1 **Risk Factors for Chikungunya Outbreak in Kebridhar City, Somali Ethiopia,**

2 **2019. Unmatched Case-Control Study**

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Abstract

Background; *Chikungunya Virus* is a Ribose Nucleic Acid (RNA) virus transmitted by a mosquito bite. *Aedes Aegypti* and *Aedes Albopictus* are responsible vectors for *Chikungunya Virus* transmission. CHIKV outbreaks are characterized by rapid spread and infection rates as high as 75%. A combination of health system efforts and healthy behavior practices by the community is essential for effective control.

Methods; Unmatched case control study was done to identify risk factors of this outbreak. One case to two controls ratios was calculated. All cases during the study period (74 cases) and 148 controls were included in the study. Bivariate and multivariable analysis were implemented. Serum samples were tested by Real Time Polymerase Chain Reaction at Ethiopian Public Health Institute laboratory.

Results; A total of 74 chikungunya fever cases were reported starting from 19th May 2019 to 8th June 2019. Not using bed net at day time sleeping (P- value < 0.001, AOR 20.8, 95CI 6.4 – 66.7), presence of open water holding container (P- value 0.023, AOR 4, 95CI 1.2 – 13.5), presence of larvae in water holding container (P- value 0.015, AOR 4.8, 95CI 1.4 – 16.8), ill person with similar sign and symptoms in the family or neighbors (P- value <0.001, AOR 27.9, 95CI 6.5 – 120.4) and wearing not full body cover clothes (P- value 0.002, AOR 8.1, 95CI 2.2 – 30.1) were significant risk factors.

Conclusion; Using bed nets at day time sleeping, cover the water holding containers, wearing full body cover cloths are protective factors.

Keywords: Risk factor, Chikungunya, Outbreak, Kebridhar, Ethiopia

2

Background

Chikungunya Virus (CHIKV) is an RNA virus that belongs to the *Alphavirus* genus of the *Togaviridae* family transmitted by the bite of mosquitoes *Aedes aegypti* and *Aedes albopictus*. CHIKV outbreaks are characterized by rapid spread and infection rates as high as 75%; 72%–93% of infected persons become symptomatic. The disease manifests as acute fever and potentially debilitating polyarthralgia [1].

The *Aedes Mosquitoes* breed in domestic settings such as flower vases, water-storage containers, etc. and peri-domestic areas such as construction sites, coconut shells, discarded household junk items (vehicular tyre, plastic and metal cans, etc.). Adult mosquitoes rest in cool and shady areas in domestic and peri-domestic settings and bite humans commonly during the daytime [2].

Since the first outbreak in Tanzania in 1952 Chikungunya Virus has caused outbreaks in various parts of Africa. Chikungunya Virus has been found to circulate in Eastern and Central Africa. Chikungunya fever is commonly a self-resolved disease. Whereas, patients with coexisting conditions such as cardiovascular, neurologic, and respiratory disorders or diabetes needs hospitalization. Additionally, *Chikungunya Virus* may present with bleeding when co-exist with dengue fever [3-5].

Chikungunya Virus is a highly contagious disease that can affect up to 70% of the total population of the outbreak affected area. The virus can easily transmit across continents and the current growing of movement of people from one country to another country as well as international trade facilitate the importation of the virus [6].

Typical presentations of *Chikungunya Virus* infection are sudden onset of fever and joint pain but sometimes it may cause severe complications including myocarditis, meningitis, encephalitis, and flaccid paralysis [7].

61 Frequent outbreaks of *Chikungunya Virus* infection suggest that health system efforts for vector

62 control alone may not be sufficient for effective control. A combination of health system efforts

63 and healthy behavior practices by the community is essential for effective control of chikungunya

64 outbreak [8].

65 The prevention mechanisms for *Chikungunya Virus* are reduce human mosquito contact or

66 eliminate vector populations. In this regard, control measures should be focused on eliminating

67 the immature stages of the mosquitoes and their larval developmental sites [9]. This study helps to

68 identify the potential risk factors for this chikungunya outbreak in order to implement appropriate

69 vector control measures. This study can also be used as an information source for future planning

70 in regard to efforts towards arboviral disease controls.

