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Features, evaluation and treatment of COVID-19 infected patient: A case study in 31 hospitals in Nepal

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Abstract
An outbreak of most recently discovered severe acute respiratory syndrome coronavirus infection occurred in Wuhan, China at the end of December 2019 and spread to almost 210 countries around the world and has become a great global public health concern. Along with the rest of the world, Nepal with poor health care infrastructure is also struggling to contain the COVID-19. In this context, our research attempts to investigate the symptoms, conditions, comorbidities, laboratory abnormalities of the infected patient along with the condition of medical facilities all over Nepal. A quantitative and observational study is conducted among 109 health professionals who were involved directly in the care of the infected patient in 31 different hospitals within seven states across the country. The data is collected through the questionnaire which consists of answers to the above objectives of the research. The research reports the most common symptoms in the context of Nepal with fever, dry cough, and shortness of breath while the less common symptoms were fatigue, sore throat and loss of taste and smell. Interestingly, 30 % of the patients were found to be asymptomatic Moreover, about 60 % of the patient are found to be hemodynamically stable with mild illness. About 55 % of the infected patients were associated with comorbidities such as Diabetes, Hypertension, Cardiovascular and respiratory disease. The medical professionals are beavering away to cure the infected patient but most of them feel insecure, and they are yearning for a greater number of PPE and other medical facilities.

Keywords: clinical trials, Coronavirus disease 2019 (COVID-19), health care, clinical care, Nepal

1. Introduction
Person-to-person transmission of COVID-19 infection led to the isolation of patients that were subsequently administered a variety of treatments. China was the only affected by COVID-19 until February 2020 resulting in an epidemic followed by increasing disease to South Korea beginning of March, with Italy in the second week of March and spread all over the European countries [1]. During the third week of March, the virus crossed the Atlantic and entered into the United States and other several countries causing a declaration of pandemic by WHO on 11th March 2020 [2]. In Nepal, as of February 24, the first case was confirmed [2], a Nepalese student studying in Wuhan, with symptom-onset on January 3 [3, 4]. The infected 32-year-old male had returned on January 9 to spend winter holidays in Nepal. After the first case, the second case emerged on March 23 2020 who also had travel history from Italy [3]. Seemingly, being travel history as a risk factor, all the citizens traveling to Nepal had been filled with contact tracing at the help desk of Tribhuvan International Airport and at the border check-point for the case investigation per provinces with their ToR for initiation of RDT test for prevention of transmission [5, 6]. Since the country was ordered for lockdown and travel from borders were restricted, people started to walk and cross the border due to the crisis which led to further cases in Nepal causing local transmission starting April 17,2020 [2]. The main purpose of this research is to express the clear overview of the health conditions of COVID-19 infected patients and medical facilities to cure them in Nepal. Contributing an interesting fact that most of the Nepalese people are showing very less or no symptoms at all which will deliberately help in further research of COVID-19.

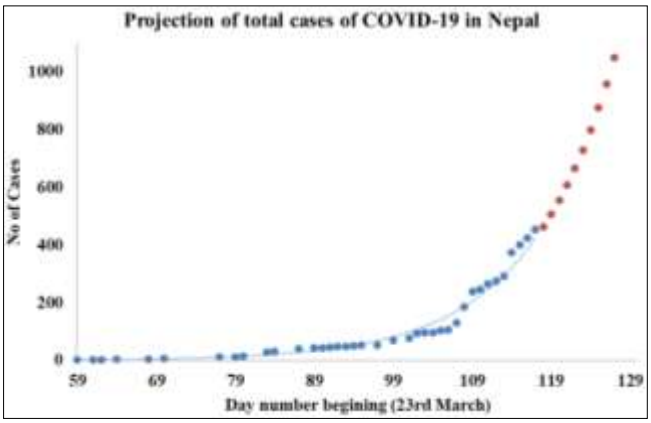

Fig 1: Projection of total cases of COVID-19 in Nepal

Figure 1 shows the scatter plots of the total confirmed cases in Nepal. The first case was confirmed in Nepal on January 24, 2020. After fifty-nine days of the first confirmed case, the second case was confirmed on March23, 2020. In the ten days interval from the last week of March until the second week of April (59-69 days) there is a slight rise in the confirmed case. From (69-89 days) the pattern continues but after 99th days the cases started to peak its pace and have been increasing upto the date. Through the projected value

we can estimate that in 10 days there will be more than 1000 cases and in the next two months the cases will rise to about 9000.

