

Evaluation of Hepatic Enzyme levels and Haematological Profiles in Chikungunya patients- An institutional study

Abstract

Background: Chikungunya is a viral infection caused by the Chikungunya virus (CHIKV) belonging to the Togaviridae family. The transmission of the virus is taking place through the bite of infected daytime biting female mosquitoes – primarily *Aedes aegypti* and *Aedes albopictus*. There were many reports which highlighted the number of reported cases of Chikungunya has been increasing in India in recent years, especially since 2016-2017.

Materials and Methods: Blood samples were collected from patients diagnosed with having Chikungunya. Routine laboratory investigations were carried out for analysing haematological and serum enzyme profiles.

Result: Our results highlighted that the alterations of haematological and hepatic dysfunction are prevalent in Chikungunya infection, with SGPT rising significantly more than SGOT. Hepatic Enzymes levels appear to have a directly proportional correlation with severity of infections.

Conclusion: Our study demonstrated that haematological and hepatic enzymes levels should be explored as routine laboratory markers for assessing the severity of Chikungunya infection, as they will help in employing an appropriate patient therapy, and thus optimise the use of available resources.

Keywords: Chikungunya, Dengue, Hepatic, Haematological

Comment [S1]: the objective of the study was not clearly stated.

Comment [S2]: More details required

Comment [S3]: More details required

Introduction

Chikungunya is a viral illness transmitted by mosquitoes affecting all age groups, but severe complications are more often observed in children. Over the past two decades, there has been global increase in the frequency of Chikungunya and its epidemics. Symptoms generally start 4-7 days after the mosquito bite. The acute phase is characterised by joint and muscle pain, high fever, extreme weakness, headache, vomiting, and rashes. In the chronic phase, various neurological syndromes and non-neurological manifestations can occur [1]. In 2006, the CHIK virus (CHIKV) re-emerged in India after 32 years, causing the epidemic affecting more than 1.4 million people across the 13 States, and post epidemic, a declining trend was seen till 2011 [1-3].

The WHO South-East Asia Regional Office has reported a significant number of Chikungunya cases in almost 151 districts in 8 states of India suffered from many cases of chikungunya fever. The most affected states are Andhra Pradesh, Andaman & Nicobar Islands, Tamil Nadu, Karnataka, Maharashtra, Gujarat, Madhya Pradesh, Kerala and Delhi [1,2]. As usual, the outbreaks of Chikungunya infections are most likely to occur in the post-monsoon period when the vector density significantly increases. There are 3 epidemiological factors: the host (man and mosquito), agent (virus), environment (abiotic and biotic factors) agent for Chikungunya viruses. Human beings are considered as the reservoir for the chikungunya virus during the epidemic time.

The rapid spread of the disease in Southern part of India from 2004 has afflicted millions of people and left many of them with crippling disabilities. Chikungunya disease continues to cause epidemics in many countries in the region. The patient in this context acts as the reservoir of infection for others in the household and the community. Therefore, public health measures to minimise the transmission of infection become imperative to prevent and control the outbreak from spreading [3-5].

Fever with or without arthralgia is a prevalent manifestation of several other diseases. CHIK fever may not have typical manifestations, or it may co-exist with other infectious diseases like dengue fever or non-infectious diseases like rheumatoid arthritis [6].

The analysis and diagnosis of the case in the community need to be communicated immediately to the nearest public health official for identification of clusters by person, place and time and expansion of the control measures in the community and district levels.

The most significant features seen in CHIKV-positive patients are lymphopenia, leukopenia, hypocalcemia, and elevated transaminases; but these features were not consistently reported in all studies and vary depending the clinical phase of infection.

The general laboratory diagnosis of Chikungunya often reveals lymphopenia, neutrophils and thrombocytopenia, an elevated creatinine, and elevated hepatic transaminases. In this study we tried to establish the relationship between the severity of Chikungunya infection and its impact on levels hepatic enzymes and haematological profiles of individuals.

Materials and Methods

Recruitments of Patients and Healthy Individuals: This study was carried out in the Department of Biochemistry and General medicine at mamata Medical College and general Hospital, Khammam, Telangana from the period of July 2021 to November 2021.

Study Design: It was a prospective cohort study over two years through sample and sampling techniques. A total of 50 patients admitted to the hospital with a history of fever of more than 38.50C and CHICKV positive were selected using purposive sampling techniques. Clinical signs and symptoms, severity, and outcomes with relevant laboratory parameters were compared in detail. They are followed from the onset of fever to time of recovery or discharge according to WHO discharge criteria whichever is earlier. Same numbers of normal healthy individuals were also recruited for this study. Duly signed Informed consent forms were collected from all the participants during the study.