71 **Methods**

72 **Study area and period**

73 This study was conducted at Kebridahar City Administration of Somali Region. Kebridahar City

74 is located 1006 kilometers to the East direction of Addis Ababa and 380 kilometers away from

75 Jigjiga. The city administration has ten kebeles. The area is lowland with temperature ranged from

76 $32^{o}C$ to $40^{o}C$. According to census 2007 of Ethiopia, the city administration has a total population

77 of 117,222. Fifty seven percent (66,817) of them were males and 12% (14,067) were children

78 below five years of age. There were two public hospitals in Kebridahar City Administration. This

79 outbreak investigation was conducted for one month, from 25th May 2019 to 25th June 2019.

80 **Study Design**

81 Unmatched case control study was conducted to determine the risk factors of chikungunya fever

82 disease outbreak and to design appropriate intervention strategies in Kebridahar City

83 Administration of Somali Region.

84   **Source Population**

85   All the residents of Kebridahar City were the source population.

86   **Study Population**

87   The study population for this study were all people diseased with chikungunya fever and controls

88   selected for the study from the source population.

89   **Sampling Method and Sample Size**

90   For this study the case to control ratio was 1 to 2. All cases and two controls for each case were

91   included. Therefore, 74 cases and 148 controls were participated in the study.

92   • **Selection of Cases**

93   All individuals who full fill the case definition of chikungunya fever and who was willing to

94   participate in the study were included in the study as a case. The cases were identified both from

95   health facility and from the community by active case search.

96   • **Selection of Controls**

97   Two controls for each case were selected from the neighbor households. One control was taken

98   randomly by lottery method from members of the household on the right side of the case's house

99   and the other control was selected by the same method from the household on the left side of the

100   case's house.

101   **Case Definitions and Outbreak Threshold**

102   • **Suspected Case**

103   A person with acute onset of fever and severe arthralgia or arthritis not explained by other medical

104   conditions, and who resides or has visited epidemic or endemic areas within 2 weeks before the

105   onset of symptoms [10].

106   • **Confirmed Case**

107   A suspected case with one of the following laboratory findings

108   • Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue,

109   blood, or other body fluid, OR

110   • Four-fold or greater change in virus-specific quantitative antibody titers in paired serum

111   samples, OR

112   • Virus-specific IgM antibodies in serum with confirmatory neutralizing antibodies in the same

113   or a later specimen [10].

114   • **Outbreak Threshold**

115   In non-endemic area a single case of suspected Chikungunya Virus is considered as a suspected

116   outbreak and if one case is confirmed by one of the laboratory methods it is considered as a

117   confirmed outbreak [11].

Operational Definitions

119   Breteaue index: - Number of containers which have larvae of *Aedes Mosquito* per 100 households

120   inspected.

121   House index: - Percentage of households from where larvae of *Aedes Mosquito* was identified per

122   the number of households inspected.

123   Container index: - Percentage of containers which have at least one larvae or pupa of *Aedes*

124   *Mosquito* per the number of containers inspected.

125   Positive household: - A household in which at least one larvae or pupa of *Aedes Mosquito* was

126   identified in at least one water container.

127   Negative household: - A household in which no larvae or pupa of *Aedes Mosquito* was identified.

128 Positive container: - A water holding container in which at least one larvae or pupa of *Aedes*

129 *Mosquito* was found.

130 Negative container: - A water holding container in which larvae or pupa of *Aedes Mosquito* was

131 not found.

132 Kebele: - The lowest political administration structure in Ethiopian administration system.

133 Epidemiologically linked: - Cases who have evidence of contact with confirmed cases.

Data Collection

135 Epidemiological data were collected by face to face interview of cases and controls. Entomological

136 data was collected by observation of water containers among selected households from four high

137 case reporting kebeles (02, 03, 09, and 10). Larvae and pupas were collected by dipper and pipette

138 and put them in to a well labeled cup with net covers to allow them to grow into adult mosquito.

139 Once the adult mosquitos were grown, *Aedes Mosquito* was identified by mosquito identification

140 key.

141 Regarding the human (laboratory) sample for confirmation, five serum samples were collected

142 from suspected cases and transported to Ethiopian Public Health Institute (EPHI) Arbovirus

143 Laboratory as per the recommended cold chain protocol. The laboratory expert from the hospital

144 was transported the sample to EPHI as per the recommended cold chain protocol.

Data Analysis and Presentation

146 After the data was cleaned and checked for completeness, entered into Epi Info Version 7.2 and

147 exported to SPSS version 23. Descriptive analysis by person, place and time were done. Bivariate

148 and multivariable binary logistic regressions were performed to identify risk factors for this

149 chikungunya outbreak. The result was interpreted by using odds ratio with 95% confidence level

150 and P-value of 0.05.

