Epidemiological Features of COVID - 19 in Hodeidah, Yemen

ABSTRACT

Background: Acute respiratory infection namely coronavirus disease 2019 (COVID -19) is a great public health problem in the world and causes(**something is missing here**) leading to morbidity and mortality in developing and developed countries.

Objectives: The research aims to study the epidemiological features of COVID-19 in Hodeidah , Yemen.

Methodology : 505 patients were diagnosed clinically according to case definition with COVID-19 (from 3 to 80 years old) and triaged into suspected, probable and confirmed in COVID- 19 Isolation Department , Center of Tropical Medicine and Infectious Diseases (CTMID) , AL Thawara Public Hospital Authority ,Hodeidah, Yemen from 1st June 2020 to 31st December 2020. Nasopharyngeal swabs for severe and critical cases were collected from patients and detected by Real Time - Polymerase Chain Reaction (RT-PCR) and admitted according to severity of disease.

Results: The results showed that 386/505 (76.43 %) of suspected cases and 70/505 (13.86 %) of probable cases were isolated and treated at home while a total of 49/505 (9.70 %) were confirmed and admitted in COVID-19 isolation department, where the males were more exposed to COVID-19 with (81.6%), 33 cases (67.3%) of old age (define which specific age range,) 65.3 % were chronic diseases where the most prevalent diabetic mellitus and diabetic

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mellitus associated with other (which other) chronic diseases chronic diseases were 18.36% and 16.32 % respectively, followed by 12.24 % of cardiac disorder and hypertension , 12.24percentate or of what of respiratory disorders, 4.08 % of cardiac diseases associated with respiratory disorder and 4.08 % of renal failure. On the other hand, 4.08 % of coinfection.(this sentence does not make sense). In addition, COVID -19 was not found through the whole year;(this could help if you mention how many months instead of seasons) however, higher frequency during the spring season 69.4% and lower frequency during the summer season 24.5% and autumn 6.1%.The case fatality rate (CFR %) of confirmed cases was 23 /49 (46.9 %) namely 30.6 % of death cases had chronic diseases,(it would help if specific chronic illness were mentioned)12.2 % had not any chronic diseases, and 2 % had coinfection. However 19/49 (82.6 %) of deaths ~~was~~ were over the age of 50 years.

Conclusion:The research concluded that, old age and chronic diseases may be contributing factors to excess morbidity and mortality among COVID-19 patients. Coinfections with other infections are concern.

Keywords: Epidemiological , COVID-19, Morbidity , Mortality , Risk Factor , Hodeidah, Yemen

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1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a respiratory disease that is caused by novel single-stranded positive sense RNA virus (nCoV-19) that was firstly isolated in December 2019 ~~when~~ which emerged in Wuhan, China [1,2], the resulting diseases so called COVID 19 which then emerged worldwide and caused mortality globally at the rate of 3.7% till the 12th of March 2020 when it was declared by WHO (in full) as a pandemic [3]. The emergence of COVID-19 expanded to 216 countries~~y~~ causing 1,153,176 deaths and 42,838,516 confirmed cases all over the world till October 24 , 2020 [4]. However, chronic pulmonary diseases and lower respiratory infections are two of the top ten global causes of morbidity and mortality[5]. Disease severity is ranging from mild non-fatal respiratory illness to more serious complications that may lead to death while associated with social determinants , risk factors , chronic diseases or other communicable diseases [6,7].

Mainly the most susceptible patients for mortality were those who experienced COVID-19 and a co-morbidity, with hypertension being the most common co-morbid followed by diabetes and coronary heart disease and older aged patients [8-12] . Clinical features of COVID-19 include lower respiratory tract

infection related symptoms mainly fever, dry cough and dyspnea as reported in the initial case series from Wuhan, China.

In addition, headache, dizziness, weakness, vomiting and diarrhea were also observed. [13-15] In Yemen the first case was registered in April 10,2020 in Hadramout then emerged to other parts of the country. A lot of morbidity and mortality were reported in Yemen, and the main question ~~about~~ is what are the epidemiological features of COVID -19 in Hodeidah , Yemen ? Hodeidah governorate at the Western part of Yemen was exposed to COVID-19 pandemic like other governorates in Yemen, adding to the current chronic problems. Hodeidah is facing complex spectrum of determinants of health; including poverty, illiteracy, food insecurity, malnutrition and multiple epidemics as well as humanitarian crises resulting from the ongoing armed conflicts since 2015. No study ~~till now~~so far has documented the COVID-19 pandemic process in Hodeidah especially on morbidity and mortality. The aim of this research was~~is~~ to describe the epidemiological features of COVID – 19 in Hodeidah , 2020.

