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THE OUTBREAK OF COVID-19 IN MIZORAM, INDIA

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DEDICATION

This book is dedicated to all the so-called 'COVID-19 warriors' – Scientists, Researchers, Doctors, Nurses, Paramedical staff, other health workers, hospital staff, and volunteers from diverse professions in recognition of their selfless contribution in fighting COVID-19.

Pharmacist form an integral part in the fight against COVID-19. However, apart from community/clinical pharmacists, their contributions in the fight against many diseases including COVID-19 are often left unnoticed. This is because, in comparison to other health care professions, many of the works accomplished by Pharmacists that benefit the healthcare system often take place in environments that are lesser exposed to society such as in academic institutions, research laboratories, pharmaceutical industries, drug testing labs, and so on.

Thus, this book is especially dedicated to all my fellow Pharmacists worldwide in appreciation for their contribution to the healthcare system and also in their fight against many diseases including COVID-19.

THE OUTBREAK

For a better understanding, this book represents the incidence of COVID-19 in Mizoram as three different outbreaks. The first outbreak started from the 2nd week of June and lasted till about the 1st week of July. The second outbreak started from the 2nd week of July and lasted till about the 3rd week of October. The third outbreak started from the 4th week of October and as of 26th November 2020, it is still an on-going outbreak with a trend in declining of active cases. The basis of classification into different outbreaks is purely based on the viewpoint of the authors. Also, each outbreak should not be considered as a wave of COVID-19. Thus, the first outbreak of COVID-19 does not mean that it is the first wave of COVID-19 and so on.

PROLOGUE

Coronavirus disease 2019 (COVID-19) is an on-going pandemic that is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Originating from Wuhan, Hubei, China, SARS-CoV-2 had infected and induced COVID-19 in more than 61 million individuals. Also, COVID-19 has claimed the lives of more than 1.4 million individuals. Since its initial outbreak in Wuhan, China, COVID-19 had spread throughout the world. The first case in India was detected in the state of Kerala on 30th January 2020. In India, there are more than 9.6 million cases with more than 0.13 million deaths. The first COVID-19 case in Mizoram, India was declared on 26th March 2020 while the first fatality was reported on 28th October 2020. Thus, apart from highlighting important topics related to COVID-19 like the epidemiology, adverse health effects, and pharmaceutical interventions; this book mainly describes the incidence of COVID-19 in Mizoram between 26th March 2020 to 26th November 2020.

EPILOGUE

The first outbreak of COVID-19 in Mizoram started from the 2nd week of June and ended by the 1st week of July. The second outbreak of COVID-19 in Mizoram started from the 2nd week of July and ended by the 3rd week of October. The third outbreak of COVID-19 in Mizoram started from the 4th week of October and as of 26th November 2020, it is still an ongoing outbreak with a trend in declining of active cases. As there are still very few written reports on the incidence of COVID-19 in Mizoram, this book may serve as a referential document for the outbreak of COVID-19 in Mizoram. Thus, this book might aid in prospective or retrospective studies. However, the data presented in the book covers up to 26th November 2020 only.

CONTENTS

THE OUTBREAK OF COVID-19 IN MIZORAM, INDIA

1
INTRODUCTION

1.1. Background

Coronaviruses (CoVs) are a type of virus that are enveloped with positive-sense RNA. From the surface of the virus, there is a projecting spike glycoprotein trimer and this is accountable for the crown-like appearance of CoVs. CoVs are single-stranded and are also non-segmented. CoVs that infect humans fall under the genus *Alphacoronavirus* and *Betacoronavirus*. Likewise, the disease induced by the novel coronavirus that originated from Wuhan, Hubei province, China is called 'Coronavirus disease 2019' (COVID-19). On 30th January 2020, the World Health Organization (WHO) declared COVID-19 as a global health emergency. Subsequently, on 12th March 2020, the WHO declared COVID-19 as a pandemic. In India, the first case of COVID-19 was detected on 30th January 2020 in Kerala. Following its initial detection, COVID-19 had become prevalent throughout India (Zothantluanga *et al*. 2020).

Mizoram shares its border as international borders with neighboring countries like Myanmar and Bangladesh. Even during the COVID-19 pandemic, interstate movements seem unavoidable. Thus, this might increase the vulnerability of Mizoram to the notorious COVID-19 pandemic (Zothantluanga *et al*. 2020). The number of total COVID-19 cases, active cases, and recovered as of 26thNovember 2020 were 3765, 408, and 3352 respectively (Zoram Medical College 2020; DIPR 2020d; HFWD 2020).

1.2. A glimpse of Mizoram (DIPR 2020a)

The state of Mizoram (Figure 1) is located in Northeast India. It has a population of 1.2 million making it the least populous state in India after Sikkim (PopulationU 2020a). Mizoram has a literacy rate of 91.85%. It is a mountainous region in the north-eastern corner of India that is sandwiched between Myanmar in the east and south and Bangladesh in the west (21° 58' & 24° 35' N and 92° 15' & 93 ° 29' E). It has a total of 722 km. international boundary with Myanmar and Bangladesh. Mizoram occupies an area of 21,087 sq. km. only.

Mizoram has the most variegated hilly terrain in the eastern part of India. The hills are steep and are separated by rivers which flow either to the north or south creating deep gorges between the hill ranges. The average height of the hills is about 1000 meters. The highest peak in Mizoram is the Blue Mountain (Phawngpui) with a height of 2210 meters above sea level.

Mizoram has a pleasant climate. It is generally cool in summer and not very cold in winter. During winter, the temperature varies from 11°C to 21°C and in the summer it varies between 20°C and 32°C. The entire area is under the direct influence of the monsoon. It rains heavily from May to September and the average rainfall is 250 cm. per annum. Winter in Mizoram is rain-free and is very pleasant; the skies are wonderfully blue, and in the morning the mist formed between the hills gives an enchanting view of wide stretches of a vast lake of cloud. Mizoram has great natural beauty and an endless variety of landscapes and is also very rich in flora and fauna. Almost all kinds of tropical trees and plants thrive in Mizoram. The hills are also marvelously green.

Majority of the inhabitant, the Mizo's are Christians, that greatly influenced the society in the right way. Mizo's are a

close-knit society with no class distinction and no discrimination on the grounds of sex. The society had a culture of good administration under the leadership of the biggest Non-Government Organization called Young Mizo Association that is deeply involved in the management of the local society. This Young Mizo Association takes an active part in fighting COVID-19 in coordination with the state government.

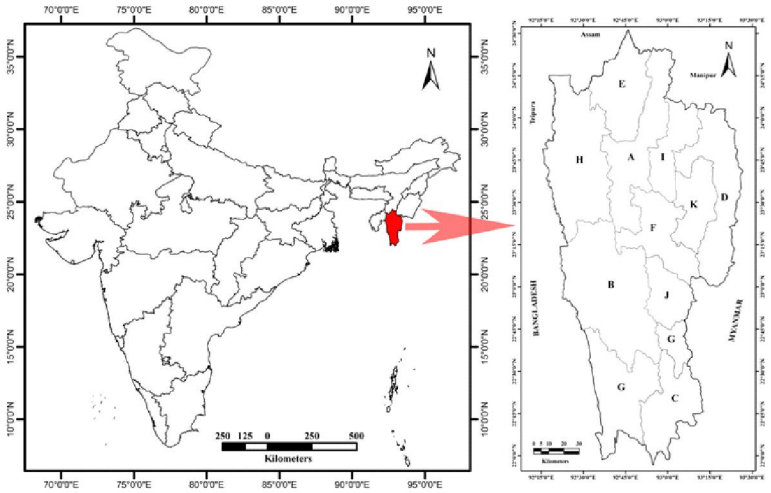

Figure 1:
Map of Mizoram showing different districts
(A = Aizawl, B = Lunglei, C = Siaha, D = Champhai,
E = Kolasib, F = Serchhip, G = Lawngtlai, H = Mamit,
I = Saitual, J = Hnahthial, K = Khawzawl); inter-state borders
(Assam, Manipur and Tripura) and international borders
(Bangladesh and Myanmar).

