ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info

ISSN
0976-9595
Research Article

MDA IN JHARKHAND: CAN IT BE AN OPPORTUNISTIC INTERVENTION TO REDUCE COVID-19 INFECTION, SIMDEGA DISTRICT JHARKHAND

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ABSTRACT

Ivermectin, an FDA approved drug was used earlier for the control of various parasitic diseases such as Onchocerciasis, Lymphatic Filariasis in African and Asian countries. In the current pandemic situation, Ivermectin has also been explored as a prophylactic and therapeutic option for COVID-19 infection. This study explores the role of single dose Ivermectin as a part of triple drug therapy (IDA: Ivermectin + Diethylcarbamazine + Albendazole) along with Mass drug administration (MDA) under the National Filariasis Elimination Programme in Simdega District of Jharkhand state in India. MDA with IDA was conducted during 10-31st August 2020 in Simdega. Trend of COVID-19 cases before and after MDA was analyzed to assess the effect of a single dose of Ivermectin in reducing the number of COVID-19 cases in Simdega. In this study, a One Way ANOVA test was used to find the significance shows that less significant difference in the mean number of cases reported before and after the MDA in Simdega. Time series analysis also didn't show any significant difference in predicted and actual number of COVID-19 cases during the subsequent follow up after MDA in Simdega. The study also concludes that age appropriate single dose of Ivermectin was not associated with any significant decrease in the number of COVId-19 cases in Simdega.

Keywords: COVID-19, Ivermectin, MDA, Simdega, filariasis.

1. INTRODUCTION

Ivermectin chemically is a macrocyclic lactone produced by the soil microorganism, *Streptomyces avermitilis,* and chemically they are called avermectins. The Ivermectin is a wonder drug, acting at various fronts, ranging from antiparasitic (both endo/ecto parasite) to antiviral, antibacterial, anticancer and even showing immuno-modulation effects [1].

Satoshi Ōmura, a microbiologist and his colleague William C Campbell invented the drug, Ivermectin in 1970 [2]. For their invention, they got the Nobel Prize for physiology and medicine in 2015. The drug since its invention has been approved for use under various programs, e.g., for Onchocerciasis (in African countries) Mass Drug Administration (MDA, in India), for elimination of Lymphatic filariasis by 2021. It exerts its antihelminthic effect by irreversibly activating glutamate-gated chloride channels expressed on the neurons and pharyngeal muscle cells of the helminths, which results into the paralysis, and death of the parasite [3]. Due to its inability to cross the BBB in hosts, the hosts are relatively resistant to the effects of this agent [4].

Lymphatic filariasis (LF) is a serious public health problem in rural and urban areas of 256 districts 16 states and five union territories of India [5]. In the affected communities, it is a cause of huge economic loss, and associated with physical & psychological morbidity and social stigma.

In India, the National Filariasis Control Program (1955-2000) did not achieve much success due to its operationalization in limited areas. Based on the global strategies for eliminating lymphatic filariasis, i.e., GPELF (Global Program for elimination of Lymphatic Filariasis, 2000), in 2004, Government of India launched nationwide MDA (Mass Drug Administration) in filarial endemic districts. During MDA rounds either DEC (Diethyl Carbamazine) alone or in combination with albendazole have been administered in the endemic districts as per policy decision [6].

Despite the multiple rounds of MDA, transmission interruption for LF was not achieved in India. In 2017 based on the evidence of success of triple drug combinations (Ivermectin, Diethylcarbamazine and Albendazole: IDA) from other countries, GOI approved Ivermectin as a part of triple drug

combination (IDA) for MDA in filarial endemic states and districts.

Jharkhand is one of the LF endemic states in India. In Jharkhand 17 districts reported more than 70 % of all cases in the state. As a part of MDA, in year 2020, two-drug therapy (DEC and Albendazole) was implemented in 12 endemic districts. Triple drug therapy (Ivermectin, DEC, and Albendazole/IDA) was implemented for pilot testing in Simdega (non-endemic) district of Jharkhand which has a population of 7.3 lakhs.

