

Short communication

Chikungunya virus infection in pre covid-19 and covid-19 era; an observation from a tertiary care hospital

Comment [RD1]: pre-covid-19

Comment [RD2]: hospital , the State of Uttar Pradesh

ABSTRACT

To study the impact of covid-19 pandemic on CHIKV (Chikungunya virus) infection. Data of cases which were referred for anti-Chikungunya IgM during 1st January 2018 to 31st December 2021 (four years) was analyzed retrospectively. Total 8822 serum samples were tested of which 3125 (35.42 %) were positive. Per cent positivity in Pre-covid-19 and covid-19 era was 36.5% and 33.5% respectively. Cases presenting with Acute Febrile illness had significant lower positivity in covid time (31.11%) than pre-covid-19 time (45.29%). There was a decrease in cases of CHIKV (Chikungunya virus) infection rolled due to covid-19 pandemic.

Comment [RD3]: the covid-19

Comment [RD4]: This study determined the impact of covid-19 pandemic on CHIKV (Chikungunya virus) infection.

Comment [RD5]: that

Comment [RD6]: from

Comment [RD7]: A total of 8822 serum

Comment [RD8]: significantly

Comment [RD9]: Finding of this revealed a decrease in cases of CHIKV (Chikungunya virus) infection during the covid-19 pandemic.

KEYWORDS: COVID-19 PANDEMIC; PRE-COVID 19, Chikungunya, Chikungunya virus, anti-Chikungunya IgM.

INTRODUCTION-

Chikungunya fever (CHIKF) is an arthropod borne viral disease [1]. Chikungunya virus (CHIKV) belongs to the family *Togaviridae*, genus *Alphavirus*. It was first recognized as a human pathogen after its isolation from the serum of an infected patient during an outbreak of debilitating arthritic disease in 1952 in Tanzania [2]. Infection by CHIKV typically results in mild and self-limiting disease in infected humans, characterized by fever, skin rash, myalgia, and arthralgia that can last few weeks to months [3]. Although it is a self-limiting disease and the associated fatality rate is low, chikungunya-related death has been reported in young infants, the elderly, and people with pre-existing conditions such as cardiovascular disease, diabetes, kidney disease, and chronic liver disease [4]. It can cause different sequelae like AES (acute encephalitis syndrome), AFI (Acute Febrile Illness), Arthralgia, Chronic Febrile illness and others [5]. For the first time

Comment [RD10]: arthropod-borne

Comment [RD11]: the debilitating

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in 1963, CHIKF was reported in India. It re-emerged in 2005 after a 32 years long period of quiescence. Currently it has become a global health concern affecting every part of India too [6]. The adapted virus has subsequently threatened to undergo both endemic and epidemic spread in Africa, Asia, Europe, and America [7].

Comment [RD15]: 32-year-long period

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Here, we are reporting our observation on CHIKV positivity in chikungunya suspected cases in Covid (2020-21) and pre-Covid (2018-19) era.

MATERIAL AND METHODS

VRDL (Viral Research Diagnostic Laboratory) at King George's Medical University, UP (KGMU) collects desired data of every patient who is referred to the laboratory for tests related to viral infections, on a predesigned questionnaire. Data of cases which were referred for anti-Chikungunya IgM during 1st January 2018 to 31st December 2021 (four years) was analyzed retrospectively. All cases provided consent to use their data for future research. Their identity was kept anonymous. Approval from Human ethical committee of KGMU was given.

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Testing for CHIKV infection was done by detecting anti CHIKV IgM using kits manufactured and supplied by National Institute of Virology (NIV) Pune, India. Laboratory was under external quality assurance under NIV throughout study.

Comment [RD21]: anti-CHIKV

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Data was analysed to study any shift in demography, geography and clinical syndromes in Pre-covid (2018-19) and Covid (2020-21) era in Chikungunya positivity. For purpose of analysis cases were divided in five clinical syndromes; AES (Acute Encephalitis Syndrome), AFI (Acute Febrile Illness), Arthralgia, CFI (Chronic Febrile Illness) and others and State of Uttar Pradesh (UP) was divided into 5 geographical zones; **Central** (included districts; Farrukhabad, Hardoi, Kannauj, Etawah, Auraiya, Kanpur Nagar, Kanpur Dehat, Hamirpur, Unnao, Lucknow, Barabanki, Raebareli, Amethi, Fatehpur, Pratapgarh, Faizabad, Sultanpur, Ambedkar Nagar) **West** (included districts; Gonda, Siddharthanagar, Maharajganj, Basti, Sant Kabir Nagar, Gorakhpur, Kushinagar, Deoria, Azamgarh, Mau, Ballia, Jaunpur, Ghazipur, Sant Ravidas Nagar, Varanasi, Chandauli) **East** (included districts; Saharanpur, Shamli, Muzaffarnagar, Bijnor, Bagpat, Meerut,