2. Methodology

A quantitative and observational study was used to identify the condition, symptoms, co-morbidities and laboratory abnormalities of patients along with conditions of medical facilities all over Nepal. This was accomplished by conducting the survey of five multiple questions to 109 health professionals working as front liner in different hospitals within seven states of Nepal from May 20, 2020 to May 27, 2020 via the Google form. The questionnaire was based on the majority of symptoms seen over the world and included the condition, symptoms, presence or absence of co-morbidities and laboratory abnormalities. The survey included health professionals working in different hospitals via random sampling technique. Participants were given an entire day to fill in the survey and 109 health professionals responded and the survey was fully completed. The data was checked for missing data and analyzed by the descriptive and statistical analysis with the use of excel spreadsheet. The results have been based on the evaluation and outcomes from the analysis.

3. Epidemiology of COVID-19

Coronavirus is one of the major pathogens that primarily targets the human respiratory system which includes previous outbreaks like SARs and MERs and has been characterized as great public health threats [1]. The first cases were reported in December 29, 2019 in Wuhan, Hubei province, China where five patients were hospitalized due to acute respiratory distress syndrome [4, 7].The patients were linked to a seafood and wet animal wholesale market where outbreak progressed and human to human spread became the main mode of transmission [8, 4].The exact mode of transmission occur mainly via respiratory droplets resembling the spread of influenza and close physical contact [4]. COVID-19 was first isolated in the bronchoalveolar lavage fluid (BALF) of three patients from Wuhan on December 30, 2019. SARS CoV-2 has been detected in non-respiratory specimens including stool, blood, ocular secretions and semen although fecal-oral transmission has not been clinically described by WHO [9]. In terms of susceptible populations, all groups were generally susceptible to COVID-19 regardless of age or sex [10] including children accounting 1 to 5% of confirmed cases but the clinical manifestations of children were generally less severe than those of adult patients [11]. Data from the largest case series in China found that 87% of confirmed case were aged 30-79 years and 3% were aged 80 years and older and 2.1% were aged 0 to 19 [12]. The Gender ratio (male/female) of confirmed was 0.99:1 and 1.06:1 respectively [13]. The overall case fatality rate is 1.4% with 98.6% recover [14]. Globally, more than four million confirmed cases of COVID-19 have been reported with 328,227 deaths [15] and spread of this virus reached to almost 210 countries around the world and WHO has declared it as "global pandemic" [16, 17]. The COVID-19 cases have been reported in all continents, except for Antarctica [9]. The United States is currently leading the total number of confirmed cases together with mortality rate in all 50 states and all least four territories [15, 18]. The precise interval during viral shedding and period of infectivity is uncertain and appears to be transmitted prior to the development of symptoms and throughout the course of illness [10]. The mean incubation period has been noted to about five days which could range from 1 to 14 days where 95% infected are more likely to experience symptoms within 11 to 12 days of contact [4]. Nevertheless, transmission from asymptomatic individuals has been well documented. A COVID-19 case in Singapore, transmission during the incubation period was estimated to account for 6.4% [8] while China estimated 7.3% [10].

