

Epidemiological characteristics of COVID-19 in Hodeidah, Yemen: based on clinical surveillance and triage.

ABSTRACT

Background: The epidemiological features of the Coronavirus disease 2019 (COVID -19) in different settings can help health system better manage cases and mitigate transmission risks.

Objective: Therefore, the objective of this study was to investigate the epidemiological features of COVID-19 namely the incidence rate, socio - demographic features, seasonality of COVID -19 and risk factors of morbidity and mortality rate and among peoples in Hodeiadh, Yemen.

Methodology: 505 patients were diagnosed clinically and epidemiologically with COVID-19 according to national case definition between 1 June and 31 December 2020 at Al Thawara Public Hospital Authority, Hodeidah, Yemen. The patients, ranging in age from 3-80 years old, were triaged into suspected, probable and confirmed categories in the isolation department. Epidemiological and clinical data were collected from patients. The cases were confirmed by RT-PCR and the chronic diseases and other infections were tested.

Results: The results showed that 386/505 (76.43%) of cases were classified as suspected, and 70/505 (13.86%) as probable cases that were isolated and treated at home. A total of 49/505 (9.70 %) were confirmed and admitted in isolation department. Males were more exposed to COVID-19 namely 40/49 (81.63%) of cases. 33/49 (67.3%) of old age, 32/49 (65.3 %) had chronic diseases where the most prevalent were diabetic mellitus and diabetic mellitus associated with other chronic diseases 8/49 cases and 8/49 (18.36 % and 16.32 % respectively), followed by 6/49 (12.24%) of cardiac disorders and hypertension , 5/49 (10.20%) of respiratory disorders, 2/49 (4.08 %) of cardiac disorders associated with respiratory disorder and 2/49 (4.08 %) of acute renal failure. 2/49 (4.08 %) of co-infection. Seasonal variation of COVID-19 cases was observed; there was higher frequency during the spring season, which accounted for 34/49 (69.4%), and lower frequency during the summer 4/49 (8.16%) and autumn 5/49 (10.2%) seasons. The overall case fatality rate (CFR) of confirmed cases was 23/49 (46.9%). Of these fatal cases, 15/49 (30.6 %) had chronic diseases, 7/49 (14.2 %) did not have any chronic diseases, and 1/49 (2.0%) had co-infection. However 19/49 (82.6 %) of deaths was over the age of 50 years.

Conclusion: The research concluded that, old age , chronic diseases and co-infection may be contributing factors to excess morbidity and mortality among COVID-19 patients.

Keywords: Epidemiological , COVID-19, Hodeidah, Yemen

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a respiratory disease caused by a single-stranded positive sense RNA virus that was first isolated in December 2019 after it emerged in Wuhan, China ^(1,2). The virus rapidly spread worldwide and was declared a pandemic by the World Health Organization (WHO) on 12 March, 2020 ⁽³⁾. As of October 2020, the virus had spread to 216 countries and territories, and had caused a reported 1,153,176 deaths and 42,838,516 confirmed cases, with the Number continuing to rise ^(4,5). The basic reproduction number R_0 of COVID-19 to be around 2.2 (90% high density interval: 1.4-3.8), indicating the potential for sustained human-to-human transmission. Transmission characteristics appear to be of similar magnitude to severe acute respiratory syndrome-related coronavirus (COVID-19) and pandemic influenza, indicating a risk of global spread ^(6,7).

One of the challenges of controlling COVID-19 is the wide spectrum of disease severity, ranging from asymptomatic infection and mild non-fatal and self-resolving respiratory illness to more serious complications that may require hospitalization and lead to death. Common clinical features of COVID-19 include lower respiratory tract infection-related symptoms such as fever, dry cough and dyspnea as reported in the initial case series from Wuhan, China, and supported by numerous other global studies. Headache, dizziness, weakness, vomiting and diarrhea have also been observed as symptoms. Fatal outcomes are particularly associated with certain social determinants, chronic diseases or other communicable disease co-infections ^(8,9). The risk of mortality from COVID-19 increases dramatically with age, as well as in those who have underlying co-morbidities, with hypertension being the most common followed by diabetes and coronary heart disease ⁽¹⁰⁻¹⁶⁾.

In Yemen, the first case was registered on April 10, 2020 in Hadhramout ^(17,15), with further cases later identified in other parts of the country as the disease spread. Hodeidah governorate lies in the western part of Yemen, and has been similarly exposed to the COVID-19 pandemic to other governorates in Yemen, adding to the on-going chronic challenges in the region. Hodeidah is facing a complex spectrum of determinants of health, including poverty, illiteracy, food insecurity, malnutrition and multiple epidemics as well as humanitarian crises resulting from the armed conflict that has been on-going since 2015. At the time of writing, no research has been conducted to document the COVID-19 pandemic in Hodeidah, especially related to morbidity and mortality. **The aim of this research is therefore to describe the epidemiological features of COVID-19 in Hodeidah, Yemen 2020 (First Wave), with an emphasis on identifying risk factors associated with morbidity and mortality of severe and critical cases disease.**

2. METHODOLOGY

2.1. Study area

Hodeidah governorate is located on the western flat and narrow coastal plain of Yemen, between the foothills of the highlands and the Red Sea. It is the fourth largest governorate in Yemen in terms of population, which is estimated to be 2,157,552 people. It has a land area of 13,500 km², including numerous islands in the Red Sea, and is divided administratively into 26 districts. The region has been substantially affected by conflict since March 2015. Hodeidah is also considered an endemic zone for numerous infectious diseases, including cholera, dengue and malaria. As the Yemeni civilian population is already suffering in an enormous man-made humanitarian crisis, the COVID-19 crisis has added a new stress to a health system which has already been shattered by war. Under-resourced and buffeted by years of conflict, it is inadequately prepared to care for COVID-19 patients and contain the spread of the virus. Nonetheless, the pandemic has been only one of Yemenis' many health concerns. Prior to COVID-19, several other notable disease outbreaks including cholera, diphtheria, measles and dengue fever were reported in Yemen. Cholera alone has affected nearly every Yemeni family in some way, with almost two million suspected cases since 2016 (19-21).