2. METHODOLOGY

2.1. Study area

Hodeidah Governorate is located on the western ,flat and narrow coastal plain between the foothills of the highlands and the red sea.

Hodeidah is the fourth largest Governorate in Yemen in the term of population which reaches to about (2157552) .The area is 13500 km2 involves 26 Districts, and a lot of islands in the red sea. The weather is typically hot and humid and the temperatures sometimes exceeding 38 to 40° C. During the rest of the year temperature range between 27-35° C. This region is known to have high conflict area since the 26th of March 2015. Hodeidah also is considered as an endemic zone for numerous infectious diseases [16-18].

2.2. Study Design

~~This study is~~ This was a cross sectional study that targeted ~~.~~ ~~The~~ patients who were admitted in 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

There were 505 cases (age ranged from 3 years to 80 years), diagnosed in COVID-19 emergency department according to case definition. The cases were triaged into suspected , probable and confirmed. The severity of patients were assessed based on radiological and hematological findings. ~~m~~ild and moderate cases were isolated and treated at home . Severe and critical cases were

admitted to COVID -19 Isolation Department, Center of Tropical Medicine and Infectious Diseases (CTMID), AL Thawara Public Hospital Authority of Hodeidah, Yemen. Nasopharyngeal swabs were collected from severe and critical patients only and detected by Real Time - Polymerase Chain Reaction (RT-PCR) [19-22].

2.4. Data collection and analysis

This study was conducted on the epidemiological features of COVID - 19 patients where the COVID-19 was the major cause of morbidity and mortality.The independent variables studied were age, gender, co-morbidity , co-infection , seasons , and residence . Data was collected ,checked and displayed i_ na nExcel format .Then the data was analyzed using tables , graphs, median, range, frequency and percentages were the main descriptive tools. State how many days/weeks or months was the data collected,who collected the data, whether data was retrieved from records or otherwise, there is also need for consenting process to be stated.

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3. RESULTS

3.1. Suspected – probable and confirmed cases

~~On the other hand,~~ A~~a~~ total of 49 confirmed cases (9.70%) of 505 patients were admitted as inpatients for intravenous support therapy in isolation department, while 386 suspected cases and 70

probable cases (76.43% ; and 13.86 %) respectively were isolated as outpatient for receiving oral support therapy at home (Table 1) .

Table 1. Suspected – probable and confirmed cases according to screening , triage and admitted criteria (N :505)

	Suspected cases *		**Probable cases** **		**Confirmed cases****		**Total**		
	Male	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Total**
<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 and treated at home
- **: Probable cases were diagnosed according to case definition, radiological and hematological finding . 16 cases were received and died in triage department namely 11 cases of males and 5 cases of females ., all cases **were** over 50 years old .
- ***: Confirmed cases were confirmed according to molecular biological method namely RT-PCR and radiological and hematological finding assessed the severalty of cases and admitted in isolation center of COVID-19 , AL Thawara Public Hospital Authority , Hodeidah, Yemen

3.2. Socio - demographic features

COVID – 19 infection was detected in 9.70 % using RT-PCR technique. The general characteristics of patients were shown in Table 1 and 2. COVID – 19 infection was represented in the males as 79.59 .5% while in the females it was represented as 20.41 %. However, this difference was statistically significant (P = 0.00). The age range of patients was from 3 to 80 years old and the median age of subjects was 51 year. The higher frequency of COVID – 19 infection was in elderly between 50 and 80 years (67.34 % % (P = 0.00) and the lower frequency was in children and young between 0 and 15 years old and 16 – 29 years old respectively (6.12 %; 10.40 %) (Table 2). The relationship between the COVID – 19 infection and area of residence was not found, regarding the area of residence, only 44.89 % of COVID – 19 infection was from the urban whereas 55.10 % were from rural area. However, this difference was not statistically significant (*P* = 0.47) (Table 2).