Amroha, Moradabad, Gautam Budh Nagar, Bulandshahr, Sambhal, Aligarh, Mathura, Hathras, Agra, Firozabad, Mainpuri and cases referred from other neighbouring states), **North** (included districts; Rampur, Bareilly, Budaun, Pilibhit, Shahjahanpur, Lakhimpur Kheri, Sitapur, Bahraich, Shravasti, Balrampur and cases referred from other neighbouring states) and **South** (included districts; Jalaun, Jhansi, Lalitpur, Mahoba, Banda, Chitrakoot, Kaushambi, Prayagraj, Mirzapur, Sonbhadra and cases referred from other neighbouring states). (Table 1 and Figure 1)

Chi-square test was applied to study association between CHIKV positivity and different variables in pre-covid and covid era.

Comment [RD33]: The Chi-square test

Comment [RD34]: the association

Comment [RD35]: the pre-covid

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RESULTS and DISCUSSION

During 1st January 2018 to 31st December 2021, total 8822 serum samples were tested for anti CHIKV IgM by ELISA of which 3125 (35.42 %) were positive. The table shows the positivity in different groups in pre-covid and covid era. Number of cases tested in Pre-covid era was 5720 and per cent positivity was 36.45% compared to covid era when number of references were 3102 and per cent positivity was 33.52%. Number of references in covid era dropped significantly. There was no significant difference in case positivity rate among different age groups and gender groups during pre-covid and covid era. On syndrome wise analysis of case positivity, cases presenting with AFI had significant lower positivity in covid time (31.11%) than pre-covid time (45.29%). while cases presenting with Arthralgia showed significant increase in positivity (64.28%) during covid era. Cases presenting with chronic febrile illness and undefined syndromes also showed mild rise in positivity. Needless to state that cases tested during covid period were much less than those tested during pre-covid era (Table). On observing the zone wise data, central zone has maximum enrollment of cases due to location of the laboratory in central zone. Districts located far from laboratory referred lower number of cases than those situated geographically closer to laboratory. Positivity from central zone

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Comment [RD38]: a total of 8822

Comment [RD39]: anti-CHIKV

Comment [RD40]: the pre-covid and covid eras

Comment [RD41]: The number of cases in the Pre-covid era was 5720 representing a percent positivity of 36.45% compared to the covid era when the number of references was 3102 with a percent positivity of 33.52%..

Comment [RD42]: The number

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Comment [RD46]: 45.29%). Besides,

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Comment [RD50]: cases of CHIKV

Comment [RD51]: the covid

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Comment [RD53]: the pre-covid

Comment [RD54]: Table 1

Comment [RD55]: enrolment

Comment [RD56]: On observing the zone-wise data, the central zone has a maximum enrolment of cases due to the location of the laboratory in the central zone.

Comment [RD57]: Districts located far from the laboratory referred to a lower number of cases than those situated geographically closer to the laboratory.

dropped during covid-19 period while from rest of the state positivity in covid and pre-covid era was comparable.

Comment [RD58]: Positivity from the central zone dropped during the covid-19 period while from the rest of the state positivity in the covid and pre-covid era was comparable.

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Comment [RD60]: the enrolment

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Comment [RD62]: the covid

Comment [RD63]: the pre-covid

The COVID-19 pandemic has generated huge challenges. We focused on impact of covid 19 pandemic on enrollment of chikungunya cases where we found that references of cases reduced drastically during covid era (2020-21) as compared to pre-covid era (2018-19). Case positivity for CHIKV during covid-19 and pre-covid-19 era has no significant difference. Cases presenting with acute febrile illness had shown positive impact of pandemic as case positivity decreased during pandemic. Case positivity increased in cases presenting with Arthralgia, chronic febrile illness and other illnesses, although number of cases in these groups were less. Lock down or lack of hospital admission of noncovid-19 illness during pandemic time may have contributed to lower number of hospital references. Even outdoor services were limited to covid-19 cases only. Most of the general hospitals were converted as Covid-19 facility. An earlier study reported CHIKV outbreak in Uttar Pradesh, India in 2016.[8] Inflammatory polyarthrititis was the most common long-term sequelae to occur with chikungunya infection.[9] The Department of Health Research (DHR), Ministry of Health and Family Welfare, Government of India, is constantly making effort to establish and strengthen the network of laboratories across country to timely diagnosis of viruses causing outbreaks. [10]

Comment [RD64]: Finding of this study however, showed significant difference between case positivity for CHIKV during covid-19 and pre-covid-19 eras.

Comment [RD65]: The result showed that the covid-19 pandemic had a positive impact on acute febrile illness of CHIKV as the positivity decreased.