2.2. Study Design

This study is a cross sectional study It focuses on the patients who sought care at the COVID-19 isolation department , Center of Tropical Medicine and Infectious Diseases (CTMID), Al Thawara Public Hospital Authority ,Hodeidah, Yemen from 1st June to 31st December 2020.

2.3. Screening and triage process for patients

Five hundred and five cases (age range :3-80 years) were diagnosed in the COVID-19 emergency department according to national case definition. The cases were triaged epidemiologically into suspected, probable and confirmed (Figure 1) and clinically into mild , moderate , severe , and critical cases (Figure 2) . The severity of illness was assessed based on radiological and hematological findings. Mild and moderate cases were isolated and treated at home (Figure 2). Severe and critical confirmed cases were admitted in the COVID-19 isolation department, which is also located at CTMID. Nasopharyngeal swabs were collected from severe and critical patients only and confirmed by Real Time - Polymerase Chain Reaction (RT-PCR) (22-26).

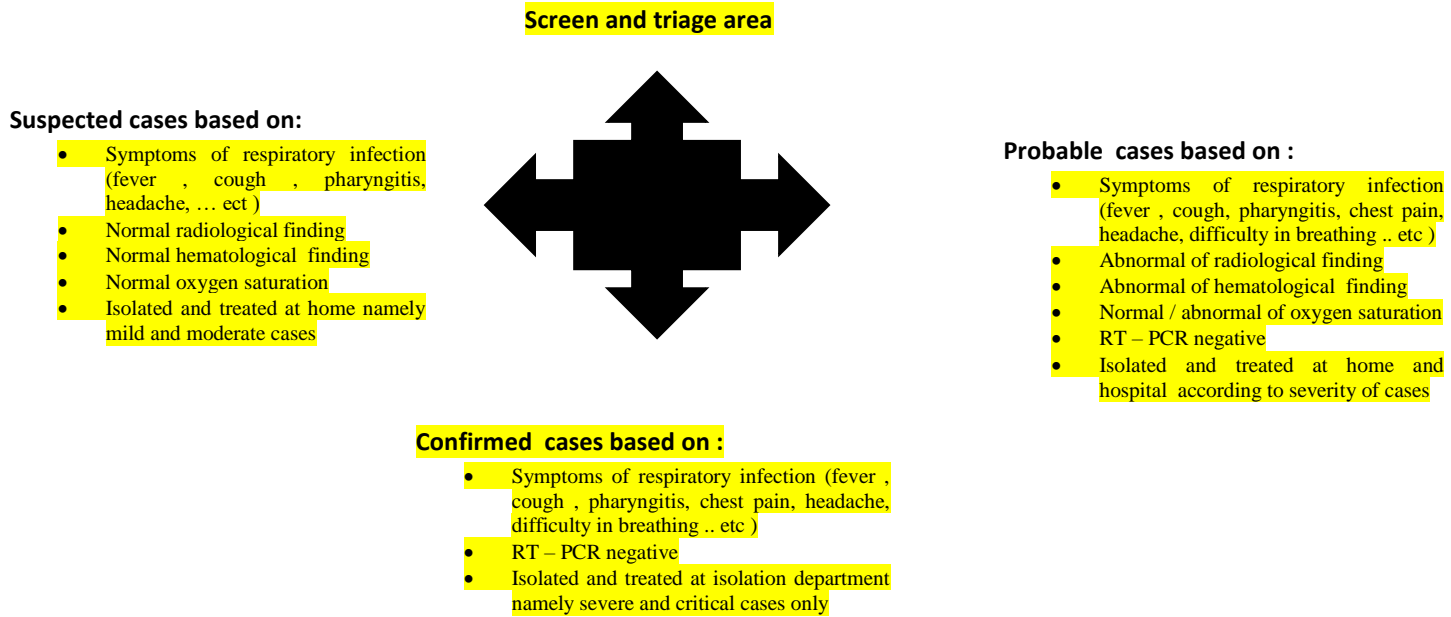


Figure 1. Screening and triage process for COVID-19 patients based on epidemiological criteria

(22-26)