151   Breteaue index, house index and container index were calculated for entomological data.

152   To confirm the etiologic agent of the outbreak, serum samples were tested by Real Time

153   Polymerase Chain Reaction (RT-PCR) after viral Ribose Nucleic Acid (RNA) was extracted.

154   **Ethical consideration**

155   Support letter was written by Ethiopian Public Health Institute, Center for Public Health

156   Emergency Management (PHEM) to Somali Regional Health Bureau and Kebridahar City

157   Administration Health Office. Permission to investigate the outbreak was obtained from regional

158   health bureau and the city health office as well as the mayor office of Kebridahar City

159   Administration. This study is an outbreak investigation. Hence, it was not pass through ethical

160   review process because outbreak investigation is not a planned study rather it is part of the outbreak

161   control and prevention activity.

162   The interviewers had explained about the objectives, the process and the benefits of the study for

163   each participant. Each participants were asked for their informed consent and interviewing was

164   conducted after written consent was received from the participant. In case of interviewing children,

165   the consent was obtained from their parents and guardians. Cases identified during data collection

166   were sent to health facility for treatment.

167   **Result**

168   **Socio demographic characteristics of respondents**

169   A total of 222 participants, 74 cases and 148 controls, were interviewed for this study. None

170   response rate was zero.

171   From the total participants, 59% (132) were female and 14% (32) were children below five years

172   old (Table 1).

173   Table 1 Socio demographic characteristics of study participants, Kebridhar City Administration,

174   Korahe Zone of Somali Region, Ethiopia 2019.

Variable		Cases		Controls		Total	
Sex	Female	33	45%	95	64%	132	59%
	Male	41	55%	53	36%	90	41%
Age	Under 5	2	3%	30	20%	32	14%
	5-14	16	22%	33	22%	49	22%
	15-45	49	66%	54	36%	103	46%
	45+	7	9%	31	21%	38	17%
Educational status	No formal Education	51	69%	78	53%	129	58%
	NA	1	1%	12	8%	12	5%
	Primary school	15	20%	43	29%	58	26%
	Secondary school	7	9%	15	10%	22	10%
Marital status	Married	56	76%	75	51%	131	59%
	NA	18	24%	47	32%	65	29%
	Single	0	0%	15	10%	15	7%
	Widowed	0	0%	11	7%	11	5%
Occupation	Daily laborer	11	15%	0	0%	11	5%
	House wife	24	32%	68	46%	92	41%
	Merchant	21	28%	22	15%	43	19%
	NA	0	0%	12	8%	12	5%
	Student	18	24%	46	31%	64	29%

Family size	Above 10	9	12%	20	14%	29	13%
	Less than 5	25	34%	49	33%	74	33%
	5 to 10	40	54%	79	53%	119	54%
Total		74	100%	148	100%	222	100%

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Description of cases

177 A total of 74 chikungunya fever cases were reported from Kebridhar City Administration starting

178 from 19th May 2019 to 8th June 2019 (Figure 1).

179 Figure 1 Distribution of Chikungunya fever cases by date of onset of fever in Kebridhar City

180 Administration, Somali, Ethiopia 2019.

181 Of five samples sent to EPHI laboratory three were positive for Chikungunya Virus (positivity rate

182 is 60%) and the rest of cases were epidemiologically linked. Eighty nine percent (66) were treated

183 as an outpatient and 10.8% (12/74) cases were treated as an inpatient.

184 Among a total of 74 cases, 41 (55.4%) were males and 33 (44.6%) were females. Two cases were

185 children less than five-year-old and seven cases were above 45 years old. The overall attack rate

186 of the outbreak was 63 cases per 100,000 at risk population. The highest attack rate was among

187 the age group of 15 – 44 (83/100,000) and the lowest attack rate was among the age group of

188 bellow five years (22/100,000) (Table 2). The median age of cases was 25 years (IQR: 20 – 33).

189 The case fatality rate of this outbreak was zero. The attack rates among males and females were

190 62 and 66 cases per 100,000 risk population respectively.

191 Table 2 Distribution of chikungunya cases by age group, Kebridhar City Administration, Somali,

192 Ethiopia, 2019

Age group (in years)	Number of cases	Percent	At risk Population	Attack Rate per 100,000 at risk population
Less than 5	2	2.70%	9,050	22
5 – 14 Years	16	21.60%	35,970	44
15 – 44 Years	49	66.20%	59,047	83
Above 45 Years	7	9.50%	13,155	53
Total	74	100.00%	117,222	63

Sign and symptoms

All cases had fever and joint pain. None of the cases had bleeding (Table 3).