One and a half months after the first confirmed case in China, the first case in Nepal was reported on 24th January 2020 [2, 19]. In context to Nepal, all the infections detected were the imported cases [4] with the travel history. Also, many of the Nepali people are engaged in the business related to India, source of spread has been spiked in Nepal as Nepali workers working in India returned to home from borders due to the crisis [19]. Thus, a higher number of patients affected with COVID-19 has been seen over the border areas such as Parsa, Banke, Udayapur, Rautahat, Rupandehi being the border between India and Nepal [2]. The first local transmission was a ninth case of Nepal, a 34-year-old woman from Kailali acquired from the fourth case from Nepal who had a travel history from Dubai [4]. In Nepal, as of May 18 2020, the total number of confirmed cases of COVID-19 is 304. The major epicenter at the moment has been Parsa as local transmission is increasing rapidly and has reported to be the highest number to be infected [2]. The confirmed case has been seen over 38 districts in 7 provinces so far in Nepal [20]. The cumulative incidence varies by state and likely depends on a number of factors, including high risk over border areas, population density, extent of implementation of strict lockdown orders, quarantine orders, extent of testing and reporting and timing of mitigation strategies. In Nepal, outbreaks in border areas have emphasized the risk of exposure and infection in congregate settings. Thus, possible control of diseases for the extreme contagious disease are continuous monitoring [21] and timely reporting of the epidemic to the public by educating the public on awareness [3]. Rapid and effective contact tracing can reduce the number of cases during the early stages of epidemics [22] and nevertheless a strong health promotion strategy of maintaining hand hygiene, public use of masks and maintaining social distancing with minimal cluster [23]. Together with the personal precaution, expand capacity to manage critically ill patients and provide personal protective equipment and disposables for health workers to protect the limited skilled manpower in our country [15] and increased number of trained health care workers to deal with a surge of cases [24].

4. Clinical manifestation

The most common symptoms as per WHO has been fever, dry cough, tiredness, with less symptoms like aches and pains, sore throat, diarrhea, conjunctivitis, loss of sense of smell and taste or also rashes over the skin and discoloration of the fingers and toes. The serious symptoms like shortness of breath or difficulty of breathing, chest pain or pressure and loss of speech or movement. It has been found that most common symptoms in China were reported with fever (98%), cough (76%) and fatigue (44%) while the less common symptoms were sputum production (28%), headache (28%) and hemoptysis (5%) and diarrhea (3%) [25]. Studies from Taiwan stated the most common symptoms

were cough (60%), fever (50%), flu symptoms (40%), myalgia ai (10%) and shortness of breath (10%) [26]. Report from Italy stated severe symptoms (24.9%), mild symptoms (46.1%), critical (5%), few symptoms (6.7%), asymptomatic (6.7%) and unspecified symptoms (10.6%) [27]. Studies from the United states reported the fever (52%), shortness of breath (76%), cough (48%) [28]. Studies from Canada reported cough (82%), fever (48%), sore throat (30%), diarrhoea (10%) and fatigue (17%) [29]. Studies from Australia reported cough (71%), fever (65%), sore throat (50%), headache (35%), nasal congestion (29%), diarrhoea (26%), fatigue (18%) and nausea (6%) [30]. Hospital-associated transmission has caused transmission to (29%) and hospitalized patients (12.3%) [10]. Co-morbidities and other conditions that have been associated with severe illness and mortality including cardiovascular disease, diabetes mellitus, hypertension, chronic lung disease, cancer, chronic kidney disease, obesity and smoking. The most prevalent co morbidities were hypertension (21.1%), diabetes (9.7%) followed by cardiovascular disease (8.4%) and respiratory system disease (1.5%) [31]. It has been found that COVID-19 in immunocompromising conditions, liver disease with pre-existing co-morbidities has been causing severe illness with advanced age [32]. The most common laboratory features associated with COVID-19 are lymphopenia (35--75%), increased values of CRP (75-93%), LDH (27-92%), ESR (upto80%) and D dimer (36-43%) as well as low concentrations of serum albumin (50-98%) and hemoglobin (41-50%) [33]. Also, the prothrombin time was prolonged to 13.0 seconds. (58%) [34].