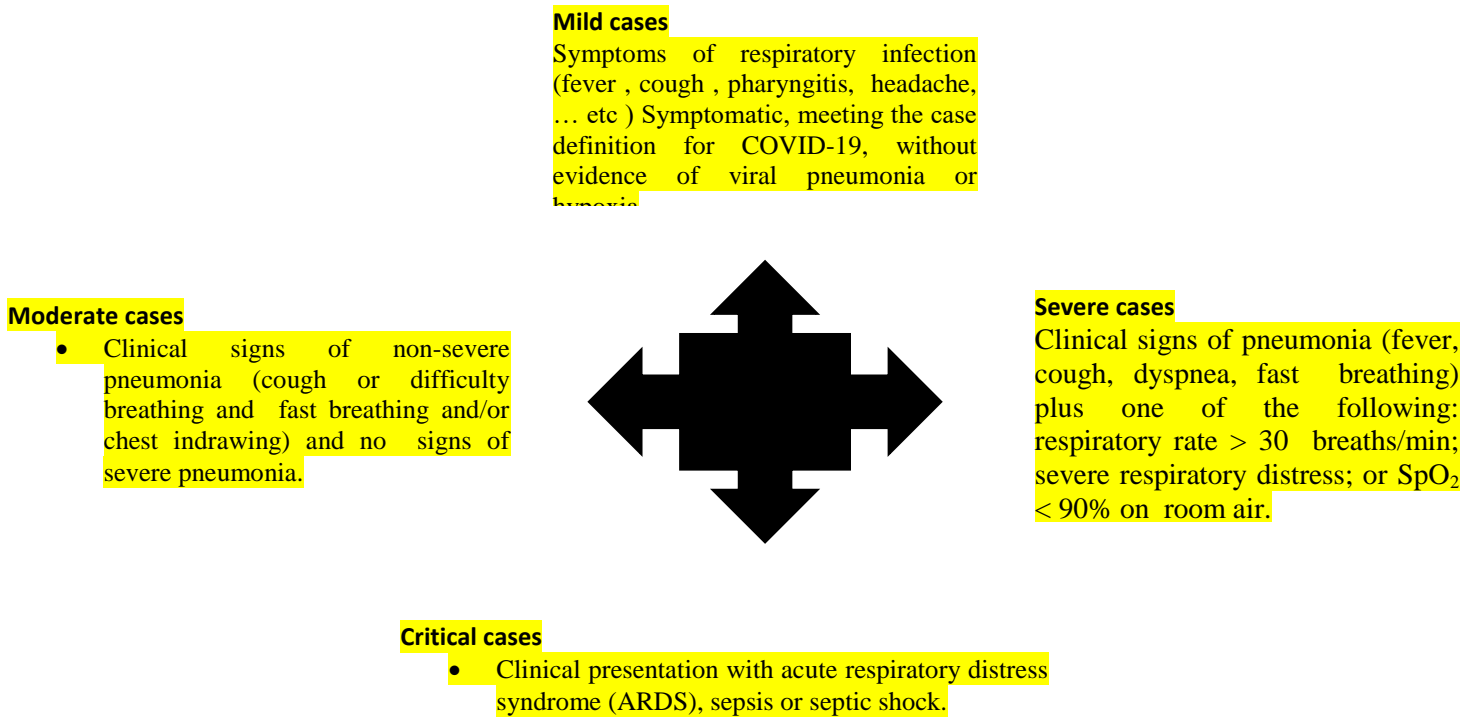


Figure 2. Screening and triage process for COVID-19 patients based on clinical criteria (22-26)

2.4. Data collection and analysis

The independent variables studied namely age, gender, co-morbidity, co-infection, seasonality, and place of residence that were collected from triage area. Data on clinical symptoms experienced by patients with severe COVID-19 were also recorded. Data were checked and entered in Microsoft Excel. The data were subsequently visualized using tables, graphs and text. Data were described through calculations of medians, ranges, frequencies and percentages. Comparisons between counts were analyzed using Chi-squared statistics. The level of alpha was set at 0.05 to determine the signification.

3. RESULTS

3.1. Suspected, probable and confirmed cases

Out of the 505 total patients presenting to the triage area during the study period, 386 (76.43%) were classified as suspected cases, 70 (13.86%) were classified as probable cases, and 49 (9.70%) classified as confirmed cases. All the confirmed cases were admitted as inpatients for treatment in the isolation department. The suspected and probable cases were treated as outpatients, and provided support therapy to take while self-isolating at home. (Table 1).

Table 1: Suspected, probable and confirmed cases by gender and age, according to screening, triage and admission criteria (N = 505)

| Age | Suspected cases * | | Probable cases ** | | Confirmed cases *** | | Total | | Total |
|--------|-------------------|--------|-------------------|--------|---------------------|--------|-------|--------|-------|
| | Male | Female | Male | Female | Male | Female | Male | Female | |
| <15 | 4 | 5 | 2 | 3 | 3 | 0 | 9 | 8 | 17 |
| 15-29 | 55 | 82 | 6 | 4 | 1 | 1 | 62 | 86 | 148 |
| 30 -49 | 47 | 60 | 10 | 7 | 8 | 2 | 65 | 69 | 134 |
| 50-59 | 19 | 35 | 13 | 3 | 12 | 3 | 44 | 41 | 85 |
| 60+ | 41 | 38 | 16 | 7 | 15 | 4 | 72 | 49 | 121 |
| | 166 | 220 | 47 | 23 | 39 | 10 | 252 | 253 | 505 |
| Total | 386 | | 70 | | 49 | | 505 | | |

- *: Suspected cases were diagnosed according to case definition , isolated and treated at home
- **: Probable cases were diagnosed according to case definition, oxygen saturation , radiological and hematological finding. They were also isolated and treated at home.
- ***: Confirmed cases were confirmed according to molecular biological method namely RT-PCR and radiological and hematological finding assessed the severity of cases and admitted in isolation center of COVID-19 , AL Thawara Public Hospital Authority , Hodeidah, Yemen .

3.2. Socio - demographic features

A total of 49 patients (9.70%) were confirmed and classified as having 21 patients of severe (4.15%) and 28 patients of critical (5.54%) . Males were significantly overrepresented in this group compared with females ($p < 0.05$). The age range of patients was from 3-80 years old and the median age of subjects was 51 years. We observed a statistically higher frequency of COVID–19 infection in older patients, with 33 of

confirmed cases (67.34%) occurring in patients between 50 and 80 years old, and the lowest frequency was in children under 15 years old (3 cases ; 6.12%; $p < 0.05$). On the other hand , no relationship between the risk of COVID-19 infection and area of residence was found in Table 2 ($p > 0.05$).

Table 2. General socio-demographic data of severe and critical COVID-19 patients in Hodeidah , Yemen (N = 49)

| Variables | Number (n) | Ratio (%) | X^2 | P – value |
|------------------|------------|-----------|-------|-----------|
| Gender | | | | |
| Male | 40 | 81.16 | | |
| Female | 9 | 18.36 | 19.62 | 0.00001 |
| Total | 49 | 100 | | |
| Age | | | | |
| <15 | 3 | 6.12 | | |
| 15-29 | 2 | 4.10 | | |
| 30 -49 | 11 | 22.44 | 0.19 | 0.00079 |
| 50-59 | 17 | 34.69 | | |
| 60+ | 16 | 32.65 | | |
| Total | 49 | 100 | | |
| Residency | | | | |
| Urban | 22 | 44.89 | 0.51 | 0.47 |
| Rural | 27 | 55.10 | | |
| Total | 49 | 100 | | |

3.3. Clinical symptoms associated with severe and critical COVID-19

The most common clinical symptoms were observed in the patients with severe COVID-19 namely difficulty breathing, followed by fever, cough, pharyngitis and chest pain. (Table 3) All cases had Acute Respiratory Distress Syndrome (ARDS). The onset date of symptom were two weeks before hospitalization.