Comment [RD66]: The case positivity of CHIKV infection although increased among patients presented with Arthralgia, chronic febrile illness, and other symptoms. The number of CHIKV infection in these groups, however, were less.

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Conclusion- There was a decrease in CHIKV cases enrolled due to covid-19 pandemic. Per cent positivity in Pre-covid-19 and covid-19 era was 36.5% and 33.5% respectively.

Comment [RD73]: The 2020-21 covid-19 pandemic decreased the CHIKV cases enrolment in the State of Uttar Pradesh. Percent positivity in the Pre-covid-19 and covid-19 eras were 36.5% and 33.5% respectively.

REFERENCES

1. Padmakumar, B., Jayan, J. B., Menon, R. M., Krishnankutty, B., Payippallil, R., and Nisha, R. Comparative evaluation of four therapeutic regimes in chikungunya arthritis: a prospective randomized parallel-group study. Indian J. Rheumatol.2009; 4: 94–101.

2. Lumsden WH. An epidemic of virus disease in Southern Province, Tanganyika Territory, in 1952–53. II. General description and epidemiology. *Trans R Soc Trop Med Hyg.* 1955;**49**(1):33–57.
3. N .Goupil BA, Mores CN. A review of chikungunya virus-induced arthralgia: clinical manifestations, therapeutics, and pathogenesis. *Open Rheumatol J.* 2016;10:129–40.
4. Mohan A, Kiran DH, Manohar IC, Kumar DP. Epidemiology, clinical manifestations, and diagnosis of Chikungunya fever: lessons learned from the re-emerging epidemic. *Indian J Dermatol.* 2010;55(1):54-63. doi: 10.4103/0019-5154.60355. PMID: 20418981; PMCID: PMC2856377.
5. Imad HA, Matsee W, Kludkleeb S, Asawapaithulsert P, Phadungsombat J, Nakayama EE, Suzuki K, Leungwutiwong P, Piyaphanee W, Phumratanaprapin W, Shioda T. Post-Chikungunya Virus Infection Musculoskeletal Disorders: Syndromic Sequelae after an Outbreak. *Trop Med Infect Dis.* 2021 Apr 15;6(2):52. doi: 10.3390/tropicalmed6020052. PMID: 33921055; PMCID: PMC8167736.
6. Charrel RN, Leparc-Goffart I, Gallian P, de Lamballerie X. Globalization of Chikungunya: 10 years to invade the world. *Clin Microbiol Infect.* 2014;20(7):662–3.
7. Padbidri VS, Gnaneswar TT. Epidemiological investigations of chikungunya epidemic at Barsi, Maharashtra state, India. *J Hyg Epidemiol Microbiol Immunol.* 1979;23(4):445-51. PMID: 575900.
8. Ozair A, Khan DN, Prakash S, et al. Upsurge of chikungunya cases in Uttar Pradesh, India. *Indian J Med Res.* 2020;152(5):527-530. doi:10.4103/ijmr.IJMR_2303_18
9. Rodríguez-Morales, A.J.; Calvache-Benavides, C.E.; Giraldo-Gómez, J.; Hurtado-Hurtado, N.; Yepes-Echeverri, M.C.; García-Loaiza, C.J.; Patiño-Barbosa, A.M.; Sabogal-Roman, J.A.; Patiño-Valencia, S.; Hidalgo-Zambrano, D.M.; et al. Post-chikungunya chronic arthralgia: Results from a retrospective follow-up study of 131 cases in Tolima, Colombia. *Travel Med. Infect. Dis.* **2016**; 14: 58–59.

Comment [RD74]: Referencing style must be UNIFORM and strictly conform to the Journal guidelines.

10.Devendra T. Mourya, Pragya D. Yadav, P.T. Ullas, et al, Emerging/re-emerging viral diseases and new viruses on the Indian horizon; Indian J Med. Res. 2019 April; 149(4): 447-467.

UNDER PEER REVIEW

Table and Figure Legends:

Table 1: Positivity of CHKV in pre-covid-19 (2018-19) and covid-19 (2020-21) era analyzed in various groups

Figure 1: Division of Uttar Pradesh into Central, North, East, West and South zone for the convenience of analysis.