2
EPIDEMIOLOGY OF COVID-19

2.1. Origin

On 8th December 2019, there were several cases of pneumonia with unknown etiology that were reported in Wuhan, Hubei province, China. Interestingly, the seafood and live animal market of Wuhan were previously visited by the patients (Chen *et al*. 2020).

2.2. Causative agent

The causative agent of COVID-19 was found to be severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Amanat and Krammer 2020). SARS-CoV-2 belongs to the genus of *Betacoronavirus* and *Sarbecovirus* as the subgenus. SARS-CoV-2 showed similarities with other CoVs such as SL-CoV-RaTG13 of *Rhinolopus sinicus* (96% nucleotide similarity), bat-SL-CoVZC45 and bat-SL-CoVZXC21 (88% similarity), severe acute respiratory syndrome coronavirus (79% similarity) and Middle East respiratory syndrome coronavirus (50% similarity) (Zothantluanga *et al*. 2020; Lu and Shi 2020). Studies had reported that several mutations had occurred in SARS-CoV-2 (Phan 2020; Tufan *et al*. 2020).

2.3. Mode of transmission

SARS-CoV-2 spreads via human to human transmission (through respiratory droplets or by close contacts) (Chan *et al*. 2020; Kolifarhood *et al*. 2020). SARS-CoV-2 was also found on the surfaces of gloves, mask, glass, steel, wood, and plastic. Thus, fomite transmission was also considered a possibility (Dhillon *et al*. 2020). Once a host is infected, SARS-CoV-2 uses a receptor called angiotensin-converting enzyme 2 (ACE-

2) that is expressed in oral mucosa, nasal, lungs, liver, stomach, heart, kidney, ileum, brain stem, and adipose tissue to enter the cells of the infected host (South *et al*. 2020; Hoffmann *et al*. 2020). The spike protein of SARS-CoV-2 is primed by a serine protease called transmembrane protease, serine 2 (TMPRSS2) and this facilitates the binding of SARS-CoV-2 to ACE-2 of the host cell (Hoffmann *et al*. 2020).

2.4. Diagnosis

Diagnosing a COVID-19 case or a SARS-CoV-2 infection based on clinical features might be unreliable because many viral and bacterial infections showed similar symptoms (Herberg *et al*. 2020). Thus, real-time polymerase chain reaction (RT-PCR) of pharyngeal swabs, nasal swabs, and sputum or bronchoalveolar lavage fluid is a preferred diagnostic test to confirm the presence of SARS-CoV-2 (Zothantluanga *et al*. 2020; Pascarella *et al*. 2020). In addition to this, simpler diagnostic testing like rapid antibody testing (RAbT) and rapid antigen testing (RAgT) that produces results within minutes are also employed to detect a SARS-CoV-2 infection (Zainol *et al.* 2020; Scohy *et al*. 2020).

2.5. Incubation period

A mean incubation period of 5-6 days was observed although it could vary from 2 to 14 days (Kolifarhood *et al*. 2020; Bai *et al*. 2020). A study also reported an incubation period of 24 days (Bai *et al*. 2020). During the incubation period, the virus can be transmitted by an asymptomatic individual. Interestingly, even after weeks of not showing symptoms, patients might also show positive results in the RT-PCR test. Thus, pathogenic transmission might not be correlated with a positive RT-PCR test (Pascarella *et al*. 2020).

2.6. Re-infection

Cases of re-infection after negative RT-PCR test was observed in several patients (Hoang *et al*. 2020). A study had reported that RT-PCR produced false-negative results at an alarming rate of 12.5% (Li *et al*. 2020a). Although antibodies like immunoglobulin (Ig) G and Ig M seem to offer protection against re-infection, a patient can be re-infected with a different strain of SARS-CoV-2 as it had undergone several mutations (Long *et al*. 2020; Mumoli *et al*. 2020; Hoang *et al*. 2020; Phan 2020; Tufan *et al*. 2020).

2.7. Age

The severity of COVID-19 increases with age wherein the case fatality rate (CFR) is high for 60 years and above. In general, maximum deaths were observed in patients whose ages were above 60. Prevalence of comorbidities, weakened immune system, and dysregulated immune response (resulting in cytokine storm and chronic systemic inflammation) may be attributed to higher CFR in the elderly (Kang and Jung 2020). Although severe cases were also reported in children, milder cases with good clinical prognosis were generally observed in children (Kang and Jung 2020; Ludvigsson 2020). Premature ACE-2 and the absence of elevated inflammatory markers might be accountable for milder cases in children (Ludvigsson 2020).

2.8. Sex

Men were reported to have a higher chance of developing severe cases in comparison to females. The CFR of COVID-19 is higher in males when compared to females. However, severe cases were also reported in female patients. Immune response is stimulated by estrogen while it is inhibited by testosterone.

Low levels of testosterone results in a greater risk of cytokine storm as well. Estrogen allows faster viral clearance. Moreover, males have a higher level of soluble ACE-2 (Maleki Dana *et al*. 2020).

2.9. High-risk individuals

Healthcare workers, sanitation workers, police personnel, pregnant women and their fetuses, individuals with comorbidities such as cerebrovascular disease, cardiovascular disease, diabetes, hypertension and chronic obstructive pulmonary disease, elderly (+60 years of age) and men may be classified as high-risk individuals as they have a higher chance to get infected or show a more severe COVID-19 induced illness (Rimmer 2020; Shirzad *et al*. 2020; Dashraath *et al*. 2020; Wang *et al*. 2020; Maleki Dana *et al*. 2020).

2.10. Ventilation

Poor ventilation can increase the risk of pathogenic transmission (Wang *et al*. 2020b). Hand washing or social distancing might not offer protection against viral respiratory droplets (Somsen *et al*. 2020). Moreover, some people might be reluctant to wear mask owing to various reasons and as clustered cases were often reported in closed environments (buses, cruise ships, hospitals, and prisons), proper ventilation might be beneficial in terms of reducing the risk of exposure to SARS-CoV-2 (Wang *et al.* 2020b; Wang *et al*. 2020c).

2.11. Population mobility

Population mobility was correlated with an increase in influenza infection (an infectious disease that spreads through respiratory droplets) (Cui *et al*. 2020). Zothantluanga *et al*. (2020) reported that an increase in interstate movement led to a

COVID-19 outbreak among migrant workers. It was also reported that increased population mobility during the spring festival of China may also attribute to the outbreak of COVID-19 (Jiang and Luo 2020). Interestingly, lockdown interventions decreased population mobility thereby reducing COVID-19 cases (Kraemer *et al*. 2020; Jiang and Luo 2020). Thus, the spread of COVID-19 is associated with population mobility (Jiang and Luo 2020).