Routine Laboratory Investigations: The 5-7ml of blood samples were collected from all these participants' investigations were done- blood counts, clinically patients are monitored and for platelets, hematocrit count, haemoglobin count, total leukocyte count.

Liver Function Test: SGPT, SGOT were estimated by using protocol prescribed by the International Federation of Clinical Chemistry. ALP, Total Protein, Albumin, Total Bilirubin were estimated by colourimetric assay.

Statistical analysis: The collected data analysis was done using SPSS software. The results were presented as mean \pm standard deviation (SD) and percentages. Mean, and SD was computed for all continuous variables and comparisons were done using Student's t-test.

Comment [S4]: • Regarding the recruitment of the patients it is preferable to use study population instead.

- In this part the author not mention the exact number of the healthy individual and their selection criteria to be used as control group.
- Generally the author required to determine the inclusion and exclusion criteria for the study.
- The author not declare the approval of this study

Comment [S5]: • More details required to describe the process of specimen collection, preservation and preparation before analysis

- For specimen analysis more information required for the analysis methods and instruments used
- For LFTs some information mentioned but for haematological investigation not.

Comment [S6]: • More details required about the normality of the data and the bases used to select the analysis tests

- No indicator for the significance of the statistical tests. The author must determine when the statistical test be significant

Results

The total numbers of 50 cases of acute febrile illness were recruited based on their clinical report as seropositive for CHIKV infection, an equal number of healthy individuals also participated in this study. There were altogether 67 (63.6%) men and 33 (36.4%) women participants. Most of the participants were in the 20–30-year age group. A seasonal peak with 42 (34.7%) cases was seen in monsoon season. The patient characteristics and salient clinical features of acute chikungunya infection, and biochemical parameters are compared in Tables 1 and 2. The rural residency was prominent in all groups. Fever was seen in all cases (100%). The symptomology of chikungunya included headaches, joint pain, weakness, and restricted joint movement. No complications were reported. Deranged liver function was seen in all patients (100%).

Table 1: Comparison of characteristics and clinical features in between normal healthy individuals and patients groups.

Characteristics	Control Group	Patient Group
Age Group (Years)	<20	4 (8)
	20-30	21 (42)
	31-40	11 (22)
	41-50	3 (6)
	51-60	2 (4)
	>60	3 (6)
Gender	Male	37 (74)
	Female	23 (46)
Residence	Urban	22 (44)
	Rural	28 (56)
Symptoms	Fever	50 (100)
	Joint Pain	31 (62)
	Backache	15 (30)
	Vomiting	4 (8)

Comment [S7]: • The number of study cases mentioned only, instead of that the author prefer to mention this number as proportion of total number including the control group.

- Some of the inclusion criteria mentioned and this not preferred.
- There is some mistake in the written number of total men should be revised.
- While the age number is not mentioned in the study design part, the mentioned range should be revised.

Comment [S8]: the age, gender compared between the two groups as number and percentage but the relation not tested for significance. It is recommended that the author preferable to used suitable statistical test to determine the relation significance between the groups.

Out of 50 patients, 37 were male and 23 were female and in control group of 50 healthy individuals 40 were male and 10 were female. Most of the participants were in the age group of 20 – 40 and none of them were below 20 years and above 70 years of age. All the patients had fever as a presenting complaint. Most of them had myalgia at the time of presentation.

Table 2: Comparison of biochemical parameters in between normal healthy individuals and patients groups.

Comment [S9]: the laboratory investigations including haematological investigation and LFTs mentioned . I recommend to separate them in two tables so as to be simple for the reader interest.

Parameters	Control Group	Patient Group	p Value
Hb	13.15±1.82	11.55±2.36	0.5012
TLC	8560±2634	4781±2219	0.0082
PC	155,700±23,523	67,622±44,254	0.0015
HCT	36.67±4.52	38.66±6.07	0.523
SGPT	28.87±4.23	239.68±589.25	0.5215
SGOT	25.92±6.22	345.52±1356.52	0.633
ALP	34.21±14.21	144.21±110.26	0.2231
Total Bilirubin	0.98±0.29	1.84±0.28	0.001
Direct Bilirubin	0.51±0.18	0.98±0.33	0.001
Total Protein	7.4±0.59	6.29±0.89	0.0747
Albumin	4.11±0.47	3.15±0.69	0.0130

Hb: Hemoglobin, TLC: Total leukocyte count, PC: Platelets count, HCT: Hematocrit, RBS: Random blood sugar, ALP: Serum alkaline phosphatase, SGPT: Serum glutamate pyruvate transaminase, SGOT: Serum glutamic-oxaloacetic transaminase.