Ivermectin which has a promising *in vitro* antiviral activity as well, has been investigated for its efficacy against the corona virus during current COVID-19 pandemic along with other drugs, e.g., Hydroxy-chloroquine, and Remdesivir/ritonavir etc. Many researches in past have proven *in vitro* antiviral activity of Ivermectin in both RNA virus (ZIKa, Influenza A, Chinguniya, HIV-1, Dengue and JE) and DNA virus (Pravovirus, Pseudorabies) but limited literature is available on *in vivo* efficacy except in few cases, e.g., west Nile and Newcastle disease, Pseudorabies and parvovirus [7].

MDA with IDA was done in Simdega district of Jharkhand from 10-31st Aug 2020 under National Filariasis Elimination Program. Current study was carried out to see the effect of single dose of Ivermectin as a part of triple drug combination (IDA) during MDA in reducing the number of COVID-19 cases at population level in Simdega district of Jharkhand state, India.

2. METHODOLOGY

MDA with IDA in Simdega district of Jharkhand was conducted from 10th August to 31st August 2020. Simdega has a total population of 7.3 lakhs with 6.5 lakhs target population to be covered. During this round of MDA a total of 539929 eligible population received the drug (excluding infants and pregnant, and seriously ill people). Supervised drug administration was done through house to house (drugs given to individuals at their doorstep), groups (schools, hospitals, offices, industries, bus stands, railways stations, prisons, etc.) and through booth approach drugs were given at predetermined place or booths.

As per the NVBDCP guidelines the drugs are given after the meal in a dosage of (Ivermectin: 200 microgram per kg body weight for>5 years) DEC:6mg/kg; Albendazole: 400 mg) to all the beneficiaries.

In the midst of COVID-19 situation in Jharkhand, the Government and partner organizations came up with the innovative ideas of using *katori* (bowl), for providing the contactless MDA and practicing infection prevention and control. Out of 6.5 lakhs target population a total 5.4 lakhs were covered during this round of MDA with IDA in Simdega. Daily reported COVID-19 cases by the Jharkhand state and respective districts through health bulletin were analyzed to assess the role of single dose Ivermectin in reducing the number of COVID-19 infections cases at population level.

Trends of COVID-19 cases before, during and after the MDA in Simdega district, (ii) comparison of cases in Simdega and other neighboring district; (iii) any significance difference in number of cases before, during and after the MDA and; (iv) comparison in predicted and actual number of COVID-19 cases in Simdega district after the implementation of MDA were used to assess the effectiveness of single dose Ivermectin in reducing the number of COVID-19 cases in Simdega.

3. RESULTS

Since the occurrence of first cases in March 2020, there has been a continuous rise in the number of cases in whole Jharkhand as well as in Simdega district as depicted in Fig. 1. Although, the cases of COVID-19 were being reported regularly in the Jharkhand state as well as in Simdega district but a sudden spike in cases was reported in early July 2020 and peak was reached in late August and early September 2020. State government had taken various steps for controlling the infections such setting up of quarantine centers for isolating infectious people, guidelines for facility and home based isolation of the infectious patients, active search of cases through contact tracing and house-to-house survey, ILI and SARI surveillance at Facility level.

As the number of daily reported cases was quite variable, hence the trend of seven days moving average was used to analyze the trend of CIVOD-19 cases in Simdega. As depicted in Fig. 2 the trend of seven days moving average of COVID-19 didn't change much during (10-31st Aug 2020) and after the MDA.

Fig. 3, Based on the number of cases being reported in earlier three months (May, June and July 2020), the maximum (Mean number of cases+ 2SD) and minimum number of cases (mean number of cases-2SD) which may occur during the following months (e.g., August & September) were calculated. The number of COVID-19 cases during the month of August when IDA was implemented and in following month, e.g., September were within the mean $\pm$ 2SD limit and did not show

any significant decrease in number of COVID-19 cases in following month, i.e. September 2020. More though in earlier 2-3 weeks in September, the cases were higher than the average cases reported in previous three months.

Fig. 4, Trends of Covid-19 cases in the neighboring districts, i.e., Khunti, Gumla, (where MDA without Ivermectin was implemented) were also analyzed to look into any significant difference in number of the reported cases. In all the three districts (Simdega, Gumla and Khunti), the trends of COVID-19 cases were almost similar. In the West Singhbhum district, there was a rising trend of cases. The Growth rate of cases in three districts was One Way ANOVA was applied to assess the significant difference in mean number of COVID-19 cases before, during and after the MDA in Simdega district. There were no statistically significant differences between group means as determined by one-way ANOVA ($F(2,75) = 2.408$, $p = .097$).