2.12. Prophylaxis

Nonessential travels, public gatherings, shaking of hands when greeting others, touching eyes, mouth, and nose with unwashed or unsanitized hands, touching common surface areas should be avoided (Lotfi *et al*. 2020). Washing hands, wearing face masks, social distancing, quarantine, home isolation and contact tracing are other prophylactic measures (Lotfi *et al*. 2020; Wilder-Smith and Freedman 2020; Guner *et al*. 2020; Salathe *et al.* 2020). Physical exercise and nutritional support may stimulate the immune system to fight SARS-CoV-2 infection (Messina *et al*. 2020; Fallon 2020; Ahmed 2020).

3

ADVERSE EFFECTS ON HUMAN PHYSIOLOGICAL SYSTEMS

3.1. Respiratory system

Among the human physiological systems, the system that is visibly affected by SARS-CoV-2 infection is the respiratory system. Shortness of breath, fever, dry cough, sore throat, dyspnea, myalgia, fatigue, rhinorrhoea, nasal congestion, and sputum production might be some of the clinical features of a SARS-CoV-2 infected respiratory system (Wang *et al*. 2020d). Histopathology of lungs in SARS-CoV-2 infection reveals interstitial inflammation; necrotizing bronchitis/bronchiolitis, early diffuse alveolar damage, cytolysis, interstitial pneumonia characterized by leukocytic infiltration of the alveolar septa, intra-alveolar edema followed by fibrin deposition and formation of hyaline membranes, and multinucleated giant cells (Jain 2020).

3.2. Endocrine system

COVID-19 might induce subacute thyroiditis that may result in ear pain (Bellastella *et al*. 2020). COVID-19 patients with diabetes as a comorbidity are at a greater risk of developing cytokine storms (Guo *et al*. 2020). Primary adrenal insufficiency might be caused by COVID-19 which can ultimately lead to a worsened reaction against severe respiratory distress (Bellastella *et al*. 2020; Pal and Banerjee 2020). ACE-2 is utilized to regulate ovulation, follicle development, luteal angiogenesis, alteration of endometrial tissue, and embryo development in females. Interestingly, ACE-2 is greatly expressed in the placenta, ovary, uterus, and vagina. Thus, SARS-CoV-2 might bind to ACE-2 and disturb the female reproductive system (Jing *et al*. 2020). ACE-2 is also expressed

in the Leydig cells and seminiferous tubules of the testis (Cardona Maya *et al*. 2020). Thus, SARS-CoV-2 might also be able to damage these anatomical parts (Pal and Bannerjee 2020).

3.3. Cardiovascular system

Chest pain, chest tightness, palpitations, and arrhythmias might be some of the clinical features of a SARS-CoV-2 infected cardiovascular system (Wang *et al*. 2020d; Behzad *et al*. 2020; Guzik *et al*. 2020). Acute cardiac injury in COVID-19 patients is the most common cardiac-related complication (Bansal *et al*. 2020). Apart from acute respiratory distress syndrome, cardiac arrhythmia was the second most reported complication (Wang *et al*. 2020e). Worryingly, a study also reported that COVID-19 patients with cardiac abnormality had the highest CFR (Wu and McGoogan 2020; Li *et al*. 2020b; Wang *et al*. 2020e).

3.4. Gastrointestinal system

Abdominal pain, diarrhea, nausea, and vomiting might be some of the clinical features of a SARS-CoV-2 infected gastrointestinal system (Wang *et al*. 2020e; Wong *et al*. 2020; Guan *et al*. 2020a; Zhang *et al*. 2020a; Xiao *et al*. 2020). Various anatomical regions of the gastrointestinal tract such as the esophagus, stomach, small intestine (duodenum), and rectum were found to contain SARS-CoV-2 (Parohan *et al*. 2020). The presence of SARS-CoV-2 in the liver and bile was reported. There were also evidences of liver injury in COVID-19 patients. Cytokine storm induced by COVID-19 complications might also worsen an underlying liver injury (Galanopoulos *et al*. 2020).

3.5. Nervous system

Studies reported that SARS-CoV-2 can enter the brain via the olfactory nerve pathway and the central nervous system via ACE-2 (Li *et al*. 2020d; Behzad *et al*. 2020). Dizziness, anosmia,

visual dysfunction, disturbed taste, consciousness disorder, myalgia, encephalitis, epileptic seizures, necrotizing hemorrhagic encephalopathy, Guillain-Barre syndrome, stroke, rhabdomyolysis, hypogeusia, hyposmia, fatigue, epilepsy, paralysis, ischemic stroke, cerebral venous thrombosis, intracerebral hemorrhage, encephalitis andmeningitis might be some of the neurological related symptoms of a SARS-CoV-2 infected nervous system (Chen *et al.* 2020; Carod-Artal 2020; Abboud *et al*. 2020). SARS-CoV-2 might also induce interstitial and cellular edema along with dysregulated blood flow of the cerebral and ischemia (Behzad *et al*. 2020).

3.6. Urinary system

Proteinuria and haematuria might be some of the clinical features of a SARS-CoV-2 infected urinary system (Diao *et al*. 2020; Li *et al*. 2020c). Acute kidney injury is often observed in COVID-19 patients (Li *et al*. 2020c). As the mortality rate in COVID-19 patients increases with renal complications, acute kidney injury may be inconclusively considered as a biomarker for a multi-organ failure (Pei *et al*. 2020; Ronco *et al*. 2020). SARS-CoV-2 can directly infect podocytes and renal tubular epithelium and this may also attribute to acute kidney injury and endothelial damage (Ronco *et al*. 2020). A computed tomography scan revealed a reduced density of the kidneys and this might be evidence of inflammation or edema (Cheng *et al*. 2020).

4

PHARMACEUTICAL INTERVENTIONS

To date, there are no cures for COVID-19. However, many promising drugs had emerged owing to our rapidly expanding knowledge on the virology of SARS-CoV-2 (Sanders *et al*. 2020). Moreover, there is still no drug approved by the Food and Drug Administration for COVID-19 treatment (World Health Organization 2020).

In addition to the regular pharmaceutical interventions, a blood filtration system called CytoSorb that is designed to filter out cytokines from the blood is also undergoing clinical trials with a registration number of NCT04391920 (Cytosorbents 2020).

Furthermore, mesenchymal stem cells that has immunomodulatory property are also undergoing clinical trials with a registration number of NCT04392778 and NCT04444271 (Hastanesi 2020; Akram 2020).

As of 26th November 2020, there are a total of 51 vaccine candidates with a total of 9 candidates in Phase 3 of the clinical trials (Craven 2020).

Globally, the following drugs are commonly used in COVID-19 therapy.

4.1. Remdesivir

Remdesivir is an antiviral drug belonging to a nucleotide analog. It induces chain termination at a premature stage when incorporated into a viral RNA (Wang *et al*. 2020f). Several studies had reported the beneficial effects of remdesivir for treating COVID-19 (Grein *et al*. 2020; Mehta *et al*. 2020). The

clinical trial registration number for remdesivir is NCT04292730 (Gilead Sciences 2020).

4.2. Favipiravir

Favipiravir is an antiviral drug belonging to a nucleoside analog. It inhibits RNA-dependent RNA polymerase (Guo *et al*. 2020). The administration of favipiravir in COVID-19 patients resulted in an enhanced viral clearance and faster recovery (Coomes and Haghbayan 2020; Irie *et al*. 2020). The clinical trial registration number for favipiravir is NCT04359615 (Irvani 2020).