UNDER PEER REVIEW

Table 1: Positivity of CHKV in pre-covid-19 (2018-19) and covid-19 (2020-21) era analyzed in various groups

	Jan 2018- Dec19	Jan 2020- Dec 21	χ^2 STATISTIC	P-VALUE
TOTAL CASES POSITIVE FOR CHIKV/TOTAL TESTED	2085/5720(36.45)	1040/3102(33.52)	7.51	0.006
POSITIVITY OF CHIKUNGUNYA VIRUS				
AGE -GROUPS				
0-20	897/2634(34.05)	360/1164(30.92)	3.56	0.059
>20-40	666/1681(39.61)	364/990(36.76)	2.13	0.143
>40-60	364/943(38.60)	216/647(33.38)	3.27	0.070
60 & ABOVE	158/462(34.19)	100/301(33.22)	0.07	0.780
GENDER				
MALE	1209/3377(35.80)	595/1806(32.94)	4.22	0.039
FEMALE	876/2343(37.38)	445/1296(34.33)	3.36	0.066
SYNDROMES				
ACUTE FEBRILE ILLNESS				
AES	1161/3467(33.48)	572/1682(34.00)	0.13	0.711
ARTHRALGIA	43/121(35.53)	9/14(64.28)	4.37	0.036
CHRONIC FEBRILE ILLNESS				
OTHERS	55/184(29.89)	32/70(45.71)	5.63	0.017
	94/332(28.31)	44/105(41.90)	6.82	0.009
GEOGRAPHICAL ZONE				
CENTRAL UP	1313/3451(38.04)	661/1949(33.91)	9.16	0.002
EAST UP	353/1028(34.33)	171/505(33.86)	0.03	0.853
NORTH UP	394/1147(34.35)	184/567(32.45)	0.61	0.433
SOUTH UP	21/66(31.81)	11/36(30.55)	0.01	0.895
WEST UP	4/28(14.28)	13/45(28.88)	2.06	0.151

Characteristics	Positivity of Chikungunya Virus		X ²	P-Value
	Jan 2018- Dec19	Jan 2020- Dec 21		
Total Cases Positive for CHIKV/Total Tested	2085/5720(36.45)	1040/3102(33.52)	7.51	0.006
Age -Groups				
0-20	897/2634(34.05)	360/1164(30.92)	3.56	0.059
>20-40	666/1681(39.61)	364/990(36.76)	2.13	0.143
>40-60	364/943(38.60)	216/647(33.38)	3.27	0.070
≥ 60	158/462(34.19)	100/301(33.22)	0.07	0.780
Gender				
Male	1209/3377(35.80)	595/1806(32.94)	4.22	0.039
Female	876/2343(37.38)	445/1296(34.33)	3.36	0.066
Syndromes				
Acute Febrile Illness	732/1616(45.29)	383/1231(31.11)	59	0.000
AES	1161/3467(33.48)	572/1682(34.00)	0.13	0.711
Arthralgia	43/121(35.53)	9/14(64.28)	4.37	0.036
Chronic Febrile Illness	55/184(29.89)	32/70(45.71)	5.63	0.017
Others	94/332(28.31)	44/105(41.90)	6.82	0.009
Geographical Zone				
Central Up	1313/3451(38.04)	661/1949(33.91)	9.16	0.002
East Up	353/1028(34.33)	171/505(33.86)	0.03	0.853
North Up	394/1147(34.35)	184/567(32.45)	0.61	0.433
South Up	21/66(31.81)	11/36(30.55)	0.01	0.895
West Up	4/28(14.28)	13/45(28.88)	2.06	0.151

Comment [RD75]: The table was structured for clarity



- CENTRAL UP : FARRUKHABAD, HARDOL, KANNAUJ, ETAWAH, AURAIYA, KANPUR NAGAR, KANPUR DEHAT, HAMIRPUR, UNNAO, LUCKNOW, BARABANKI, RAEBARELI, AMETHI, FATEHPUR, AMETHI, PRATAPGARH, FAIZABAD, SULTANPUR, AMBEDKAR NAGAR
- NORTH UP : RAMPUR, BAREILLY, BUDAUN, PILIBHIT, SHAHJAHANPUR, LAKHIMPUR KHERI, SITAPUR, BAHRAICH, SHRIVASTI, BALRAMPUR
- SOUTH UP : JALAUN, JHANSI, LALITPUR, MAHABA, BANDA, CHITRAKOOT, KAUSHAMBI, PRAYAGRAJ, MIRZAPUR, SONBHADRA
- EAST UP : SAHARANPUR, SHAMLI, MUZAFFARNAGAR, BUNOR, BAGPAT, MEERUT, AMROHA, MORADABAD, GAUTAM BUDDHA NAGAR, BULANDSHAHR, SAMBHAL, ALGARH, MATHURA, HATHIRAS, ETAH, AGRA, FIROZABAD, MAINPURI
- WEST UP : GONDA, SIDDHARTHANAGAR, MAHARAJGANI, BASTI, SANT KABIR NAGAR, GORAKHPUR, KUSHINAGAR, DEORIA, AZAMGARH, MAU, BALLIA, JAUNPUR, GHAZIPUR, SANT RAVIDAS NAGAR, VARANASI, CHANDAULI

Figure 1: Division of Uttar Pradesh into Central, North, East, West and South zone for the convenience of analysis.

Comment [RD76]: The figure 1 should come first before the Table 1 in arrangement.

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