Table 3. Clinical symptoms data of COVID-19 patients in Hodeidah , Yemen (N = 49)

| Variables | Number (n) | Percentage (%) |
|----------------------|------------|----------------|
| Difficulty breathing | 42 | 85.7 |
| Fever | 30 | 61.2 |
| Cough | 20 | 40.8 |
| Joints pains | 16 | 32.65 |
| Sore throat | 14 | 28.6 |
| Chest pain | 13 | 26.5 |
| Headache | 3 | 6.12 |

3.4. Co-morbidities and co-infections on severe and critical COVID-19 morbidity

32 patients (65.30%) with severe and critical COVID-19 were also affected by one or more co-morbidity caused by an underlying chronic disease, the most common of which was diabetes mellitus namely 17 patients (34.69%). 8 of these patients had diabetes alongside other chronic conditions. 8 patients (16.33%) had underlying cardiac disorders and hypertension, of which 2 also concurrently had respiratory disorders (bronchial asthma). 5 patients (10.20 %) had bronchial asthma without other co-morbidities, and a further 2 patients (4.08 %) suffered from renal failure. 2 patients (4.08%) were identified with co-infections of an

infectious disease (hepatitis C and tuberculosis). 15 of the patients (30.61 %) did not present with any underlying chronic or infectious disease or related co-morbidity.

3.5. Co-morbidity and co-infection on severe and critical COVID 19 mortality

The mortality rate was high overall, with 23 patients (44.90%) with severe and critical COVID-19 dying. Of these, the majority (65.21%, n=15) were afflicted with underlying co-morbidities, including 3 cases each of diabetes mellitus or cardiovascular disorders as single co-morbidities, and 4 cases with both diabetes mellitus and cardiovascular disorders together. 5 patients (10.20 %) had bronchial asthma, including one with cardiovascular disorders as an additional co-morbidity, and 1 case had acute renal failure. Of 2 patients (4.08 %) with underlying infections, the patient with hepatitis C succumbed to COVID-19. On the other hand, 7 cases (30.43 %) died without having any chronic diseases or co-infections.

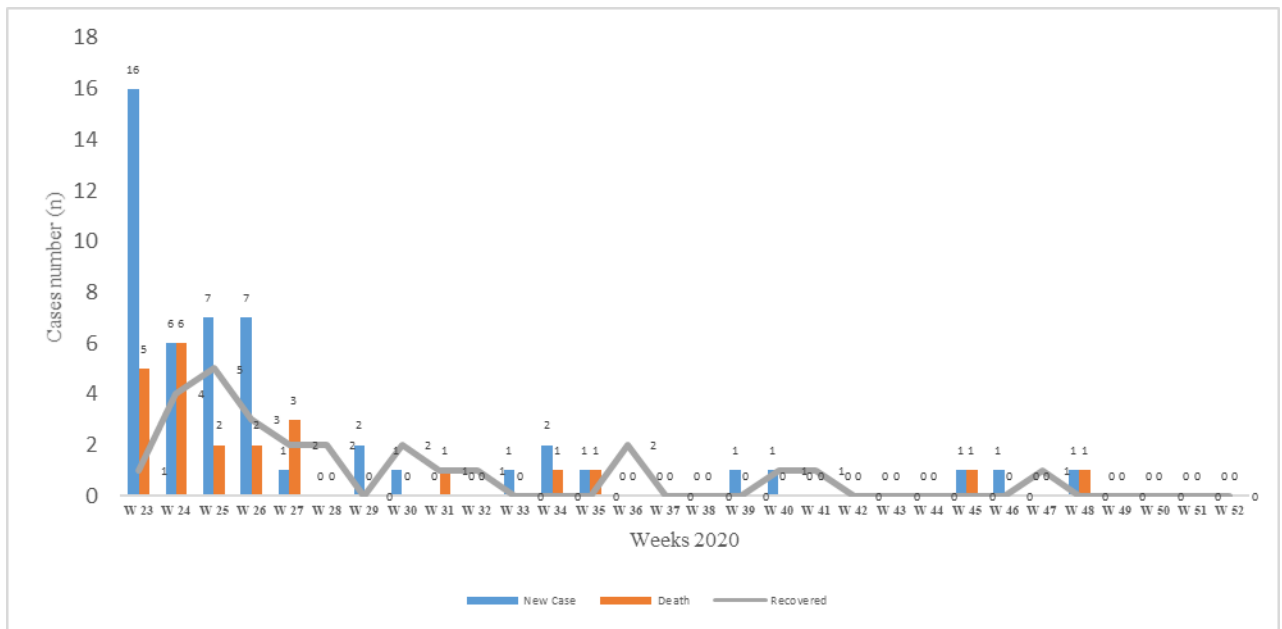


Figure 3. Epidemiological surveillance of COVID -19 in Hodeidah , Yemen

Table 4 . Association of co-morbidities and co-infections with severe and critical COVID-19 morbidity and mortality (N = 49)

| Risk factors | Recovery | | Death | | Total | |
|--------------|----------|-------|-------|-------|-------|-------|
| | n | % | n | % | N | % |
| Co-morbidity | 17 | 34.69 | 15 | 30.61 | 32 | 65.30 |
| Co-infection | 1 | 2.04 | 1 | 2.04 | 2 | 4.08 |
| Non | 8 | 16.32 | 7 | 14.28 | 15 | 30.61 |
| Total | 26 | 53.06 | 23 | 46.93 | 49 | 100 |