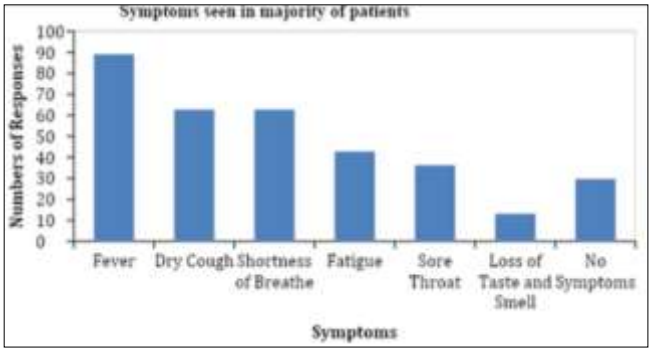

Fig 2: Symptoms seen in majority of Patients

The results of the majority of the symptoms seen in Nepal are (81.65%) fever, (57.70%) dry cough, (57.70%) shortness of breath while the less common symptoms are fatigue (39.40%), sore throat (33%), loss of taste and smell (12%) and interestingly (27.50%) patients were asymptomatic. The conditions of infected patients in Nepal are (55%) hemodynamically stable, (30.27%) pneumonia, (12%) severe pneumonia under ventilation, (15.50%) under oxygen therapy, (9.17%) ARDS. The patients were also associated with comorbidities such as (52.29%) diabetes, (57.29%) hypertension, (45.87%) respiratory disease, (30.27%) cardiovascular diseases and (6.42%) dyslipidemia. The most common laboratory abnormalities seen in infected patient in nepal are lymphopenia(43.11%), elevated erythrocyte sedimentation rate (30.27%), elevated C -reactive protein (30.27%), elevated lactate dehydrogenase (11.92%), elevated aminotransferase (9.17%), elevated ferritin (2.75%) and lastly no abnormalities were seen in 33.94% of infected patients. We also asked health professionals on their feelings about working as front liners where 23 health workers stated themselves to be safe while 23 stated they were insecure and 70 health workers are in need of more PPE and other medical equipment. Also 3 health workers stated that they didn't want to work in this situation without proper medical equipment.

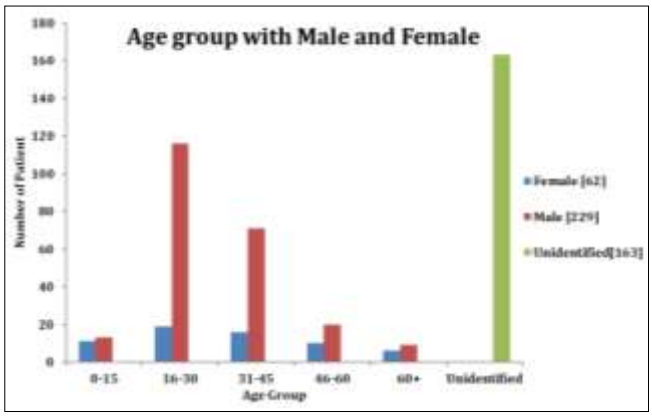

Fig 3: Graphical representation of Age group of Patients with Male and Female

The graph states the infected rate in male is greater than female [2]. Figure 3 shows the age group with male and female affected in Nepal. This chart illustrates 16-30 years age group is highly affected and age group more than 60 years are the least affected in Nepal. From this chart we can conclude that male is more susceptible from COVID-19 as compared to female.

5. Clinical Trials and Care

The major diagnosis for COVID-19 has been considered on the basis of signs and symptoms together with the travel history within 14 days or had close contact with confirmed or suspected cases of COVID-19. The patients undergo screening and triage if suspected with the COVID-19. The laboratory confirmatory test for COVID-19 has been made by direct detection by nucleic acid amplification test (NAAT's), primarily Reverse Transcription Polymerase Chain Reaction (RT-PCR). The Upper Respiratory (URT) samples such as nasopharyngeal aspirate are the primary specimens where two or more genes including nucleocapsid (N), envelope (E), and spike (S) genes are detected [34]. The sensitivity and specificity of RT-PCR has sensitivity of 95% and specificity of 100% [19]. RDT has also been used widely for the early identification which is tested through the blood via the antibodies. The presence of IgM and IgG antibodies confirms that the patient is carrier of COVID-19. The sensitivity of RDT has been 86%. Thus, WHO has suggested that the RT-PCR has been more appropriate for confirmation [19]. The result with positive confirmatory tests should undergo screening and triage into mild, moderate to severe illness. The patient with mild illness can be considered with home care with proper precautions with the family members and should keep active contact with the hospital. The patients will need symptomatic treatment such as antipyretics for fever and should consult a doctor in case of development of complications. During the home care, daily cleaning and disinfecting surfaces frequently touched, use of dedicated linen and eating utensils, cleaning and disinfecting surfaces and lastly used gloves, mask and other waste should be disposed properly in order to prevent