4.3. Ivermectin

Ivermectin is a well-known anti-parasitic drug. It possesses immunomodulatory property and also exhibits an antiviral activity against SARS-CoV-2 *in vitro*. Studies showed that ivermectin was useful against many DNA and RNA viruses (Heidary and Gharebaghi 2020). The clinical trial registration number for ivermectin is NCT04523831 (Mahmud 2020).

4.4. Doxycycline

Doxycycline is an antibiotic. It is a lipophilic analog of tetracycline whose antiviral activity had been reported. It also has an immunomodulatory property and can downregulate the inflammatory markers. Doxycycline inhibits NF-kappaB which downregulates dipeptidyl peptidase-4 expression which might be a factor in blocking the entry of SARS-CoV-2 into cells (Alam *et al*. 2020). The clinical trial registration number for doxycycline is NCT04523831 (Mahmud 2020).

4.5. Convalescent plasma

Convalescent plasma might be able to provide passive immunization against COVID-19 as it might contain antibodies

if it is obtained from a recovered COVID-19 patient (Mehta *et al*. 2020). When convalescent plasma was administered in COVID-19 patients, it was observed that neutralizing antibody titers were increased. A better clinical prognosis was also observed in COVID-19 patients (Rajendran *et al*. 2020).

4.6. Interferons

Interferons are known to inhibit the replication of a virus and helps support the immune system to aid in viral clearance (Zhou *et al*. 2020). A study demonstrated that interferons were able to significantly improve the condition of COVID-19 patients when they were simultaneously administered with other antiviral drugs (Shalhoub 2020; Hung *et al*. 2020). Currently, remdesivir and interferon-β1a are undergoing human trials (National Institute of Health 2020).

4.7. Vitamins and minerals

Vitamin C reduces inflammation, modulates cytokines, and modulates the immune system (Colunga Biancatelli *et al*. 2020; Carr 2020). Vitamin D has immunomodulatory properties and also increases the production of antiviral peptides (Ali 2020). Zinc has an immunomodulatory property and antiviral properties as well. It can prevent the entry of pathogens into the cell (Wessels *et al*. 2020). Vitamin C, D, and zinc are undergoing clinical trials with a registration number of NCT04335084 (ProgenaBiome 2020).

4.8. Corticosteroids

Corticosteroids reduces the production of inflammatory mediators like cytokines. They alter the transcription of mRNA by binding to cytoplasmic receptors (Mehta *et al*. 2020). Several studies had reported the beneficial effects of administering corticosteroids in COVID-19 patients like reduced mortality

rate (Mehta *et al*. 2020; Wu *et al*. 2020; Ye *et al*. 2020). With our current knowledge on the ability of corticosteroids being able to reduce inflammation, it might be logical to administer them in critically ill or ICU patients.

4.9. Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen or acetaminophen had been recommended by the WHO as COVID-19 is associated with fever (Mehta *et al*. 2020). NSAIDs are beneficial for treating fever and inflammation as they inhibit cyclooxygenase (COX)-1 and COX-2 thereby preventing the production of prostaglandins (Mehta *et al*. 2020; Guan *et al*. 2020b). A drug called ibuprofen that belongs to the class of NSAIDs is undergoing clinical trials with a registration number of NCT04382768 and NCT04383899 (Garcia 2020; Bordeaux 2020).

4.10. Monoclonal antibodies

Monoclonal antibodies can prevent cytokine storm in COVID-19 patients (Giwa *et al*. 2020). Under the class of monoclonal antibodies, drugs like tocilizumab, sarilumab, and imatinib are studied for validating their efficacy in treating COVID-19 (Wiersinga *et al*. 2020). Monoclonal antibodies are also believed to prevent systemic inflammation in COVID-19 patients (Zhang *et al*. 2020b). Currently, they are being studied under clinical trials (Wiersinga *et al*. 2020; Zhang *et al*. 2020b; Kemp 2020).

4.11. Vitamin K and anticoagulants

Deficiency of vitamin K might lead to thrombosis, cytokine storm, and enhanced elastic fiber damage in COVID-19 patients (Dofferhoff *et al*. 2020; Anastasi *et al*. 2020). Vitamin K was reported to prevent thrombosis, vascular elastic fiber damage,

and pulmonary damage (Dofferhoff *et al*. 2020). Evidences suggested that COVID-19 might be associated with disseminated intravascular coagulation (Kollias *et al*. 2020). Thus, the administration of vitamin K and anticoagulants might be considered for treating COVID-19.

5
INITIAL MEASURES TAKEN UP BY THE GOVERNMENT OF MIZORAM

SARS-CoV-2 spread effortlessly throughout the world and on 30th January 2020, the first COVID-19 case was eventually detected in Kerala, India. The Government of Mizoram was forced to take up all the possible responsibilities to prevent the entry as well as prevent an outbreak of COVID-19 in Mizoram. Throughout the state of Mizoram, task forces were formed at every level – local/community, district, and state level to mitigate the COVID-19 outbreak.With the hope to prevent the entry or outbreak of COVID-19 in Mizoram, the Government of Mizoram was forced to cancel or postpone many of its pre-planned programs that involved public gatherings.

Following this, the Government of Mizoram decided to observe a partial lockdown between 22nd March 2020 to 29th March 2020. It is also noteworthy to highlight that a commercial flight service opted not to operate any flights to Lengpui Airport of Mizoram for a total of 28 days i.e., from 19th March 2020 to 15th April 2020 (Zothantluanga *et al*. 2020). Thus, it is clear that the Government of Mizoram carried out the appropriate steps to prevent the entry or outbreak of SARS-CoV-2 in Mizoram. Table 1 provides a brief highlight on some of the precautionary measures taken up by the Government of Mizoram before a single case was detected in Mizoram.

Table 1: Highlights on the initiatives taken by the Government of Mizoram to prevent the entry or curb the spread of COVID-19 in Mizoram (Zothantluanga *et al*. 2020)

Sl.no.	Date	Initiatives
1	4th February	A COVID-19 medical screening point was set up at Zokhawthar, Champhai which is a town located near the Indo-Myanmar border.
2	2nd March	To screen the individuals entering Mizoram from Myanmar, a decision was made to deploy a medical team to Saisihchhuah, Lawngtlai.
3	7th March	In Siaha district, the movement along the Indo-Myanmar border through Lopu, Chapi, Khaikhy, Zyhno, Lodaw, Lomasu, Iana, Siasi, Laki and Khopai villages was prohibited.
4	10th March	An announcement was made to seal the international and inter-state borders until further notice. However, Bairabi and Vairengte at the Mizoram-Assam border, Khawkawn at the Mizoram-Manipur border, and Kanhmun at the Mizoram-Tripura border were excluded from the announcement. Limited movement was allowed for trucks carrying essential supplies.

		However, the details of all the passengers were recorded and they were screened for COVID-19. An advisory was issued that cautioned people to avoid public gatherings and traveling.
5	11th March	A notice was issued by the Government of Mizoram stating that various check gates may be opened during the day time but should remain closed during the night time.
6	13th March	Launching of COVID-19 helpline numbers was done.
7	16th March	Public places and educational institutions were closed by the Government of Mizoram till the 31st of March 2020.
8	19th March	Public places were closed down by the Government of Mizoram and 14 days of home quarantine was made mandatory for all returness that were coming from outside the state.
9	20th March	Several departments were instructed by the Government of Mizoram to work at 50% workforce capacity.

10	21st March	Owing to the increasing public interest, the Government of Mizoram decided to stop the movement of passengers and goods through Zokhawthar, Champhai.
11	22nd March	The higher secondary school leaving certificate examination for the year 2020 was postponed.
12	23rd March	The Lengpui airport was closed by the Government of Mizoram until further notice.