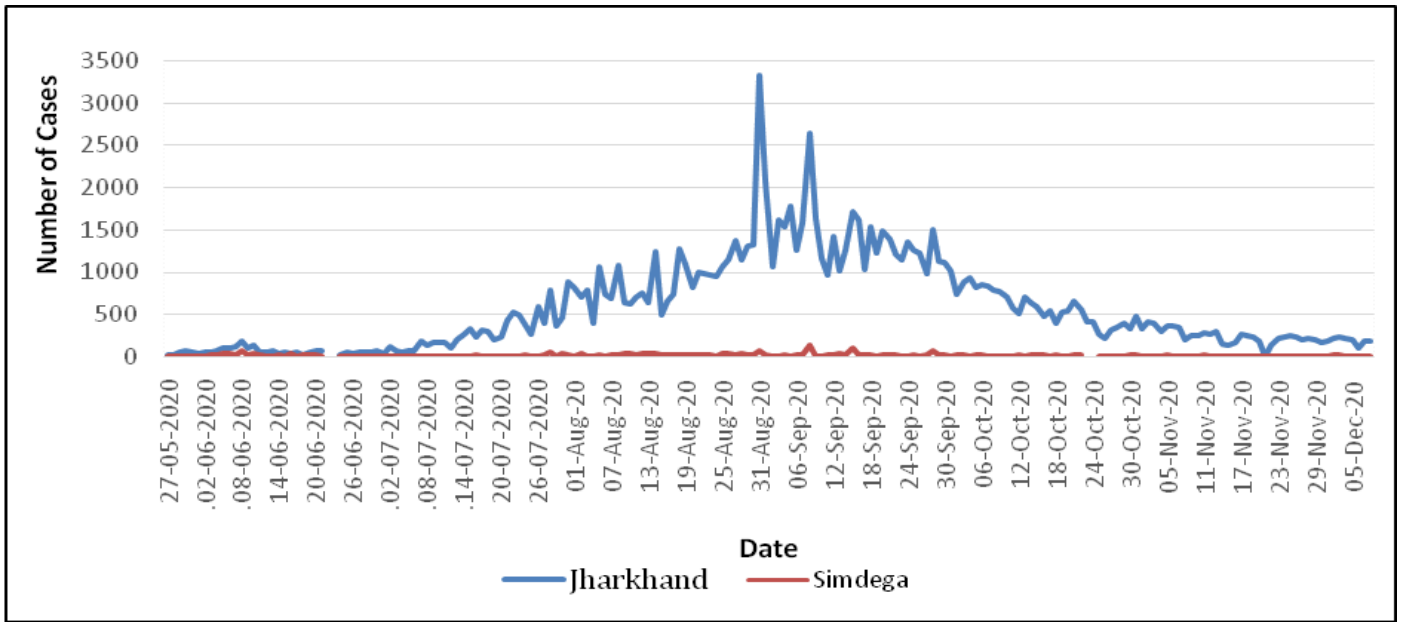

Fig. 1: Trend of COVID-19 cases in Jharkhand state Vs Simdega District

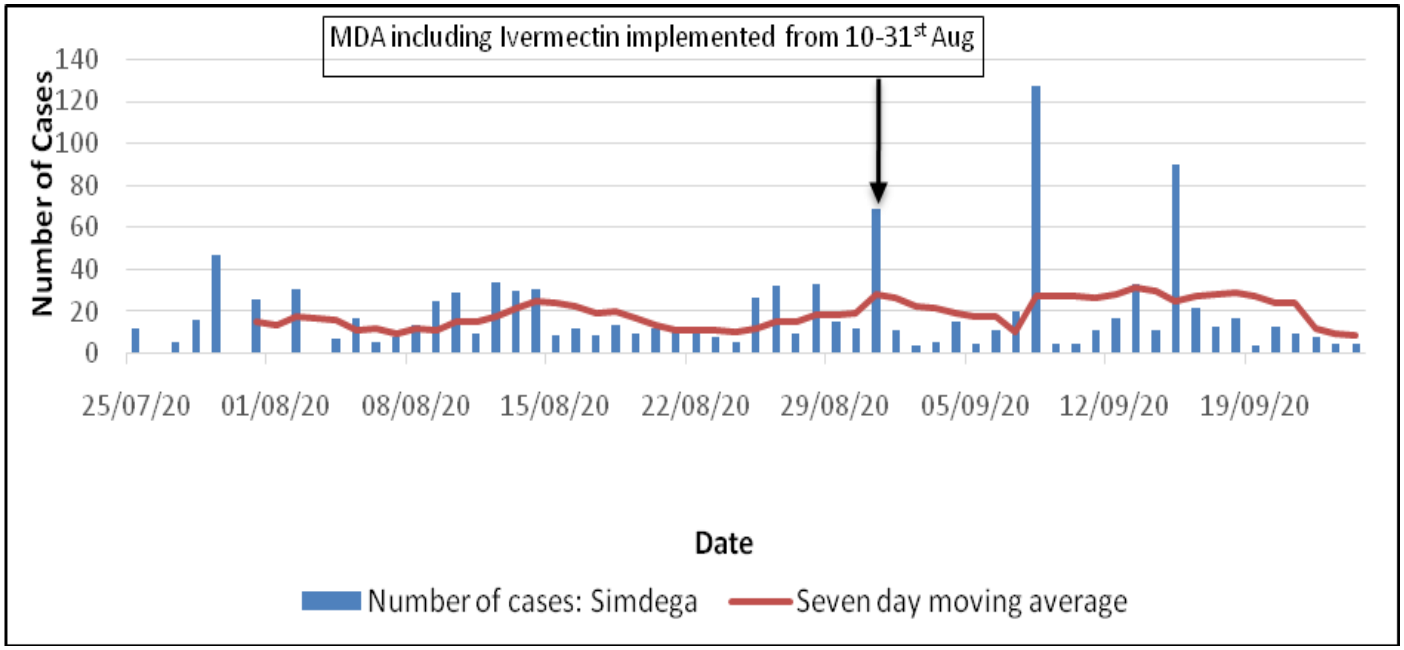

Fig. 2: Trend of COVID-19 cases before, during and after the MDA with IDA in Simdega district of Jharkhand