transmission [35]. If the patient is suspected to have moderate to severe illness, the patient is hospitalized. Once the patient is hospitalized, standard precautions should always be applied including hand hygiene, use of personal protective equipment (PPE) in direct or indirect contact. The collection of blood culture to identify bacteria and sepsis is needed in the hospitalized patients and initiation of antimicrobial therapy is required. Repeat URT and LRT should be done in hospitalized patient to demonstrate viral clearance. Oxygen supplementation is given immediately in cases of respiratory distress, hypoxemia or shock to target SpO2>94% with the use of face mask with reservoir bag. Hematology and biochemistry laboratory testing and ECG should be performed to indicate complications such as acute liver injury, acute kidney injury, acute cardiac injury or shock and further treatment should be given accordingly with precaution of drug-drug interactions. In cases of severe patients, endotracheal intubation should be performed and implementing mechanical ventilation if the patient is suggested for ARDS and sepsis induced respiratory failure. In critical patients with septic shock, the patient should be given vasopressors to maintain the mean arterial pressure and lactate and crystalloid fluid should be initiated as needed [36]. The major prevention of transmission in hospital settings are screening health care workers, universal use of masks for covering nose and mouth to contain respiratory secretions, use of PPE(gown, gloves and medical mask) when caring patients with proper hand hygiene before and after any contact [34]. Respiratory swab collection of health workers and twice daily temperature monitoring should be done to prevent transmission [37]. The health care workers should monitor themselves for fever and recommend staying home if ill. The hospital should restrict visitors in the hospitals but in cases of exemption, the visitor must be screened for exposure. Lastly, proper disposal of PPE of health workers by local sanitary authority and disinfectant use over the entire hospital [34].

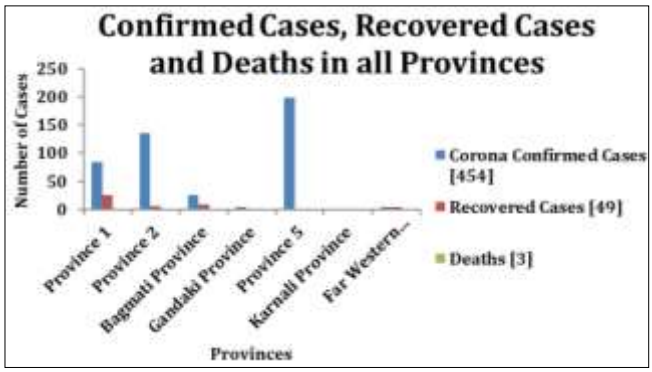

Fig 4: Graphical representation of Confirmed Cases, Recovered Cases and Deaths according to the province up to 5/21/2020

As of May 21, 2020, the total PCR tests conducted were 38,737 and RDT tests were 78,695 wherein the total PCR confirmed is 454. Over the total cases, there are 487 active cases and 49 people have recovered with 3 deaths in total. Though the cases are rising day by day, there are no serious or critical patients for now [2].