Table 3 Distribution of chikungunya cases by sign and symptoms in Kebridhar City Administration, Somali, Ethiopia, 2019

Sign and symptom	Yes (Number)	Percent	No (Number)	Percent	Total
Fever	74	100%	0	0%	74
Joint pain	74	100%	0	0%	74
Headache	53	72%	21	28%	74
Rash	8	11%	66	89%	74
Nausea/vomiting	37	50%	37	50%	74
Bleeding	0	0%	74	100%	74

Entomological findings

A total of 26 household and 49 water containers were visited from four kebeles of Kebridhar City to identify the mosquito species. Among those containers in the visited households 26.5% (13/49) were positive containers and the rest 73.5% (36/49) were negative containers.

Of the visited households 38.5% (10/26) were positive households. The highest breteau index and house index were identified from Kebele Ten, whereas the highest container index was in Kebele Two of the city (Table 4).

Table 4 Indices of Aedes aegypti mosquito by kebele in Kebridhar City Administration, Somali, Ethiopia, 2019

Location Investigated		Type of Vector Found	Aedes aegypti Stegomyia Indices		
District	**Kebeles**		Breteau Index	House Index	Container Index
Kebridhar City	02	Aedes aegypti	50%	37.5%	50%
	03	Aedes aegypti	28.5%	28.5%	22.2%
	09	Aedes aegypti	33.3%	33.3%	28.6%
	10	Aedes aegypti	66.6%	44.4%	37.5%

Risk factors of chikungunya fever

All participants responded that, they have bed net but their houses were not sprayed with in six months prior to this outbreak. Also, all the study participants had water holding container in their compound and they have never used mosquito repellants.

In bivariate analysis ten variables were analyzed and eight of them had a P-Value of less than 0.05. Sex, knowing the symptoms and prevention mechanisms of chikungunya, knowing that *Aedes*

212   *Mosquito* bites commonly at day time, using LLINs at day time sleeping, status of water holding

213   container, presence of larvae in water holding container, ill person with similar sign and symptoms

214   in the family of neighbors and type of close they commonly were are significant in bivariate

215   analysis.

216   In multivariable analysis eight variables significant by bivariate analysis were entered in to the

217   model. The odds of being affected by chikungunya disease was 21 times higher among people not

218   using LLINs at day time sleeping (P- value < 0.001, AOR 20.8, 95CI 6.4 – 66.7), four times higher

219   among people who have open water container (P- value 0.023, AOR 4, 95CI 1.2 – 13.5), five times

220   higher among people whose water container had mosquito larvae (P- value 0.015, AOR 4.8, 95CI

221   1.4 – 16.8), 28 times higher among people who have neighbors with chikungunya sign and

222   symptoms (P- value <0.001, AOR 27.9, 95CI 6.5 – 120.4) and eight times higher among people

223   who usually wears cloths not full body cover (P- value 0.002, AOR 8.1, 95CI 2.2 – 30.1) (Table

224   5).

225   Table 5 Multivariable analysis of chikungunya risk factors in Kebridhar City Administration of

226   Somali, Ethiopia 2019

Variables	Controls (%)	Cases (%)	P – Value	AOR	95% CI	
Sex						
Female	95 (64.2)	33 (44.6)		1		
Male	53 (35.8)	41 (55.4)	0.331	1.8	0.6	6.1
Knowing symptoms and preventions of chikungunya						
Yes	71 (48.0)	13 (17.6)		1		

No	77 (52.0)	61 (82.4)	0.075	3.3	0.9	12.0
Knowing that Aedes Mosquito bites commonly at day time						
Yes	65 (43.9)	21 (28.4)		1		
No	83 (56.1)	53 (71.6)	0.189	2.2	0.7	7.0
Using LLINs at day time sleeping						
Yes	130 (87.8)	12 (16.2)		1		
No	18 (12.2)	62 (83.8)	<0.001	20.8	6.4	66.7
Status of water holding container						
Closed	123 (83.1)	23 (31.1)		1		
Open	25 (16.9)	51 (68.9)	0.023	4.0	1.2	13.5
Presence of larvae in water holding container						
Yes	21 (14.2)	50 (67.6)	0.015	4.8	1.4	16.8
No	127 (85.8)	24 (32.4)		1		
Ill person with chikungunya in the house hold and neighbors						
Yes	15 (10.1)	47 (63.5)	<0.001	27.9	6.5	120.4
No	133 (89.8)	27 (36.5)		1		
Kind of clothes they wear commonly since the emergence of this outbreak						
Full body cover						
Short	115 (77.7)	22 (29.7)		1		