Table 3: Comparison of deranged liver enzymes in between normal healthy individuals and patients groups.

Comment [S10]: the laboratory investigation data were separated and derangement were determined. The results in these two tables needs more clarification and also no statistical test used to determine the significance.

Parameters	Control Group	Patient Group
SGPT (U/L)	60-180 (%)	1 (2)
	181-500 (%)	0
	501-1000 (%)	0
	>1000 (%)	0
SGOT (U/L)	38-120 (%)	0
	121-500 (%)	1 (2)
	500-1000 (%)	0
	>1000 (%)	0

Elevated liver enzymes were found in almost all patients. Of the liver enzymes, SGPT levels were significantly higher than SGOT levels.

Table 4: Comparison of thrombocytopenia in between normal healthy individuals and patients groups.

Platelets Count (/μL)	Control Group	Patient Group
>150,000	26 (52)	2 (4)
150,000-100,000	23 (46)	5 (10)
100,000-50,000	1(2)	20 (40)
50,000-20,000	0	13 (26)
<20,000	0	6 (12)
<10,000	0	3 (6)
Platelets transfusion	0	1 (2)

Thrombocytopenia was noted in 43 patients, of whom 12 had bleeding, and 31 had no bleeding. Statistically, the Chi-square test was used to test the significance of thrombocytopenia and bleeding tendencies. There was no significant difference ($p = 0.945$) found between the variations in the thrombocytopenia and the bleeding tendencies. This implies that bleeding tendencies does not depend upon thrombocytopenia.

Discussion

Currently, Chikungunya is causing significant public health concern throughout the world, particularly in South-East Asian countries. Recently dengue outbreaks caused significant morbidity and mortality in certain parts of India mainly in Andhra Pradesh, Uttar Pradesh and Tamil Nadu [7]. Hepatic dysfunctions in dengue are common. It is due to either direct effect of the virus on hepatocytes or due to reactive hepatitis. Hepatic involvement in dengue fever is in the form of elevated serum aminotransferase [8]. Those patients with elevated liver enzymes are more likely to have increased risk of bleeding tendencies, shock, ARDS, renal failure. In addition to decreased platelet count, hepatic dysfunction plays a significant role in

Comment [S11]: the laboratory investigation data were separated and derangement were determined. The results in these two table needs more clarification and also no statistical test used to determine the significance.

Comment [S12]: Consideration of these Comments or opinions into account may contribute in the strength of the study discussion and help the author to formulate a useful conclusion

bleeding. Hence, it is mandatory to evaluate serum aminotransferases in all patients with dengue fever [9]. It is observed that, out of 50 patients, most of the patients had elevated liver enzymes, SGPT levels were significantly higher than SGOT levels, and these patients had severe complications.

Chikungunya viral infection is not generally fatal but can cause neurological and optical manifestations. Severe joint pain is the prominent clinical manifestation and can persist for months to a year [10]. As Dengue Fever (DF) has a high incidence and mortality rate, symptomatic patients are tested only for DENV and only in rare cases for chikungunya viral infection. This scenario is an important reason why chikungunya cases go undiagnosed in dengue-endemic regions, and the actual burden of the chikungunya viral infection has been missed. Thus, investigation for both viruses should be done, especially in endemic regions. Accurate and early diagnosis of coinfections would help inappropriate management [11, 12]. The number of cases increases during and after the monsoon months because higher humidity lengthens the life span of mosquitoes and increased temperatures shorten the extrinsic incubation period [13]. Rising of the cases during the monsoon period with highest cases in different months had been reported in previous studies from India [11-14]. November was observed as a peak among all the months of the year in this study.

Earlier studies have reported increased incidences of atypical hemorrhagic manifestations [12-14] and hepatic dysfunction [15]. Hepatic dysfunction was the most common complication in our dengue and coinfection groups. SGPT levels were significantly higher than SGOT levels.

Conclusion

Haematological profile alteration and Hepatic involvement are common in Chikungunya. It is characterized by elevated liver enzymes, i.e. SGPT more than SGOT levels. Elevated liver enzymes are associated with complications like bleeding, shock and organ impairment. In

Comment [S13]: Consideration of these recommendations or opinions into account may contribute in the strength of the study and help the author to formulate a useful conclusion

addition to thrombocytopenia, hepatic involvement plays a significant role in bleeding. Elevated liver enzymes have got prognostic value in this study. Hence, liver enzymes are mandatory in dengue fever to look for complications, and it is of prognostic value. Those patients with elevated liver enzymes should be monitored carefully than those patients with normal liver enzymes.

UNDER PEER REVIEW

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