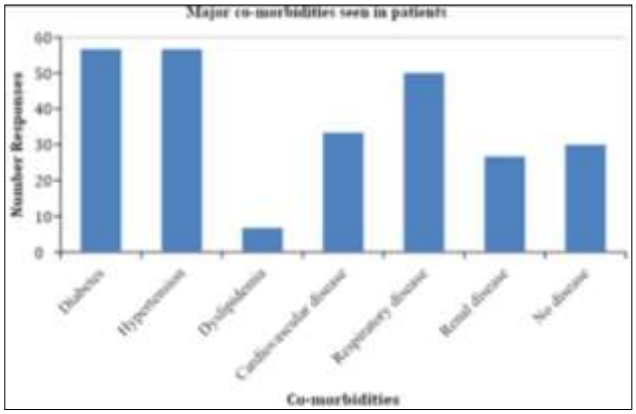

Fig 5: Major co-morbidities seen in patients

5.1 Drug delivery

The patients confirmed with COVID-19 are first classified under the severity of illness as mild illness, pneumonia, severe pneumonia ARDS, sepsis, septic shock [38]. The majority of patients in Nepal are hemodynamically stable thus considered mild illness and few are considered with pneumonia. The patient with mild illness may have non-specific symptoms such as fever, fatigue, cough w or w/o sputum production, anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion or headache. Few patients have been classified as pneumonia in adults but do not present severe pneumonia and does not require supplemental oxygen. The patients classified as mild illness are managed by isolating in the designated hospitals and treating symptomatic treatment like giving antipyretic (paracetamol) if the fever is >38C to reduce the fever.

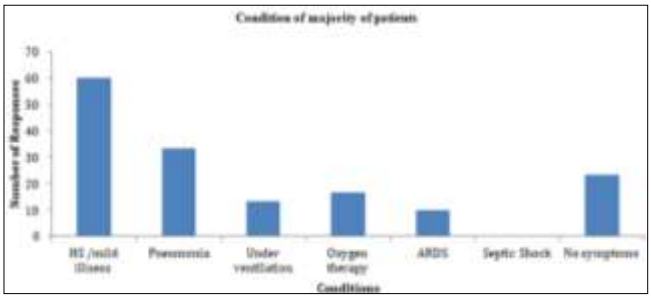

Fig 6: Condition of majority of Patients

5.2 Nursing care

The health care workers with proper personal medical equipment help in the morning with regular monitoring of vital signs (temperature, blood pressure, respiration, and heart rate). Nursing care also provides medication as kardex. Nurses who observe the irregularities, problems & improvements of every individual patient, maintain records on their every shift change. Moreover, during the care of infected patients few nurses have also been tested positive in Nepal, thus health professionals are instructed to take precautions and use of personal protective measures for control and spread of COVID-10. Despite the precautions, if a health worker shows signs and symptoms, they are placed for self-quarantine. As of now, health professionals working

as front liners are requested to stay under self-quarantine for safety and prevention.

5.3 Isolation, Quarantine and Testing

Any person who are /had been exposed to risk of developing COVID-19such as travel history, unknown exposure are allowed to stay into quarantine for a total of 14 days as to deal with the incubation period of the COVID-19.Any individual who has returned from outside to Nepal are required to stay home quarantine or at quarantine center [39]. All Nepali nationals, NRN and foreign nationals entering Nepal since 14th march 2020 were subjected to stay in self quarantine for 14 days from the date of their arrival [5]. Any symptoms persisting within 14 days are shifted to isolation. The person having fever, signs and symptoms of respiratory distress such as cough or shortness of breath are further evaluated with history of travel, contact with confirmed or probable COVID-19 cases. If one or all of the above-mentioned results are positive, the patient is suspected for COVID 19 and is kept under isolation and further tests like RDT and PCR tests are conducted. If the tests are further positive, the patient is admitted and kept under isolation for symptomatic management. If the testing shows negative results, other diagnostic modalities can be used for further management. If the symptoms persist for COVID- 19, the patient should be kept under quarantine [39, 40].