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

Variables	**Number(n)**	Ratio (%)	X^2	*P* – value
Gender				
Male	39	79.59		
Female	10	20.41	17.16	0.00
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

In addition, the clinical findings were diagnosed and recorded. 30 cases of fever , 14 cases of pharyngitis , 20 cases of cough , 3 cases of headache , 13 cases of chest pain , 16 cases of arthritis , and 42 cases of difficult breathing . Those were the main symptoms (Table 3). All cases had Acute Respiratory Distress Syndrome (ARDS) for a period of a week before hospitalization.

Table 3. Clinical symptoms data of COVID-19 patients in Hodeidah , Yemen (N = 4**9**)

Variables	Number(n)	Ratio (%)
Fever	30	61.2
Pharyngitis	14	28.6

Cough	20	40.8
Headache	3	6.12
Chest pain	13	26.5
Difficult in breath	42	85.7

3.4. Effect of co-morbidity and co-infection on COVID 19 morbidity

Morbidity rate was high in patients that experienced COVID-19 in comorbidity, namely 32 cases (65.30 %) , 9 cases (18.36%) of diabetic mellitus and 8 cases (16.32 %) of diabetic mellitus with chronic diseases ,followed by cardiac disorder and hypertension 6 cases (12.24 %) . Also 6 cases (12.24 %) of respiratory disorder (bronchial asthma). 2 cases (4.08 %) of heart disease with respiratory disorder (bronchial asthma), and 2 cases (4.08 %) of renal failure . In addition , 2 cases (4.08 %) of co- infection namely hepatitis C and tuberculosis . On the other hand , 14 cases (28.57 %) were infected without any chronic diseases .

3.5. Effect of co-morbidity and co-infection on COVID 19 mortality

Mortality rate was high in patients that experienced COVID-19 in comorbidity namely 16 cases (69.56 %) , 3 cases (13.04 %) of diabetic mellitus , 4 cases (17.39 %) of diabetic mellitus with cardiovascular diseases ,followed by cardiac disorder and hypertension 3 cases (13.04 %). Also , 4 cases (17.39 %) of asthma disorder. 1 case (4.34 %) of heart disease with asthma ,

and 1 case (4.34%) of renal failure . In addition , 1 case (4.34 %) of co- infection namely hepatitis C. On the other hand , 6 cases (26.08 %) died without having any chronic diseases .

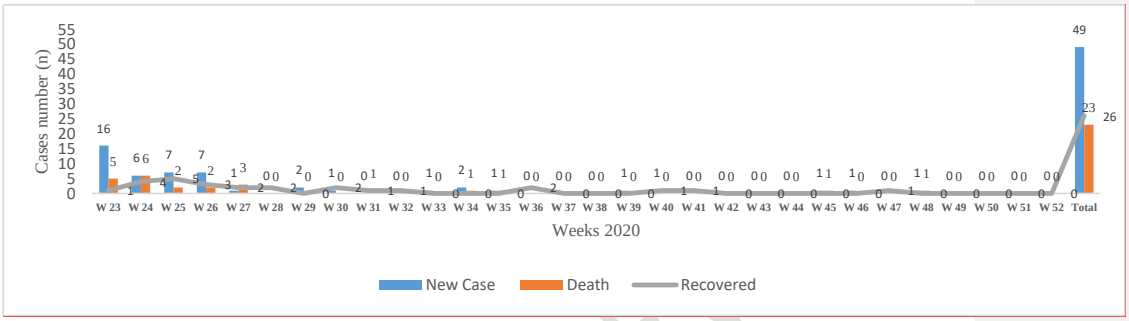

Figure 1. Epidemiological surveillance of COVID -19 in Hodeidah , Yemen

Table 4 . Effect of co-morbidity and co-infection on COVID 19 morbidity and mortality (N:49)

Risk factors	Recovery		Death		Total	
	n	%	n	%	N	%
Comorbidity	18	36.73	16	32.65	32	65.30
Co-infection	1	2.04	1	2.04	2	4.08
Non	8	16.32	6	12.24	14	28.57
Total	26	53.06	23	46.93	49	100