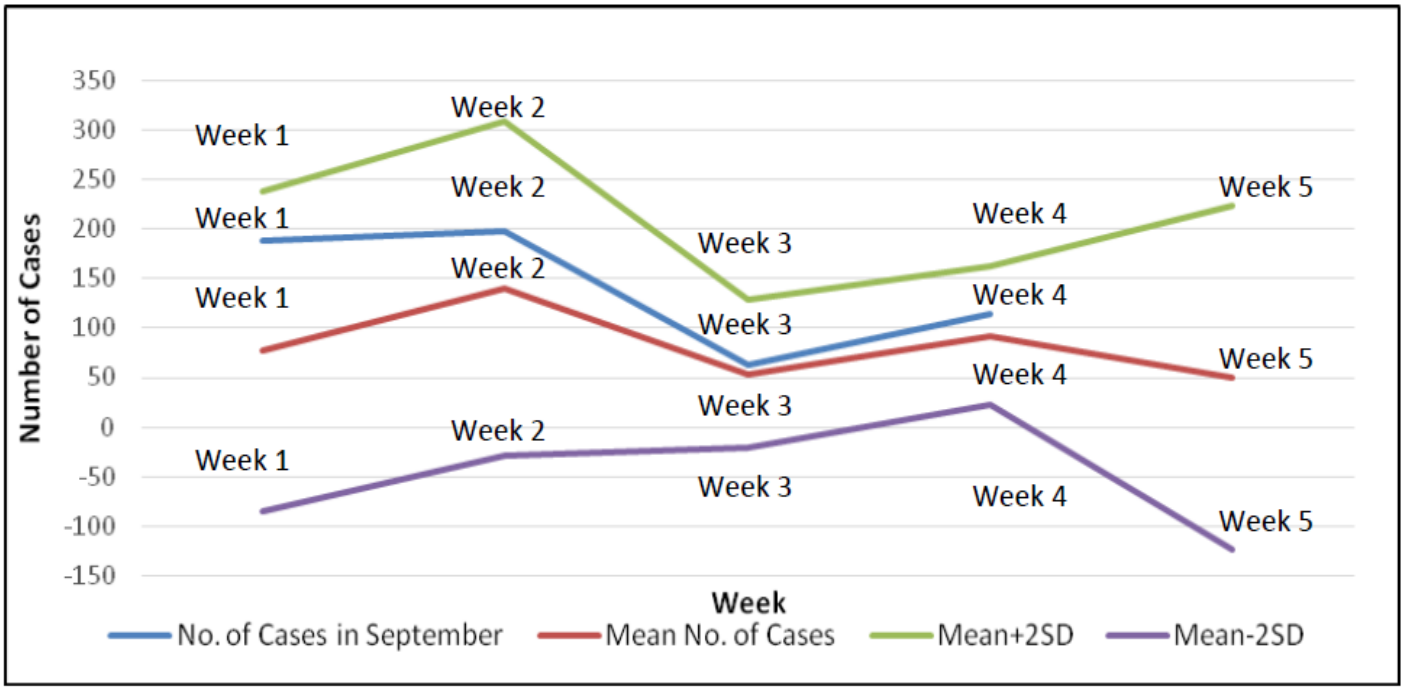

Fig. 3: Trends of COVID-19 Cases in September 2020 in Simdega (after the implementation of MDA (including Ivermectin)