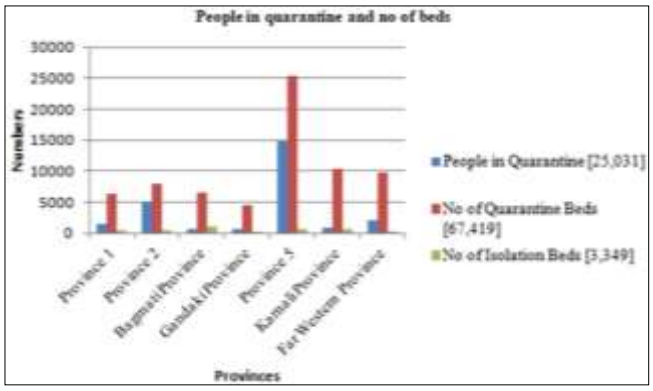

Fig 7: Graphical representation of people in quarantine and number of beds

The Government has implemented quarantine and isolation beds for precaution and prevention for further transmission. The total number of beds all over the country has been 67,419 so far. The total number of isolation beds all over the country is 3,349 and the total number of people staying at quarantine is reported to be 25,031. The chart below shows province 5 has comparatively more people in staying in quarantine than other provinces. Though the province has more people in quarantine, the government also has tried increasing more quarantine beds as compared to other provinces. The least people in quarantine are in Gandaki province.

6. Discussion and Recommendation

As of may 21, 2020 the total infection rate in Nepal is 454 where male share a higher percentage (70%) as females. Most of the confirmed cases in Nepal are of the age group 16-30 years and the age group of more than 60 years is the least affected so far. Some studies from other countries have confirmed that higher percentages are shared by the people above 50 years with a case ranging from 2 to 89 years. The survey that was carried out among 100 health care professional's reported that the most common symptoms were fever (81.65%), dry cough(57.70%), shortness of breath (57.70%) and less common symptoms were fatigue, sore throat and loss of taste and smell. Interestingly, (30%) of people were found to be asymptomatic. Moreover, 60% of the majority of patients are hemodynamically stable with mild illness and about 30% of the patients are diagnosed with pneumonia and less amount of patients are under ventilation and oxygen therapy. Almost 55% of infected patients were associated with co-morbidities such as Diabetes, Hypertension, Cardiovascular and Respiratory disease. 45% of the infected patients were seen to have reduced lymphocytes, elevated C-reactive protein and elevated erythrocyte sedimentation rate. Most of the medical professionals are not feeling secure in this situation due to the lack of proper testing facilities and less amount of medical equipment.

Reducing the risk of infection to healthcare workers is of paramount importance so the concerned authority must immediately provide the necessary PPE and standard operating procedures while dealing with the suspected confirmed COVID-19 cases. Mental health, psychosocial support and psychological first aid training must be provided to the healthcare staff to support the long term care facilities. As hypertension is seen among most of the infected patients, there must be the facility of proper counseling to the infected patients. Contact tracing, case detection and community control measures to control the transmission must be given the highest priority. Further research on major aspects of COVID-19 for a better understanding of symptoms and transmission patterns in Nepal, people risk perception, and preparedness would be of significance to establish effective prevention and control strategies both at national and local levels.

7. Conclusion

COVID-19 has infected more than two hundred countries so far including Nepal and the infection rate has been under control. In general, patients infected with COVID-19 in Nepal have shown stable condition with very few severe cases. The most common co-morbidities seen over the infected patients were diabetes and hypertension while the common laboratory abnormalities are lymphopenia and elevated erythrocyte sedimentation rate. Interestingly, 16-30 yrs age group predominantly male are more affected in Nepal. However, an aggressive approach needs to be implemented by the government in terms of increasing the number of quarantine places, hospital beds and isolation beds. The health workers working as front liners are feeling insecure due to the lack of their personal safety including enough PPE making them demand more medical equipment. Thus, the government has to play an immediate role to provide medical equipment and PPE to different hospitals and health care workers. The system's capacity to respond to implement more strict rules over borders needs to be focused. The research predicts that if this trend continues ie. exponential rise of the cases will be more than 9000 by the end of June. These measures are a step in the right direction and needs to be implemented urgently to bring control over it.

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