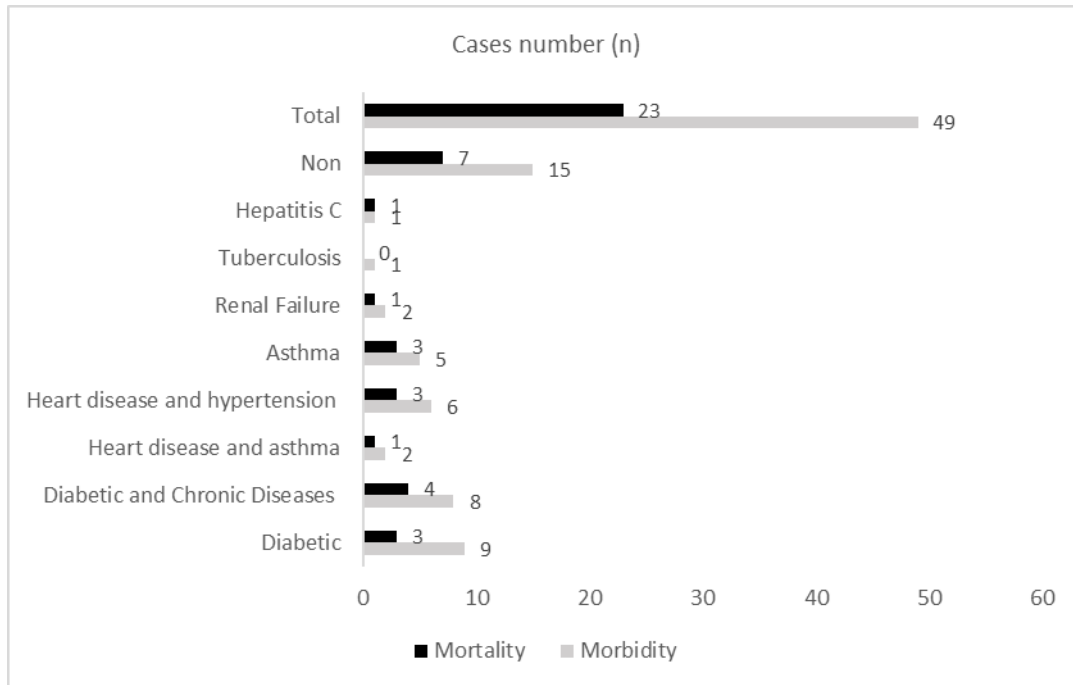


Figure 4. Different conditions associated with severe and critical COVID–19 morbidity and mortality (N=49)

3.6. Recovery and death of severe and critical case versus critical cases

Mortality rate was very high in critical cases namely 22 /28 cases (78.57 %) while the mortality rate of severe cases was 1 /21 cases (4.76 %) (Figure 5).

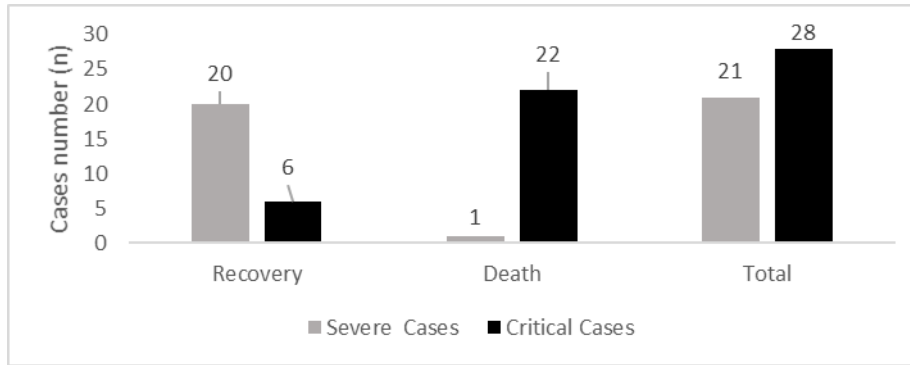


Figure 5. Mortality and recovery of COVID-19 namely severe and critical cases in Hodeidah , Yemen (N=49)

3.7. Seasonality of COVID -19

As for seasonal distribution, severe COVID-19 disease was not observed to be evenly distributed through the whole year. The spring season was significantly associated with severe COVID -19 infection (40 cases, 81.16%, and $p = 0.0001$) with lower frequency of cases observed during the summer , autumn and winter seasons respectively (4 cases , 8.15 %; 5 cases , 10.20 % ; and 0 cases, 0%) (Table 5). The peak month of COVID-19 infection, as measured by the number of severe cases, was June (Figure 6).

Table 5. : Seasonality data of COVID-19 patients in Hodeidah , Yemen , 2020 (N = 49)

| Variables | Number(n) | Ratio (%) | X^2 | $p - value$ |
|-----------|-----------|-----------|-------|-------------|
| Spring | 40 | 81.16 | 84.95 | 0.0001 |
| Summer | 4 | 08.16 | | |
| Autumn | 5 | 10.20 | | |
| Winter | 0 | 0 | | |
| Total | 49 | 100 | | |

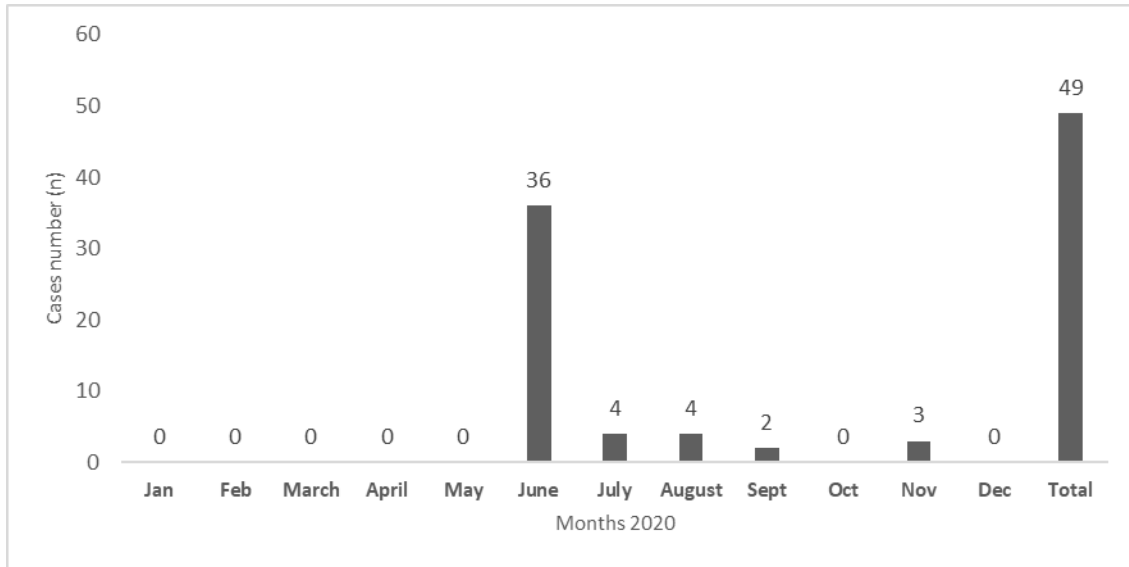


Figure 6. Monthly seasonality of severe COVID-19 among identified cases in Hodeidah, Yemen (N=49)
 Note : From 24th to 31st May 2020 , a total of 50 suspected , probable and confirmed COVID-19 patients were triaged only but not admitted where 29 cases were died in triage. The patients were admitted in 1st June after we prepared the isolation department in this time