6

ISOLATION, TREATMENT CENTRE AND TESTING FACILITIES FOR COVID-19 IN MIZORAM

To isolate and treat COVID-19 patients in Mizoram, the Government of Mizoram designated State Referral Hospital - Zoram Medical College (SRFH-ZMC) located at Falkawn, Aizawl as the isolation and treatment centre. Before 7th April 2020, all the collected swab samples had to be preserved and outsourced for testing the presence of SARS-CoV-2. From 7th April 2020 onwards, the installed COVID-19 testing laboratory at SRFH-ZMC which was equipped with RT-PCR started to function (Zothantluanga *et al*. 2020). The RT-PCR installed at SRFH-ZMC had a testing capacity of 1500 samples per day (Healthworld 2020).

It is also noteworthy to mention that Aizawl Civil Hospital and other private hospitals voluntarily made rooms to accommodate patients that were earlier admitted to SRFH-ZMC. This was done with the motive to increase the capacity of SRFH-ZMC for treating COVID-19 patients as well as to prevent cross-infection within the hospital. On 12th June 2020, the TrueNat laboratory that was setup at Lunglei Civil Hospital started to function. Since then, locals and quarantined migrants residing in the Lunglei district were frequently screened for COVID-19 using TrueNat (Zothantluanga *et al*. 2020). Currently, the Government of Mizoram had allowed private hospitals and private labs to conduct tests for COVID-19 provided they adhere strictly to prescribed guidelines (Healthworld 2020).

7

QUARANTINE FACILITIES IN MIZORAM

In addition to home quarantine, there are three types of quarantine facilities in Mizoram viz. government quarantine facilities, community quarantine facilities, and hotel/ paid quarantine facilities. Government quarantine facilities include medical quarters, circuit houses, tourist lodges, rest houses, bungalows, covid care centres, and others. A graphical representation of district wise government quarantine facilities and capacities is given in Figure 2. A representation of community quarantine facilities and capacities are also given in Figure 3. Overall, there are 723 QF (government=301; community=414; hotel/ paid=8) with 14,628 (government=9600; community=4969; hotel/paid=59) capacities (Zothantluanga *et al*. 2020; DIPR 2020b; DIPR 2020c; DIPR 2020d).

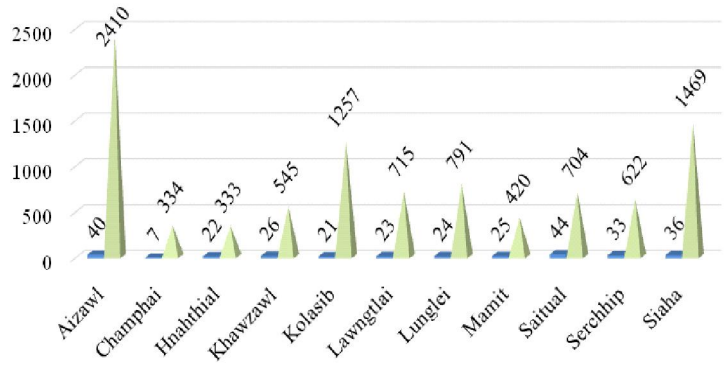

Figure: 2
District wise government quarantine facilities and capacities of Mizoram (Box – Facilities; Pyramid – Capacities)

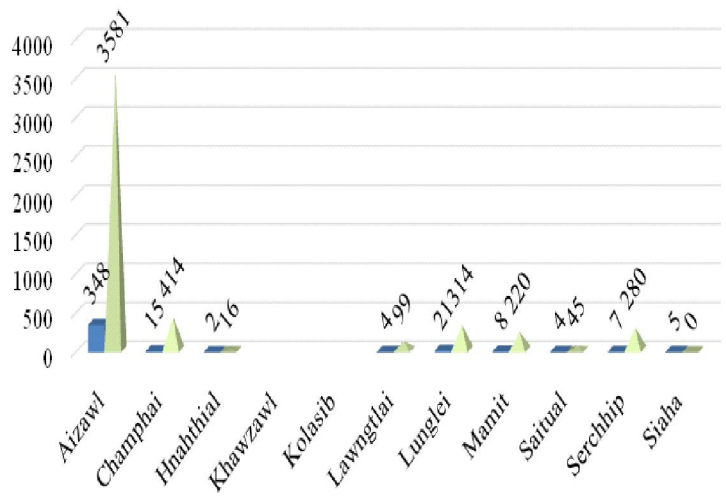

Figure 3:
District wise community quarantine facilities and capacities of Mizoram (Box – Facilities; Pyramid – Capacities)

Regarding the total quarantine facilities and capacities that are available district wise (Figure 4), Aizawl district has 396 QF with 6050 capacities, Siaha district has 41 QF with 1469 capacities, Kolasib district has 21 QF with 1257 capacities, Lunglei district has 45 QF with 1105 capacities, Serchhip district has 40 QF with 902 capacities, Lawngtlai district has 27 QF with 814 capacities, Saitual district has 48 QF with 749 capacities, Champhai district has 22 QF with 748 capacities, Mamit district has 33 QF with 640 capacities, Khawzawl district has 26 QF with 545 capacities and Hnahthial district has 24 QF with 349 capacities (DIPR 2020b; DIPR 2020c; DIPR 2020d).

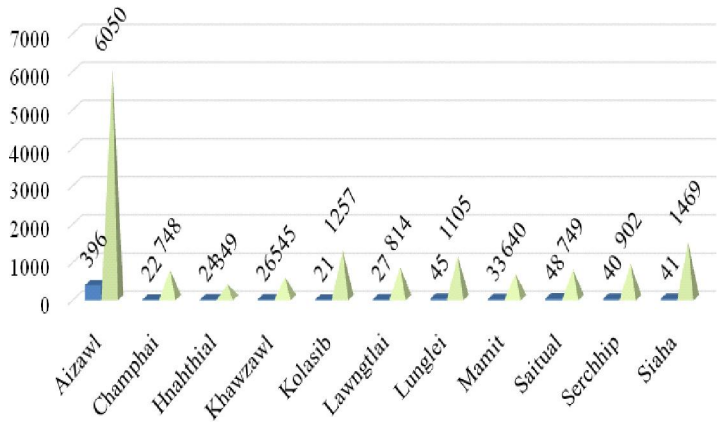

Figure 4:
District wise total quarantine facilities and capacities of Mizoram (Box – Facilities; Pyramid – Capacities)

8

INVOLVEMENT AND CONTRIBUTION BY NON-GOVERNMENT ORGANIZATIONS OF MIZORAM

To enhance security along the border of Mizoram, one of the largest non-government organizations in Mizoram called the Young Mizo Association volunteered and contributed effectively. In total, 754 task force (Figure 5) were formed at the local/ community level that operates to curb or monitor the local transmission of COVID-19 within Mizoram. The local task force efficiently cooperated with the Young Mizo Association and together, they act as a backbone for Mizoram in the fight against COVID-19 (Zothantluanga *et al*. 2020).