		33 (22.3)	52 (70.3)	0.002	8.1	2.2	30.1

Discussion

227

228   After its reemergence in 2004, CHIKV has caused numerous epidemics around the world,

229   including new spread to previously non endemic regions, such as the Americas, Europe, the Middle

230   East, and Oceania [12]. The first outbreak in Ethiopia was detected in Dolo Ado District of Somali

231   Region in 2016, since then this is the third outbreak following similar outbreak in Adar District of

232   Afar Region in March 2019.

233   To confirm this chikungunya outbreak Polymerase Chain Reaction (PCR) test was done and the

234   positivity rate was 60%. Studies in other countries also showed that, the positivity rates of CHIKV

235   among suspected cases ranges from 12.9% to 75% [13-16].

236   Among the total cases 10.8% were treated as an inpatient, which is lower than the similar study in

237   Malaysia. That study also showed that, the attack rate ranged from 0.6 to 63 per 100,000 population

238   in different districts [17]. In our study the attack rate of the outbreak was 63 cases per 100,000 at

239   risk population. Studies in Malaysia showed that the case fatality rate of chikungunya fever is zero

240   [2,17]. Similarly, the case fatality rate of the chikungunya outbreak in Kebridhar City is zero.

241   The median age of the chikungunya fever cases in Kebridhar City was 25 years, this finding is

242   almost similar to the median age of chikungunya fever cases (24 years) found from a cross-

243   sectional study in Tanzania [13].

244   Acute phase of Chikungunya Virus infection is characterized by high grade fever and sever joint

245   pain. Bleeding is less likely among individuals infected by Chikungunya Virus [18]. Our

246   investigation result also supports this evidence, which founded that all cases had fever and joint

247   pain but no case was presented with bleeding.

248   *Aedes Mosquito* larval index is categorized as high and low larval index based on house and bretue

249   indices. High larval index is when the house index is ≥ 5% and/or breatue index is ≥ 20% [19].

250   Hence, the findings of our study shows that Bretuea index and house index of *Aedes aegypti* were

251   ranges from 28.5% to 66.6% and from 28.5 to 44.4% respectively.

252   In this outbreak investigation the odds of being affected by chikungunya fever is 21 times higher

253   among peoples who did not use bed net during day time sleep compared to those used, four times

254   higher among peoples having open water holding container comparing to those properly close their

255   containers, four point eight times higher among peoples whose water container had larvae of

256   mosquitos compared to those whose water containers did not have larvae, 28 times higher among

257   peoples living with ill persons with similar sign and symptoms compared to not living with affected

258   peoples and eight times higher among peoples wearing shorts and T-shirts than peoples wear full

259   body cover closes. These findings were supported by studies done in Malaysia, South India and

260   Central Nepal. These studies shows, not using full body cover clothes, not using mosquito net or

261   coil, having uncovered plastic water containers and staying with relatives infected with

262   Chikungunya Virus are significant risk factors for Chikungunya Virus infection [8-9,17].

263   On the other hand, a retrospective study of chikungunya outbreak in India founds differences in

264   awareness of chikungunya, cause of the disease, vector responsible, mode of transmission, biting

265   time and elimination of breeding of mosquitoes are significant risk factors, which are not

266   significantly associated with Chikungunya Virus infection in our study [3].

Conclusion

268   This outbreak was the third chikungunya outbreak in Ethiopian by which females were more

269   affected than males but no death was registered. Fever and joint pain were the commonest

270   manifestation of chikungunya fever in this outbreak but no case was presented with bleeding.

271   This study indicated that, the larval indices of *Aedes Aegypti* mosquito was high in the city

272   administration during the outbreak period.

273   Not using bed net during day time sleeping, having an open water container, presence of Aedes

274   Mosquito larvae in water holding container, living with people having chikungunya sign and

275   symptoms and wearing clothes which did not cover the full body were risk factors for being

276   affected by chikungunya fever.

277   Therefore, there should be regular indoor and outdoor spraying of insecticidal chemicals, regular

278   monitoring of water containers which are difficult to drain as well as to cover and apply larvicidal

279   chemicals, awareness creation on day time bed net utilization, drainage of unusable stored water

280   and educate the community to cover all water containers in and around the house and promote the

281   people to wear full body cover cloths and use mosquito repellants in the time when there is an

282   outbreak are helpful to prevent and control chikungunya outbreaks.