4. DISCUSSION

As the COVID-19 pandemic continues, governments are warning people at high risk to be particularly stringent in observing social distancing measures because if they become infected they are more likely to need critical care including ventilation, and are also at higher risk of death ⁽²⁷⁾. However, in this study, patients access late to hospital with a serious critical condition. In our study, although , males and females presented to the hospital with suspected or probable COVID-19 infection, males were more likely to develop severe morbidity and mortality. This finding is consistent with other studies in China and Italy ⁽²⁷⁻²⁹⁾, and may be due to sex-based immunological or gendered differences, such as patterns and prevalence of smoking ^(26, 30-32).

Elderly patients are at greater risk of developing COVID-19, as are patients with underlying health conditions. These risk factors are additive; co-morbidities with chronic diseases increase the risk of mortality five times in older subjects ^(26,31). In this study, the most commonly reported co-morbidities were diabetes, hypertension, cardiovascular disease and bronchial asthma, as well as combinations of multiple of these conditions, which is similar to other published literature, in which it is hypothesized that underlying immunodeficiency caused by chronic health conditions can make patients more susceptible to COVID-19 complications and fatality ^(33-35,15).

Microbial co - infection can also play an important role in the occurrence and progression of COVID -19 infection by creating difficulties in diagnosis, treatment options, and prognosis of COVID-19,

and even increasing the disease symptoms and risk of mortality. However, there are few published reports about COVID-19 co-infections with bacteria, fungus, and other viruses ⁽³⁶⁾.

Our study identified one case of tuberculosis - COVID-19 co-infection among the 49 severe and critical cases included in the analysis. There is limited literature on the occurrence of COVID-19 in patients with tuberculosis ; to our knowledge, only eight studies have reported a total of 80 patients with this co-infection. These patients were reported from ten different countries, with Italy reporting the largest number of cases. In all eight studies, COVID-19 was treated as per the local protocol. Mortality was reported in more than 10% of patients, and was higher in elderly patients (> 70 years) and amongst patients with multiple additional medical comorbidities ^(37,38). Our study also identified one case of hepatitis C virus (HCV) in a patient with severe COVID-19. In Iran, the mortality rate among COVID-19- hepatitis B virus co-infected patients was 6%, and 13% among COVID-19-HCV co-infected patients. In the same study, 34.1% and 76.2% of these patients reported at least one co-morbidity besides hepatitis B virus and hepatitis C virus infection, mainly hypertension and diabetes mellitus type 2 ⁽³⁹⁾ highlighting the challenge of separating out the influence of different potential risk factors on COVID_19 morbidity and mortality. Other study , chronic HBV infection did not predispose COVID-19 patients to more severe outcomes, their data suggest COVID-19 and HBV co-infection poses a higher extent of dysregulation of host functions at the onset of COVID-19. Thus, caution needs to be taken with the management of COVID -19 and HBV co -infected patients ⁽⁴⁰⁾. Also, management of co-infection with malaria and dengue fever that are the most prevalent vector-borne diseases and represent major public health problems. They are transmitted by mosquito namely *Anopheles* and *Aedes aegypti*, respectively. Hodeidah is a high density with these vectors. Also, co-infection of these diseases has (malaria and dengue) become undetected due to lack of suspicious clinically and overlapping symptoms ⁽⁴¹⁾.

Finally, our study reported the maximum peak of infection in spring, in Italy , the COVID-19 pandemic was particularly invasive in Italy during the period between March and late April 2020, then decreased in both the number of infections and in the seriousness of the illness throughout the summer of 2020 ⁽⁴²⁾. Other previous studies reported that most viral respiratory infections tend to follow seasonal patterns with high incidence during winter ⁽⁴³⁾. Also previous study found the largest global peak of COVID-19 during the winter season, with the highest rate of positivity among children ⁽⁴⁴⁾.Our country , Yemen due to poor supporting of RT-PCR , early detection, isolation at home and management of COVID-19 cases (suspected and confirmed) are critical strategies for prevention and control of the disease ⁽²¹⁾. While , in other countries , the strategies include, among others, syndromic surveillance (to identify and test suspected cases at points of entry into countries, public places and health facilities), and prevention of virus shedding into the environment through respiratory hygiene, regular hand washing with soap and water or hand sanitizers which contain at least 60% alcohol. Social distancing is also vital to prevent contact with infected persons as well as avoidance of touching potentially contaminated surfaces, eyes, nose and mouth

with contaminated hands. With the risk of transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV -2) by asymptomatic and pre-symptomatic infected individuals who potentially shed the virus into the environment, the importance of these preventive measures to control the transmission of COVID-19 cannot be overemphasized ^(45,46).

Limitations of the study : There are some limitations in this study that need to be considered. The small samples size in confirmation of cases. The severe and critical cases only were confirmed. On the other mean , the sample of COVID-19 patients is limited to the hospital admitted cases .

5. CONCLUSION

Our study aligns with other epidemiological studies in highlighting old age and co-morbidity with non-communicable diseases as key potential contributing factors to excess illness and death among COVID-19 patients. Co-infections with other viral infections like tuberculosis and hepatitis is of high concern in Hodeidah, Yemen, and warrant further investigation.