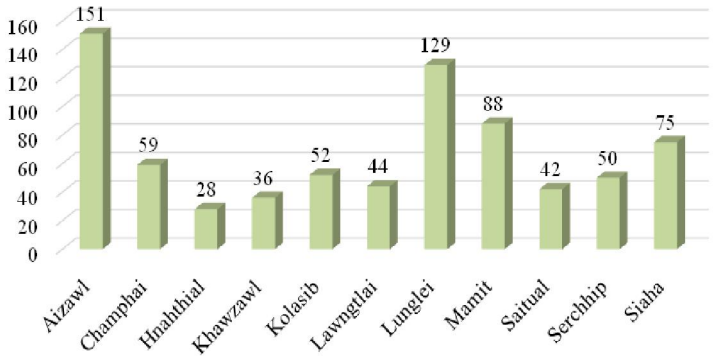

Figure: 5

Total number of district wise local task force in Mizoram

Under the supervision of the Department of Horticulture as the nodal agency, the local task force was able to effectively

manage vegetable supply chains during the nation-wide lockdown. Also, the local task force efficiently contributes to maintaining vigil along the borders of Mizoram. To prevent illegal movements along the borders of Mizoram, more than 1000 locals volunteered for duty along the Indo-Myanmar and more than 500 locals volunteered for duty along the Indo-Bangladesh borders. Many locals also volunteered to watch illegal movements along the interstate borders as well (Zothantluanga *et al*. 2020).

As the number of people returning from outside the state increased, the capacities of various quarantine facilities were quickly overwhelmed. Thus, Mizoram fell short of quarantine facilities. Then, the churches of Mizoram intervened to solve to this problem wherein a total of 194 church halls were offered for quarantine facilities. Subsequently, the quarantine capacities and facilities of Mizoram had increased. Students, health workers, nurses, drivers, lab technicians, dentists, and pharmacists including others that completed undergraduate and postgraduate courses volunteered to help fight COVID-19 (Zothantluanga *et al*. 2020).

9
OVERVIEW OF COVID-19 CASES IN MIZORAM

On 25th March 2020, the first COVID-19 positive case was confirmed through laboratory test (Zothantluanga *et al*. 2020). A weekly development of COVID-19 active cases, recovered and total cases from 26th March 2020 to 26th November 2020 is represented in Figure 6 (Zoram Medical College 2020; DIPR 2020e; HFWD 2020). Figure 7 represents the monthly data of active cases, recovered and total COVID-19 cases in Mizoram (Zothantluanga *et al*. 2020; Zoram Medical College 2020).

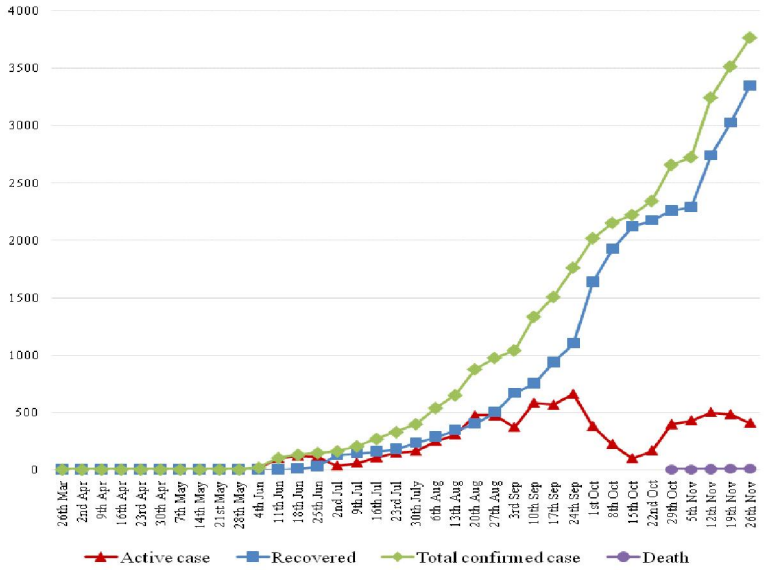

Figure 6:
Weekly development of active cases, recovered, total cases and death of COVID-19 in Mizoram from 26th March 2020 to 26th November 2020

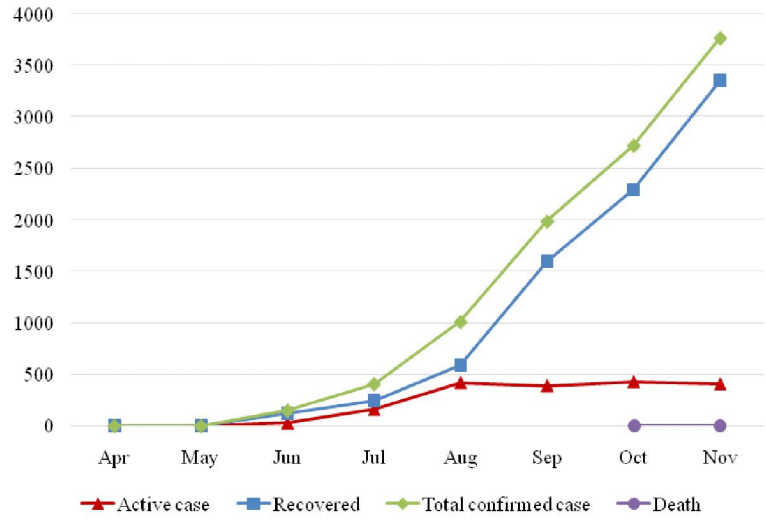

Figure 7:
Monthly development of active cases, recovered, total cases and death of COVID-19 in Mizoram from March 2020 up to 26th November 2020

As per the data obtained from the Health and Family Welfare, Government of Mizoram published and circulated by the Information & Public Relations Department, Government of Mizoram; the district wise status on COVID-19 on 26th November 2020 is given in Figure 8. With 67.91 % of total COVID-19 case, Aizawl district records the highest total COVID-19 case in Mizoram. Several factors like crowded population, business, presence of COVID-19 isolation, and treatment centre at SRFH-ZMC might the attributing factors for a high number of COVID-19 cases within Aizawl district.

As of 26th November 2020, a cumulative of 1,97,297 samples were tested for SARS-CoV-2, out of which 3765 (2.42%) tested

positive (DIPR 2020e). As of 26th November 2020, a total of 2784 males and 981 females had been infected by SARS-CoV-2 (DIPR 2020e; HFWD 2020). Figure 9 represents the prevalence of COVID-19 among different age groups as of 6th August 2020 (Zothantluanga *et al*. 2020). As of 26th November 2020, the youngest patient infected with COVID-19 is a 2-month old baby while the oldest patient infected with COVID-19 is 92 years old (DIPR 2020e).The majority of SARS-CoV-2 infected age group ranged between 21–35 years in females and between 28–42 years in males approximately (Zothantluanga *et al*. 2020). The recovery rate of COVID-19 infection up to 26th November 2020 was 89.03%. As of 26th November 2020, the fatality rate of COVID-19 in Mizoram is 0.13%.The doubling rate of COVID-19 cases from 26th March 2020 to 26th November 2020 was 20.62 days.

