs.

Although hepatic dysfunction was proportionately more common among infants and children with severe dengue, no statistically significant association was observed between hepatic dysfunction and age, sex, or disease severity in the present study ($P > 0.05$). This suggests that hepatic involvement can occur across all demographic groups and clinical categories of dengue infection.

Overall, the study concludes that hepatic involvement is a frequent but predominantly mild and reversible complication of dengue infection in children, with biochemical abnormalities occurring more commonly than clinically evident liver disease. Early recognition of hepatic dysfunction through routine assessment of liver function tests and coagulation profile can facilitate timely management, prevent complications, and improve clinical outcomes. Careful monitoring of children with dengue, particularly those with warning signs or severe disease, is therefore recommended for early detection and appropriate management of hepatic involvement.

References

1. World Health Organization. Dengue bulletin 2020. Geneva: World Health Organization; 2020. p. 148-160.
2. World Health Organization. Global strategy for dengue prevention and control 2012–2020. Geneva: World Health Organization; 2012.

3. World Health Organization. Dengue and severe dengue: Fact sheet. Geneva: World Health Organization; 2021.
4. Biswas A, Kumar S, Pangtey G, Soneja M, Gulati S, et al. National guideline for dengue case management during COVID-19 pandemic. New Delhi: Ministry of Health and Family Welfare, Government of India; 2020.
5. Bhatt P, Sabeena SP, Varma M, Arunkumar G. Current understanding of the pathogenesis of dengue virus infection. Curr Microbiol. 2021;78(1):17-32.
6. Fayyaz A, Fayyaz Z, Fatima S. Dengue fever: Hepatic involvement in children up to 12 years of age. Professional Med J. 2017;24(11):1605-1609.
7. Yasmin A, Akhter R, Shapla SP, Yeasmin L. Severity of liver involvement in children with dengue infection. Bangladesh J Infect Dis. 2020;7(2):90-94.
8. World Health Organization, Special Program me for Research and Training in Tropical Diseases. Dengue: Guidelines for diagnosis, treatment, prevention and control. New ed. Geneva: World Health Organization; 2009.
9. Biswas A, Pangtey G, Devgan V, Singla P, et al. National guidelines for clinical management of dengue. New Delhi: Ministry of Health and Family Welfare, Government of India; 2015. p. 196-206.
10. Pothapregada S, Kamalakannan B, Thulasingh am M, Sampath S. Clinically profiling pediatric patients with dengue. Journal of global infectious diseases,2016; 8(3), 115-20.
11. Setyoboedi, B., Angelika, D., Zuraida, E., Darmowandowo, W., Arief, S., & Basuki, P. S. Liver Involvement in Children with Dengue Infection. Folia Medica Indonesiana, 2011: 47(4), 215-218.
12. Prommalikit O, Thisyakorn U, Thisyakorn C. Serum Aminotransferases in Thai Children with Dengue Infection. Iranian journal of pediatrics,2017; 25(6).
13. Jagadishkumar K, Jain P, Manjunath VG, Umesh L. Hepatic involvement in dengue fever in children. J Clin Diagn Res. 2012;6(3):457-461.