ETHICAL APPROVAL

The studies involving human participants were reviewed and approved by Ethics Committee of CTMID, Al-Thawara Public Hospital Authority, Hodeidah , Yemen.

CONSENT

As per international standard or university standard, Participants' written consent has been collected and preserved by the authors. The raw data are secured in the Center of Tropical Medicine and Infectious Diseases (CTMID), Al-Thawara Public Hospital Authority, Hodeidah , Yemen.

AUTHORS' CONTRIBUTIONS

Mohammed Amod AL Kamarany is scientific consultant on COVID-19 humanitarian project in Hodeidah ,Yemen and wrote , revised and edited the final manuscript and responsible for summarizing all epidemiological and clinical data ; Khaled Ahmed Suhail is supervisor of COVID-19 humanitrien response project ; Ahmed Suliman Majam collected the epidemiological and clinical data ; Elham Abdulbari Alabsi is technical supervisor of project and contributed in establishment of COVID-19 isolation department in Center of Tropical Medicine and Infectious Diseases (CTMID), Al-Thawara Public Hospital Authority, Hodeidah , Yemen ; Mohammed Dowbalah and Abdullah Mohammed Zohairy supported the literature review and contributed in training the medical staff on control of covid-10 pandemic

FUNDING

This study was Funded by COVID-19 Humanitarian Response Project , Health and Nutrition Program , Save the Children International (SCI) , Hodiedah Office , Yemen Country . The fund is humanitarian response for diagnose and treatment , and control of COVID-19 pandemic in conflict area. The publication fee is not supported in this fund.

COMPETING INTERESTS

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

ACKNOWLEDGEMENTS

The authors would like to thank the supervisor and medical staff of the COVID-19 isolation department, Center of Tropical Medicine and Infectious Diseases (CTMID), Al-Thawara Public Hospital Authority, Hodeidah , Yemen for their fruitful assistance.

REFEENCES

1. Lai CC, Shih TP, Ko WC., Tang HJ., Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and corona virus disease-2019 (COVID-19): the epidemic and the challenges. *Int J Antimicrob Agents* . (2020) 55:3. 105924. doi: 10.1016/j.ijantimicag.2020.105924.
2. Gundlapally J, Kumar A, Kashyap A, Saxena AK, Sanyal A.. In Search of Novel Coronavirus 19 Therapeutic Targets. *Helix*. (2020) 10:02: doi: 10.29042/2020-10-2-01-08.
3. World Health Organization (WHO), Coronavirus disease 2019 (COVID-19) situation report – 52. (2020) https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200312-sitrep-52-covid-19.pdf?sfvrsn=e2bfc9c0_4 [Accessed March 12, 2020]
4. World Health Organization (WHO) , Coronavirus disease (COVID-19) pandemic. (2020). <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>
5. World Health Organization (WHO) The top 10 causes of death, 2020 . <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death> [Accessed December 19, 2020]
6. Riou J , and Althaus C L . Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. *Euro Surveill* . (2020) 25(4) doi: 10.2807/1560-7917.ES.2020.25.4.2000058.
7. Hao X , Cheng S, Wu D, Wu T, Lin X and Wang C . Reconstruction of the full transmission dynamics of COVID-19 in Wuhan *Nature* (2020) 584
8. Lipsitch M, Swerdlow DL, Finelli L. Defining the epidemiology of Covid-19—studies needed. *N Engl J Med*. (2020) 382:13. doi: 10.1056/NEJMp2002125
9. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. *The lancet Gastroenterology & hepatology*. (2020) 5(5). doi:[https://doi.org/10.1016/S2468-1253\(20\)30057-1](https://doi.org/10.1016/S2468-1253(20)30057-1)
10. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X., Guan L. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet*. (2020) 395:10229. doi:[https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)

11. Center of Diseases Control and Prevention (CDC) US. Symptoms of Coronavirus (2020) . <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html> [Accessed Feb. 22, 2021]
12. Li D, Chen Y, Liu H, Jia Y, Li F, Wang W, Wu J, Wan Z, Cao Y, Zeng R. Immune dysfunction leads to mortality and organ injury in patients with COVID-19 in China: insights from ERS-COVID-19 study. *Signal Transduct Target Ther.* (2020) 5:62. doi: 10.1038/s41392-020-0163-5
13. Du RH, Liang LR., Yang CQ., Wang W, Cao TZ, Li M, Guo GY., Du J, Zheng CL, Zhu Q, Hu M. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. *Eur Respir J.* (2020) 55:5. doi: 10.1183/13993003.00524-2020.
14. Pal R, Bhadada, SK. COVID-19 and non-communicable diseases. *Postgrad Med J.* (2020) 96:1137. doi: 10.1136/
15. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* (2020) 395:10223. doi :[https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5).
16. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, Fan Y, Zheng C. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *The Lancet Infectious Diseases.* (2020) 20:4. doi:[https://doi.org/10.1016/S1473-3099\(20\)30086-4](https://doi.org/10.1016/S1473-3099(20)30086-4)
17. Novel Coronavirus COVID-19". Yemen Supreme National Emergency Committee for Covid-19. Retrieved 9 December 2020.
18. Ghobari, Muhammad. "War-ravaged Yemen confirms first coronavirus case, braces for more". Reuters. Retrieved 10 April 2020.
19. CSO Statistical Year Book 2006; Ministry of Planning and International Cooperation: Sana'a, Republic of Yemen, 2007
20. CSO Statistical Year Book 2010; Ministry of Planning and International Cooperation: Sana'a, Republic of Yemen, 2011
21. Nasser A (Yemen Researcher, Middle East and North Africa Division). War and COVID-19 in Yemen , *Istituto Affari Internazionali* . (2020) [Accessed October 24, 2020] <https://www.hrw.org/news/2020/10/14/war-and-covid-19-yemen>
22. World Health Organization (WHO), WHO COVID-19: Case Definitions . (2020) file:///C:/Users/nt/Downloads/WHO-2019-nCoV-Surveillance_Case_Definition-2020.2-eng.pdf [Accessed December 16, 2020]
23. World Health Organization (WHO). Operation Consideration for Case Management of COVID - 19 Health Facility , (2020) https://apps.who.int/iris/bitstream/handle/10665/331492/WHO-2019-nCoV-HCF_operations-2020.1-eng.pdf?sequence=1&isAllowed=y [Accessed March 19, 2020]