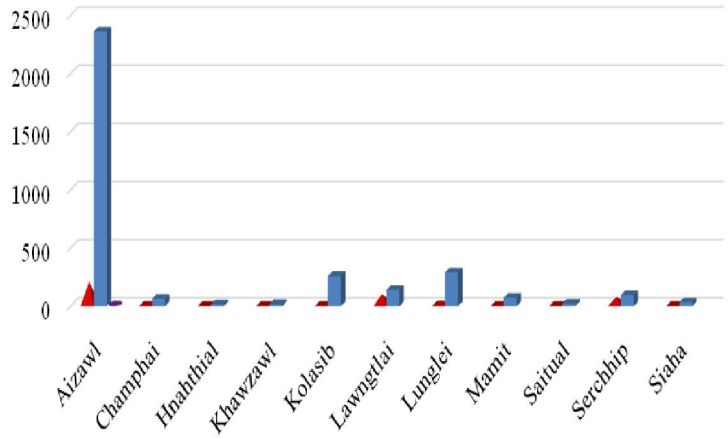

Figure 8:
District wise status on COVID-19 as on 26th November 2020 (Pyramid – Active cases, Box – Recovered, Cylindrical – Deaths)

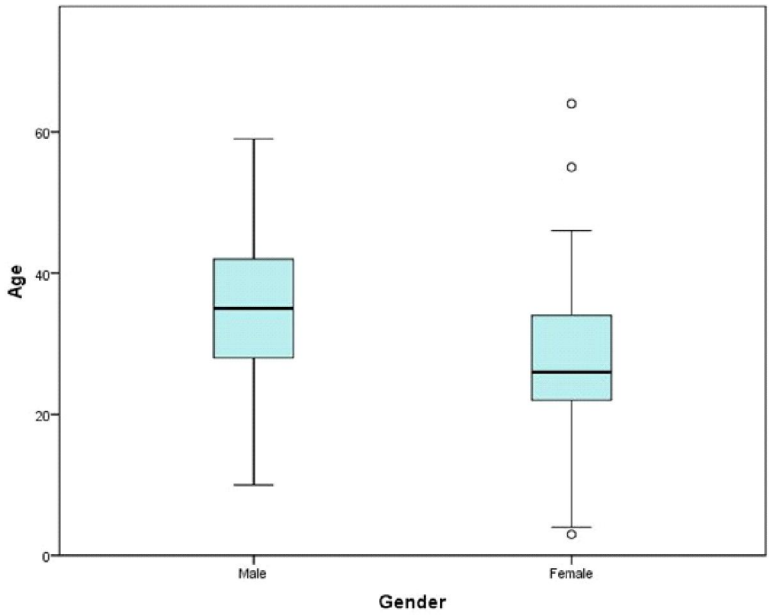

Figure 9:
Prevalence of COVID-19 among different age groups in Mizoram as on 6th August 2020 (Original figure reproduced with permission from Zothantluanga *et al*. 2020)

9.1. The first outbreak of COVID-19 in Mizoram

The total number of COVID-19 cases in Mizoram is gradually rising (Figure 6). In the 2nd week of June 2020, the first outbreak of COVID-19 occurred (Figure 10). During this period, many people that stayed outside the state for various reasons returned to Mizoram (Zothantluanga *et al*. 2020). Predictably, many of the returnees had tested positive for COVID-19 (DIPR 2020e; HFWD 2020; Zoram Medical College 2020). The interstate movement of returnees can be considered as a contributing factor for the first outbreak of COVID-19 in Mizoram.

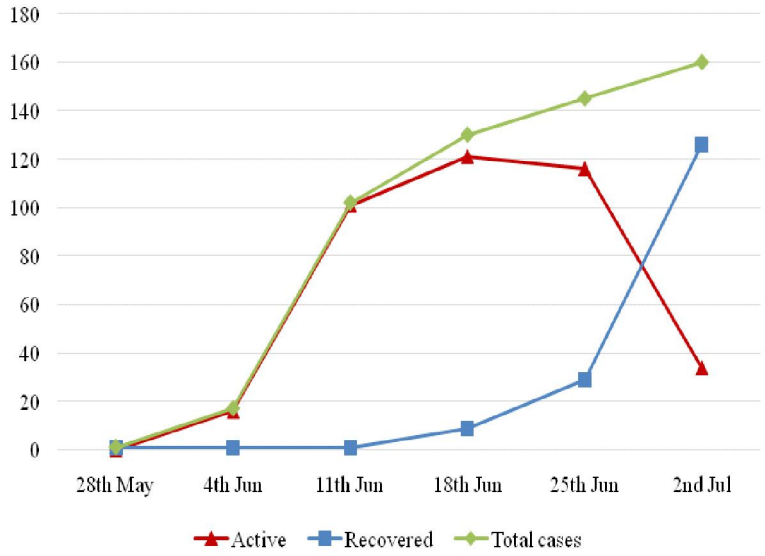

Figure 10:
Weekly development of active cases, recovered and total cases of COVID-19 during the first outbreak of COVID-19 in Mizoram

The number of active cases decreased significantly from 25th June 2020 to 2nd July 2020. On 2nd July 2020, out of a total of 160 cases, the remaining number of active cases was only 34 (Zoram Medical College 2020). It is noteworthy to mention that, the origin of infection for the majority of the individuals infected with SARS-CoV-2 can be traced in the first outbreak of COVID-19. As the majority of them were returnees from outside Mizoram, they were quarantined and screened immediately for COVID-19. Thus, the SARS-CoV-2 infected patients were not exposed to the other residents of Mizoram. This might allow early detection, isolation, treatment, and containment of the spread of COVID-19 during the first outbreak.

9.2. The second outbreak of COVID-19 in Mizoram

From the 2nd week of July 2020, the number of active cases gradually increased again (Figure 11). Here, one of the main factors that contributes to the increase in active cases was the movement of paramilitary forces. On 3rd August 2020, personnel from the paramilitary force accounts for 75% of all the active cases in Mizoram (Zothantluanga *et al*. 2020). From the above evidence, it may be inconclusively stated that the inter-state movement or travel seems to be a contributing factor to the increase in the number of COVID-19 cases. Therefore, it is advisable to avoid non-essential travels especially those that involve movement between different states.

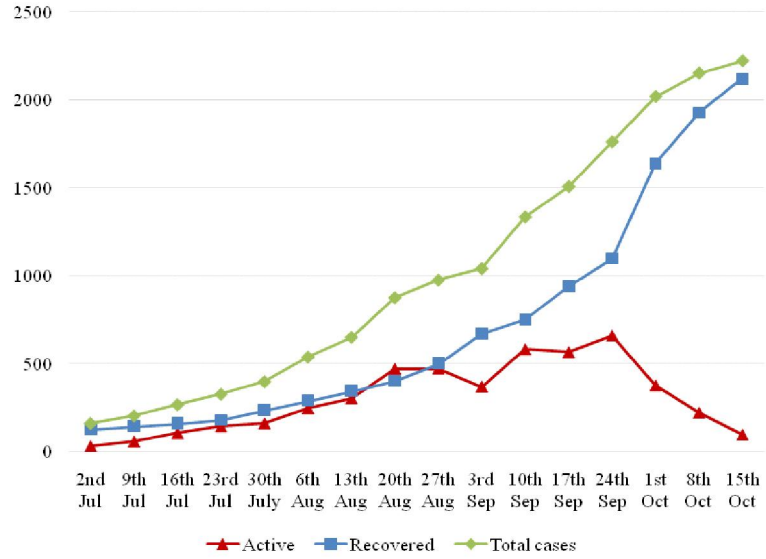

Figure 11:
Weekly development of active cases, recovered and total cases of COVID-19 during the second outbreak of COVID-19 in Mizoram

Between 27th August 2020 and 3rd September 2020, there seems to a decline in the number of active cases. However, after 3rd September 2020, the number of active cases increased till 24th September 2020. On 29th August 2020 and 4th September 2020, the village council and local council elections were held (DIPR 2020f; DIPR 2020g). This type of event involves huge public gatherings. Several guidelines were published by the authorities to prevent a possible COVID-19 outbreak after the elections. However, this event seemed to spark a chain of community transmission. Eventually, as the number of active cases fell below 100 (Figure 10), the second outbreak seemed to be contained.