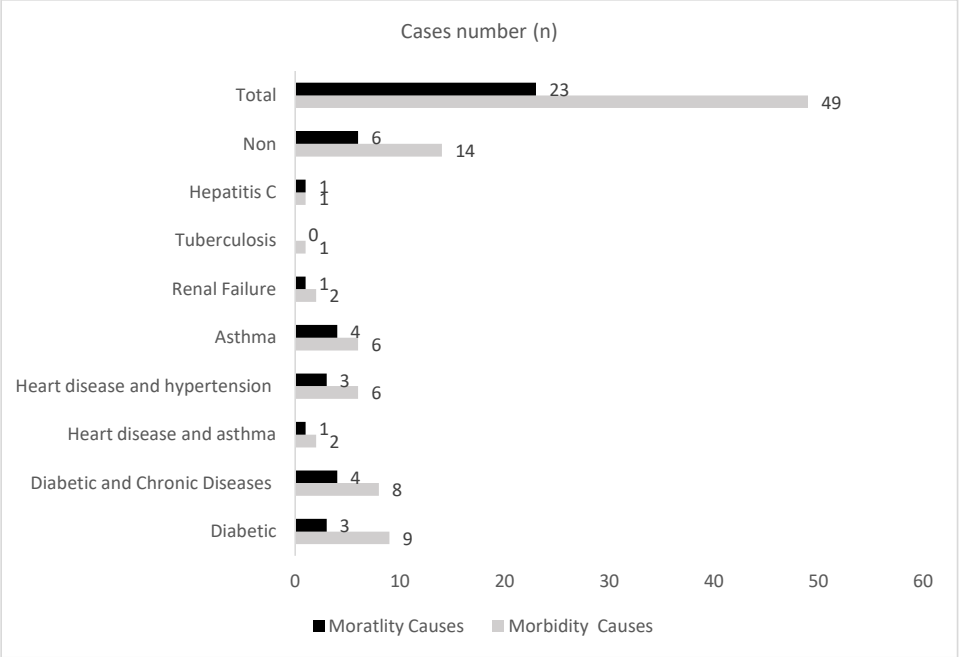

Figure 2. Risk factors associated with COVID – 19 morbidity and mortality (N:49)

3.6. Recovery and death of severe case versus critical cases

Mortality rate was very high in critical cases namely 22 /27 Cases (81.48 %) while the mortality rate of severe cases was 1 case /20 case (5 %) (Figure 3).

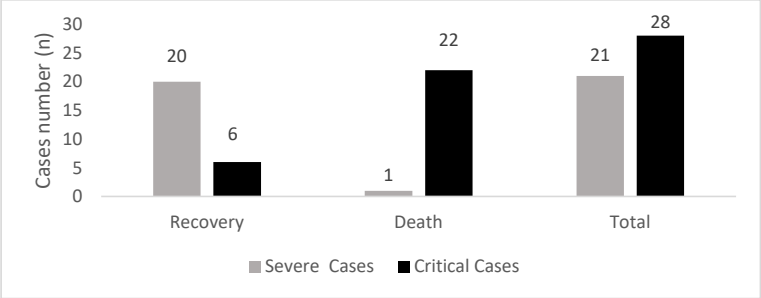

Figure 3. Morality and recovery of COVID-19 namely severe and critical cases in Hodeidah , Yemen (N:49)

3.7. Seasonality of COVID -19

~~As for seasonal distribution, COVID -19 infection was not found through the whole year.~~this sentence is confusing. However, spring season was significantly associated with COVID -19 infection (*P* = 0.0001) ; however, higher frequency during the spring season (40 cases, 81.16%, and P = 0.0001) and lower frequency during the summer , autumn and winter seasons respectively (4 cases , 8.15 ; 5 cases , 10.20 % ; and 0 cases, 0%) (Table 5). In addition, COVID -19 infection exhibited peaks in the month of June ~~month~~ (Figure 4).

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		
Summer	4	08.16	84.95	0.0001
Autumn	5	10.20		
Winter	0	0		

Total	49	100

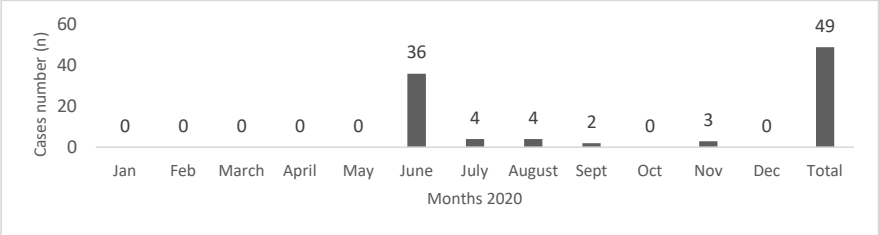

Figure 4. Monthly seasonality of COVID-19 among people of Hodeidah , Yemen (N:49)

4. DISCUSSION

~~Since~~ As COVID-19 pandemic accelerates, governments are warning people at high risk to be particularly stringent in observing social distancing measures because if they become ill they are more likely to need critical care including ventilation, to recovery or die [24]. However, in this study, patients access late to hospital with a serious critical condition. Males were more susceptible to develop morbidity and mortality and this is inconsistence with

other studies in China and Italy [25-27] and it may be due to sex-based immunological or gendered differences, such as patterns and prevalence of smoking[24, 28-30].