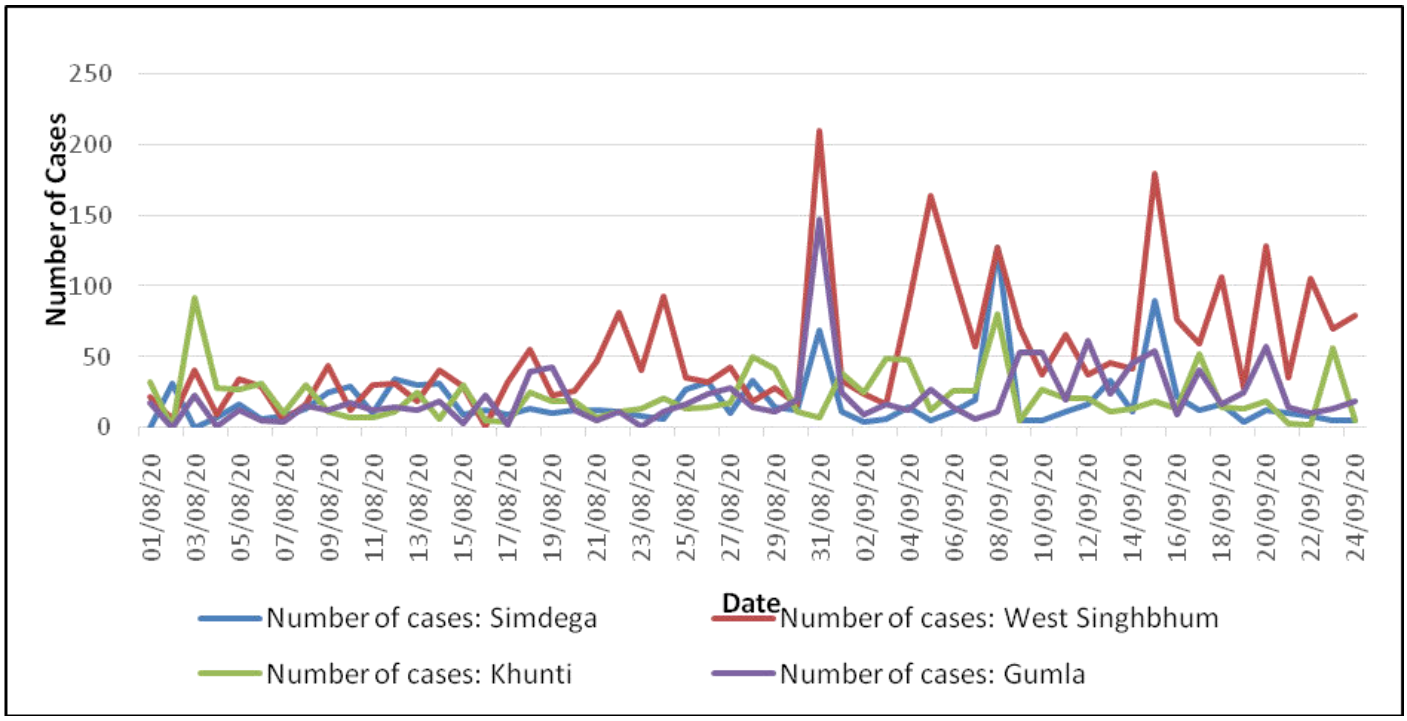

Fig. 4: Trends of Number of covid-19 cases in Simdega and Neighboring districts (West Singhbhum, Khunti, Gumla)