Competing of interest

284   All authors declare that, they have no any competing of interest.

Author's contribution

286   MA design the study, participate in field investigation, conduct analysis and write the manuscript.

287   TT participate in designing the study and manuscript writing. HA and DB involved in laboratory

288   confirmation. HA and SD participate in field investigation and data analysis. All authors review

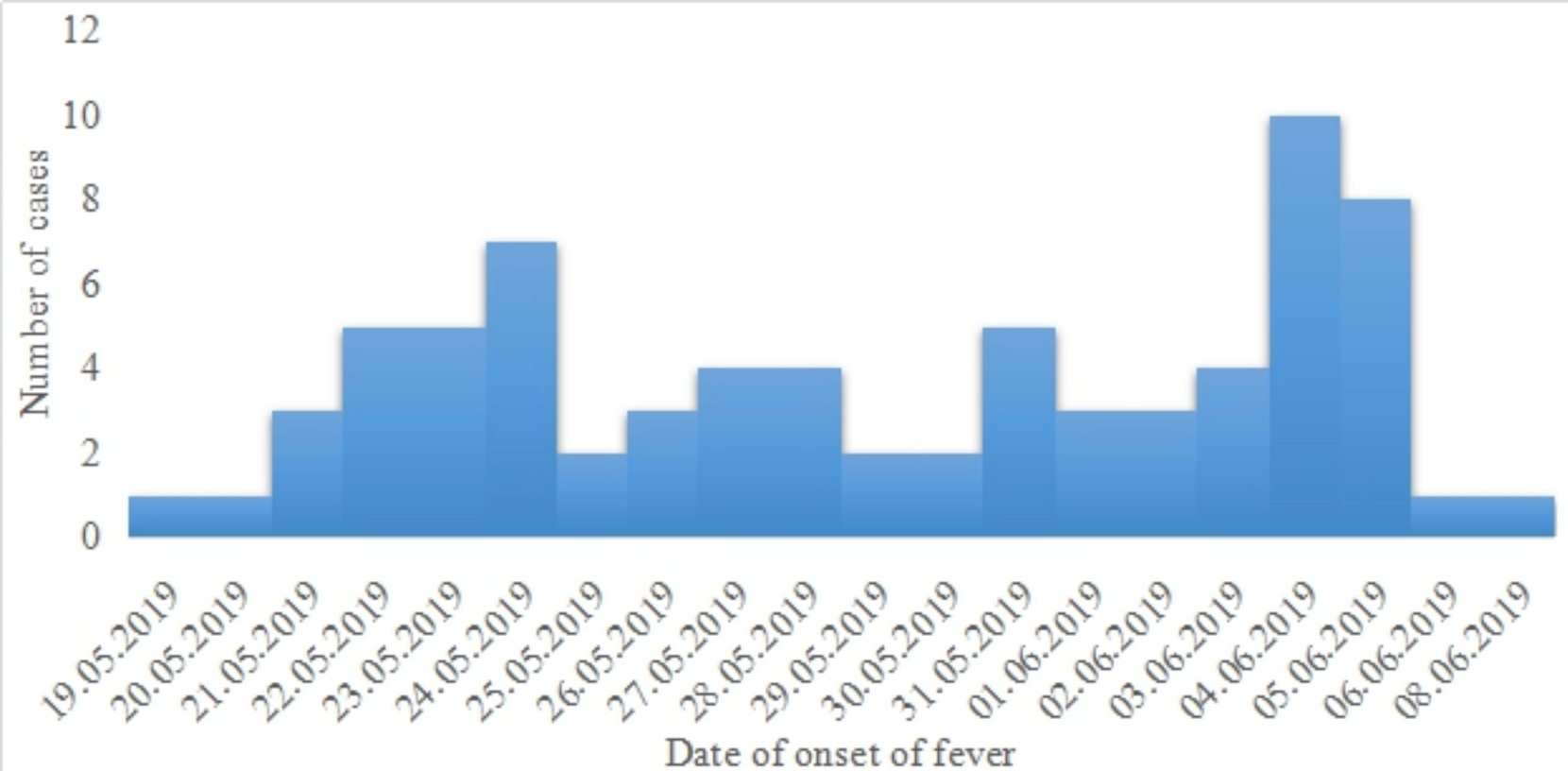289   the manuscript and approve the submission.

Acknowledgement

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