24. Ministry of Public Health and Population (MOPHP), Therapeutic Sector , Administration of Service and Emergency , National Guideline for Case Management of Mild and Moderate at Home of Coronavirus Disease 2019 (COVID-19), (2020) .
25. Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. *Clin Chem Lab Med.* (2020) 25;58(7). doi: 10.1515/cclm-2020-0240
26. Prokop M, van Everdingen W, van Rees Vellinga T, Quarles van Ufford J, Stöger L, Beenen L, Geurts B, Gietema H, Krdzalic J, Schaefer-Prokop C, van Ginneken B, Brink M. CO-RADS - A categorical CT assessment scheme for patients with suspected COVID-19: definition and evaluation. (2020) 296:2 doi: 10.1148/radiol.2020201473
27. Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. *BMJ* (2020) 368. doi: 10.1136/bmj.m1198
28. Wenham C, Smith J, Morgan R. Gender and C-W Group. 2020. COVID-19: the gendered impacts of the outbreak. *The Lancet* . (2020) 395:10227. doi:https://doi.org/10.1016/S0140-6736(20)30526-2
29. Jin J, Bai P, HeW, Wu F, Liu WF, Han DM, Liu S, Yang JK. Gender differences in patients with COVID-19: Focus on severity and mortality. *Journal.* (2020) doi.org/10.3389/fpubh.2020.00152
30. Hall KS, Samari G, Garbers S, Casey SE, Diallo DD, Orcutt M, Moresky RT, Martinez ME, McGovern T. Centring sexual and reproductive health and justice in the global COVID-19 response. *The Lancet* . (2020) 395:10231. doi:https://doi.org/10.1016/S0140-6736(20)30801-1
31. Wenham C, Smith J, Morgan R. COVID-19: the gendered impacts of the outbreak. *The Lancet.* (2020) 395:10227. doi:https://doi.org/10.1016/S0140-6736(20)30526-2
32. Public Health England. Seasonal influenza vaccine uptake in GP patients: winter season 2018 to 2019. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/804889/Seasonal_influenza_vaccine_uptake_in_GP_patients_1819.pdf [Accessed May, 2019]
33. Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA* (2020) 323(14):1335 . doi: 10.1001/jama.2020.4344.
34. Guan W- jie, Ni Z- yi, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* (2020) 382:1708-1720. doi: 10.1056/NEJMoa2002032
35. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus- infected pneumonia in Wuhan, China. *JAMA.* (2020);323:11. 1061-1069. doi:10.1001/jama.2020.158
36. Chen X, Liao B, Cheng L, Peng X , Xu X , Li Y, Hu T , Li J, Zhou X, Ren B. The microbial coinfection in COVID-19. *Appl Microbiol Biotechnol.* (2020) 104:18:7777-7785. doi: 10.1007/s00253-020-10814-6.
37. Marina T, José-María GGa, François-XB, Sergey B, Delia G, Ilaria M, Luigi RC, Simon T, Giovanni Sotgiu, Giovanni BM . On tuberculosis and COVID-19 co-infection. *Eur Respir J.* (2020) 56:2: doi: 10.1183/13993003.02328-2020

38. Ajay M, Kamal KS, Amos L, George A . Tuberculosis and COVID-19 Co-infection: An Updated Review . *ACTA BIOMEDICA*. (2021) 92:1. doi: <https://doi.org/10.23750/abm.v92i1.10738>
39. Mirzaie H, Vahidi M, Shokoohi M, Darvishian M, Sharifi H, Sharafi H, Karamouzian M. COVID-19 among patients with hepatitis B or hepatitis C: A systematic review. (2020). doi: <https://doi.org/10.1101/2020.10.22.20216317> (In press)
40. Rui L, Li Z, Xiaoming C, Huan H, Cong L, Dong L, Andrew L, Guosheng G, Feng Z, Fang L, Yingan J, Chengliang Z, Yuchen X. Clinical characteristics of COVID-19 patients with hepatitis B virus infection — a retrospective study . *Liver International*. (2021) 00:1–11. doi: <https://doi.org/10.1111/liv.14774>
41. Al-Areeqi A, Alghalibi S , Yusuf Q, Al-Masrafi I , and Amod AL Kamarany M . Epidemiological Characteristic of Malaria Coinfected with Dengue Fever in Hodeidah, Yemen . *International Journal of Tropical Disease & Health* . (2020) 40 (3) , 2020 .
42. Giuseppe DN, Lorenzo DN, Claudia T , Vito M, Antonio C, Karen G H, Renato S . The Evolution of Covid-19 in Italy after the Spring of 2020: An Unpredicted Summer Respite Followed by a Second Wave. *Int J Environ Res Public Health*. . (2020) 17:23 doi: 10.3390/ijerph17238708.
43. Lam TT, Tang JW, Lai FY, Zaraket H, Dbaibo G, Bialasiewicz S, et al. . Comparative global epidemiology of influenza, respiratory syncytial and parainfluenza viruses, 2010–2015. *J Infect*. (2019) 79:373–82. 10.1016/j.jinf.2019.07.008
44. Sangshin P, Yeonjin L, Ian C M, Young JC. Global Seasonality of Human Coronaviruses: A Systematic Review *Open Forum Infectious Diseases*. (2020) doi: <https://doi.org/10.1093/ofid/ofaa443>
45. Peck K.R.. Early diagnosis and rapid isolation: response to COVID-19 outbreak in Korea. *Clin Microbiol Infect*. (2020) . 26(7): 805–807. . doi: 10.1016/j.cmi.2020.04.025
46. Joy Luba Lomole Waya, David Ameh, Joseph Lou K. Mogga, Wamala J.F and Olu O.O . COVID-19 case management strategies: what are the options for Africa? *Infectious Diseases of Poverty* (2021) 10:30 <https://doi.org/10.1186/s40249-021-00795-7>