In the second outbreak of COVID-19, the origin of infection for many of the individuals that are infected with SARS-CoV-2 can be traced. However, there were a few instances where the origin of infection could not be traced. Consequently, this might be a predisposing factor for the third outbreak of COVID-19 in Mizoram.

9.3. The third outbreak of COVID-19 in Mizoram

On 15th October 2020, the total number of active cases was only 99 (Figure 6). Throughout the state of Mizoram, it was publicly observable that the majority of the people were increasingly careless as the entire state was set to return to normalcy. Since 16th October 2020, schools and hostels were also reopened for the students of Class 10 and 12 (DIPR 2020h).

The people of Mizoram were then caught off guard when the state witnessed the third outbreak of COVID-19 (Figure 12) towards the end of October. Worryingly, the origin of infection for the majority of the positive cases could not be traced. Furthermore, clustered case among school students that went to the same school was also reported (DIPR 2020e).

Mizoram also witnessed its first COVID-19 induced death on 28th October 2020. A 67-year-old male from Aizawl District burdened with an ongoing heart-related comorbidity passed away days after being tested positive and treated for COVID-19. As of 26th November 2020, Mizoram had reported 5 deaths due to COVID-19. Two individuals that succumb to COVID-19 were 34 and 40 years of age respectively while the other three deceased patients were all above 60 years of age (DIPR 2020e).

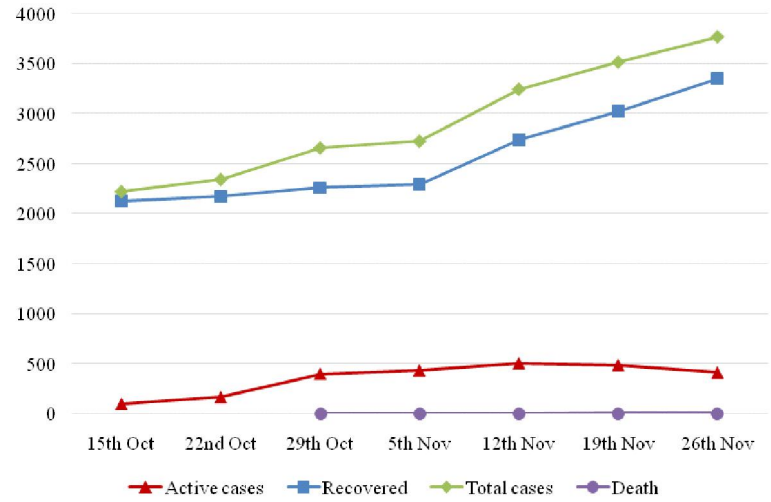

Figure 12:
Development of active cases, recovered, total cases and death of COVID-19 during the third outbreak of COVID-19 in Mizoram

To break the community transmission chain of COVID-19, the Government of Mizoram decided to observe "COVID-19 No Tolerance Fortnight" from 26th October 2020 till 9th November 2020 (DIPR 2020d). In addition to measure, Aizawl district underwent lockdown from 27th October 2020 till 3rd November 2020 (DIPR 2020e).

10

WHY WAS MIZORAM ABLE TO CONTAIN THE SPREAD OF COVID-19 AT THE INITIAL STAGE?

To some extent, the spread of COVID-19 or local transmission of COVID-19 in Mizoram might have been prevented by the decisions made by the Government of Mizoram in addition to the obedient cooperation from its people. Thus, in one way, the Government of Mizoram decisiveness at a very early stage might have curtailed the intensity of spread or transmission of COVID-19 in Mizoram (refer Table 1).

Amidst the COVID-19 pandemic, the Government of Mizoram was burdened with a lot of unforeseen and surmounting pressures to fight the pandemic. Auspiciously, many private individuals and a handful of non-government organizations made voluntary contributions that seem to have a significant impact. These crucial contributions were in the form of financial aid or providing selfless professional service (Zothantluanga *et al*. 2020). Thus, these selfless contributions by the people of Mizoram may directly or indirectly contribute to containing the spread of COVID-19.

The Government of Mizoram seems to fell short of facilities to quarantine those that return from outside the state. To aid the Government in its fight against COVID-19, churches from all over Mizoram offered their halls to the Government to be used as a quarantine facility (Figures 2, 3, and 4). This greatly increased the capacity as well as the ability of Mizoram to combat the endless rage of COVID-19. Thus, this may be also considered as a pivotal decision and also a contributing factor in limiting the spread of COVID-19 in Mizoram (Zothantluanga *et al*. 2020).

The Government of Mizoram took the responsibility to test and quarantine everyone with a travel history outside Mizoram. This sole initiative by the Government might have helped in the detection of COVID-19 at an early stage of infection. Subsequently, isolation and treatment of infected individuals were possible at the initial stage of infection. Also, the isolation of an infected individual at this stage can be considered as a factor that limits the local transmission of COVID-19 (Zothantluanga *et al*. 2020).

The Government of Mizoram mandates testing of any individual that came in contact with a COVID-19 infected patient. This initiative was undertaken as there were chances of contracting SARS-CoV-2 through primary positive contact. If there was ever any model to avoid community transmission, this initiative by the Government of Mizoram might be a good fit as an exemplary model (Zothantluanga *et al*. 2020).

11

WHY ARE THERE VERY LESS COVID-19 RELATED DEATHS IN MIZORAM?

As discussed in the previous sections, Mizoram has a population of approximately 1.2 million. So far, it had recorded 5 deaths due to COVID-19 as of 26th November 2020. Even a lesser densely populated northeastern state like Sikkim has a population of roughly 0.69 million recorded 102 deaths due to COVID-19 as of 26th November 2020 (PopulaitonU 2020b; MOHFW 2020).

The exact reason for the very low fatality rate of COVID-19 in Mizoram cannot be pinpointed. There could be several factors associated with it. Factors such as race, environment, nutrition, lifestyle, status of immunity, or other previous vaccinations can all contribute to the very less fatality rate. In one way, it is also possible a very low fatality rate was observed due to the obedience of the people of Mizoram, the selfless volunteers, the contributions from the non-government organizations and the Government's decicion to act at an early stage. However, no conclusive statement could be made regarding this matter. Thus, further studies may be conducted regarding the very low fatality rate of COVID-19.

From the available evidence, we do know that majority of the infected patients in the first outbreak and the second outbreak of COVID-19 were easily traceable with the help of an efficient local-level task force committee. This facilitates testing, isolation, and treatment at the very initial stage of infection wherein infected patients are usually asymptomatic. Moreover,

the majority of the symptomatic patients showed only mild to moderate symptoms. Luckily, many of the COVID-19 patients admitted in the intensive care unit made successful recovery (DIPR 2020e; HFWD 2020; Zoram Medical College 2020; Zothantluanga *et al*. 2020). In this way, the health care providers of Mizoram might be able to effectively treat and cure a COVID-19 patient.

Whenever the state Government imposed any form of lockdown interventions and regulations, the people of Mizoram obediently cooperated with the authorities (DIPR 2020e). Moreover, it is publicly observable that wearing of masks, sanitizing or washing of hands, maintenance of social distancing, and avoidance of public gatherings were followed by the Mizo people at their level best. This can also be attributed to preventing or reducing the intensity of local transmission. Thus, the people's obedience may have indirectly contributed to prevent the overwhelming of the healthcare system.

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