Based on the trend of the number of cases in the past three months (June, July and August) prediction was drawn (Fig. 5, a) for the expected number of cases in September and compared with the actual number of cases (Fig. 5, b) using a time series analysis. Actual number of COVID-19 cases in September was almost similar to the predicted cases (10 cases daily).

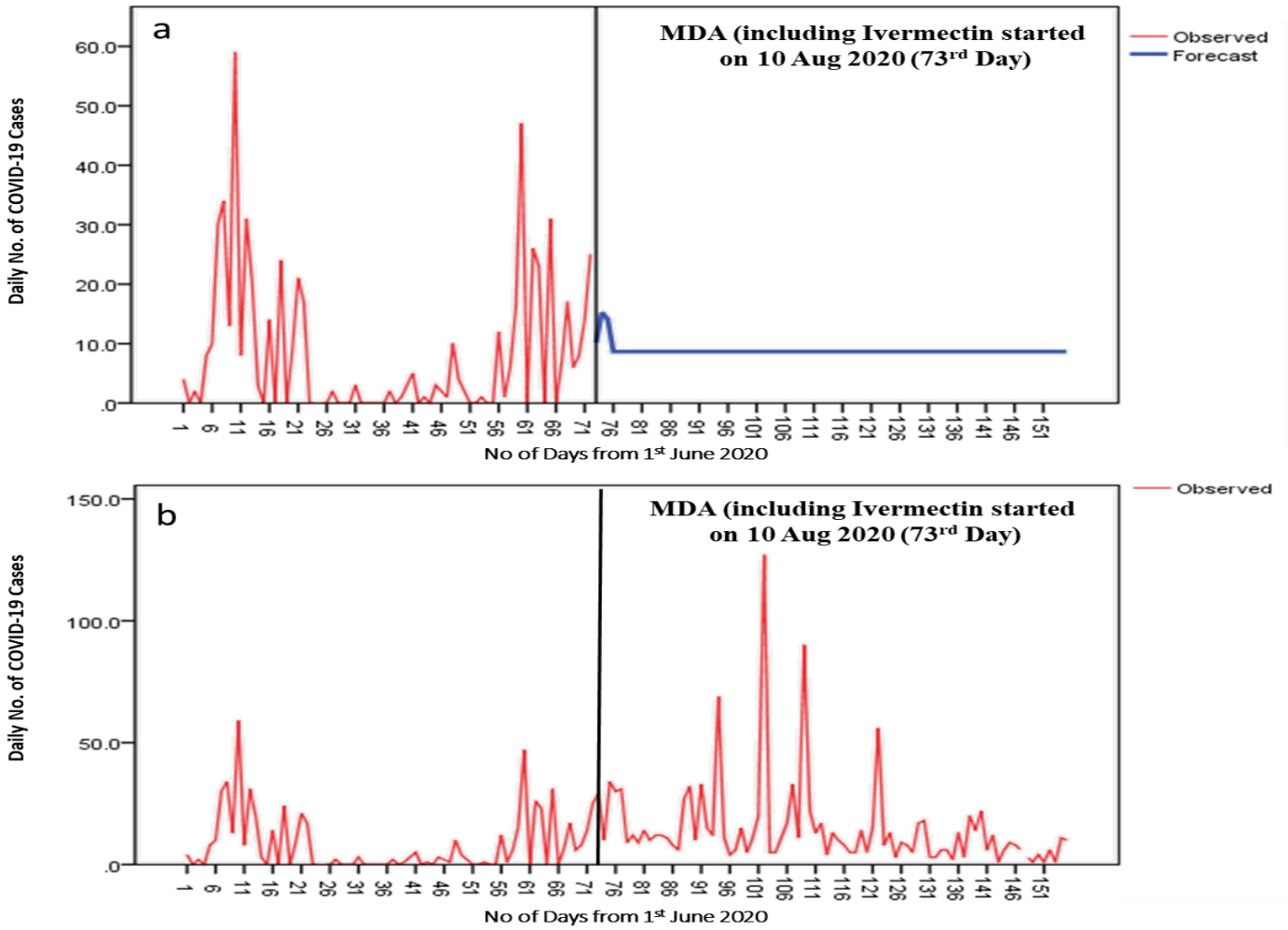

Fig. 5: Number of COVID-19 Cases in September based on the trend of cases in previous three months (June, July and August) 2020 (a) Predicted and (b) Actual

4. DISCUSSION

Ivermectin, which is a FDA approved drug for protection against various helminthic/parasitic infection, has also shown to have antiviral activity. Clay Leon and colleagues [8] demonstrated *in vitro* anti SARS-Cov-2 activity of Ivermectin. They found that a single dose of Ivermectin was able to control viral replication within 24-48 hrs and it was suggested that if given to patients early in infection, could help in limiting the viral load, prevent severe disease progression and limit person-person transmission.

A few other studies have assessed the efficacy of the Ivermectin as a prophylactic and therapeutic drug in prevention and control of COVID-19 infection [9-13]. In a retrospective study on use of Ivermectin in hospitalized patients conducted by Juliana Cepelowicz Rajter et al [8] the overall mortality was significantly lower in the group receiving Ivermectin than the group receiving usual care group (15.0% vs 25.2%, p=.03). Mortality was also lower for Ivermectin treated patients in the subgroup of patients with severe disease (38.8% vs. 80.7%, p=.001).

A clinical trial conducted by Waheed Shouman et al [9] for assessing Ivermectin as a prophylactic option in asymptomatic family close contacts with patients of COVID-19. In this trial, it was found that two doses of Ivermectin when given in age appropriate doses three days apart, was significantly associated with decreased spread of infection in close family contact. The trails showed an OR of 12.533 and 11.445 when compared to no intervention in both univariate and multivariate models, respectively, and Ivermectin protection was not affected by gender or comorbidities in multivariate model.

In another study conducted by Behra P et al [10] as a hospital-based matched case-control study in which cases and controls were healthcare workers who were tested positive and negative, respectively, for COVID-

19 by RT-PCR. Exposure was defined as the intake of Ivermectin and/or hydroxychloroquine and/or vitamin C. They found that two-dose Ivermectin prophylaxis at a dose of 300 μg/kg with a gap of 72 hours was associated 73% reduction of COVID-19 infection among healthcare workers but a single dose have no role in prevention or prophylaxis against infection.

In a white paper by a group of senior doctors on Ivermectin: as a potential therapy for COVID, recommended that Ivermectin may be used as a safe therapeutic option for mild, moderate or severe cases of Covid-19 infection [13]. The prophylactic use of the Ivermectin in prevention of infection among close contact or control of infection at a population level has not been addressed in this paper.

MDA with IDA in Simdega district of Jharkhand state provides an opportunity to assess the single dose prophylactic use of Ivermectin in reducing the infection at population level. As discussed in result both the ANOVA and trend of seven day moving average of COVID -19 cases in Simdega did not change significantly before, during and after the MDA. Even the predicted number of cases and actual cases appeared in the Simdega were almost similar. All the results indirectly confer that a single dose in 200mcg/kg of the Ivermectin has a limited role in providing the protection against the COVID-19 infection at population level.

Strength of this study is that almost 83% of the target population consumed the drug and a number of cases of COVID-19 were being reported on the MoHFW COVID portal on a daily basis, which provide real time the authentic picture of the spread of infection. Being the first study to assess the role of Ivermectin for prophylaxis against COVID-19 infection at population level, this evidence needs to be supported by other such studies. MDA with IDA being conducted or planned in future for other states should be grabbed as an opportunity to strengthen or to refute the evidence.

5. ACKNOWLEDGMENTS

We would like to acknowledge the State program officer, Integrated Disease Surveillance Programme (IDSP) and National Vector Borne Diseases Control Programme (NVBDCP), Jharkhand for sharing daily COVID 19 health bulletin and MDA report in Simdega district of Jharkhand respectively.

Conflict of interest

No conflict of interest.

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