The elderly patients are at greater risk of developing COVID-19 especially those ~~certainly~~ over 60 years old, this was according to their underlying health condition with immune response. Infection co-morbidities with COVID-19 increases the risk of mortality five times in older subjects [24,29]. Most commonly reported co-morbidities with COVID-19 and which pose~~s~~ a life threat are diabetes, hypertension, cardiovascular disease and chronic obstructive pulmonary disease, this was similar to what was found in this study due to underlying immunodeficiency, which ~~may~~ made those patients more susceptible to COVID-19 complications and fatality [31-33,12].

On the other hand , beyond the pathogenesis of COVID-19 , microbial coinfection plays an important role in the occurrence and development of SARS-CoV-2 infection by raising the difficulties of diagnosis, treatment, prognosis of COVID-19, and even increasing the disease symptom and mortality. , ~~on other~~this may mean~~s~~ , the coinfection between different microorganisms and COVID-19 is a serious problem in the COVID-19 pandemic.

However, there are few reports about COVID-19 coinfects with bacteria, fungus, and other viruses [34].

Our study reported TB – COVID-19 coinfection namely 1 case (1/49) 2.04 % , European respiratory journal reported " in the absence of previous cohorts and scientific information on TB - COVID-19 co-infection, they have described the timing of diagnosis of the two diseases, observing that one third had COVID-19 diagnosed prior to TB and 18% were diagnosed simultaneously [35] " . There is limited literature on the occurrence of COVID 19 in patients with TB. 8 studies reported a total of 80 patients with this coinfection. These patients were reported from ten different countries, with Italy reporting the largest number of cases. In all 8 studies, COVID 19 was treated as per the local protocol. Mortality was reported in more than 10% of patients. Mortality was higher in elderly patients (> 70 years) and amongst patient with multiple medical comorbidities [36]. Our study reported 1 case hepatitis C (1/49) 2.04 % and in Iran , death proportion was 6% among COVID-19-HBV and 13% among COVID-19-HCV co-infected patients. Also , among COVID-19 patients, 34.1% and 76.2% reported at least one comorbidity besides HBV and HCV infections, mainly hypertension and diabetes mellitus type 2 [37]. Other study , chronic HBV infection did not predispose COVID-19 patients to more severe outcomes, their data suggest COVID-19

and HBV coinfection 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 SARS-CoV-2 and HBV coinfected patients [38].

Finally, our study reported the maximum peak of infection in spring , in Italy , the coronavirus (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 [39]. Other previous studies reported that most viral respiratory infections tend to follow seasonal patterns with high incidence during winter [40]. Also previous study found the largest global peak of COVID-19 during the winter season, with the highest rate of positivity among children [41].

5. CONCLUSION

Old age and co-morbidity with non-communicable diseases mainly diabetes mellitus , hypertension , and heart diseases may be contributing factors to excess illness and deaths among COVID 19 patients. Co-infections with other viral infections like tuberculosis and hepatitis is of high concern in Hodeidah, Yemen.

ETHICAL APPROVAL

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

CONSENT

Written informed consent for participation was required for this study.How was this done considering critical cases

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): 01-08 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. Lipsitch M, Swerdlow DL, Finelli L. Defining the epidemiology of Covid-19—studies needed. *N Engl J Med*. 2020, 382 (13): 1194-1196 doi: 10.1056/NEJMp2002125

7. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. *The lancet Gastroenterology & hepatology*. 2020, 5(5):428-430 doi:https://doi.org/10.1016/S2468-1253(20)30057-1

8. 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) 054-1062 . doi:https://doi.org/10.1016/S0140-6736(20)30566-3

9. Center of Diseases Control and Prevention (CDC) US. Symptoms of Coronavirus (2020) . https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html [Accessed Fab. 22, 2021]

10. 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):1 - 3 doi: 10.1038/s41392-020-0163-5

11. 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) : 2000524 . doi: 10.1183/13993003.00524-2020.

12. Pal R, Bhadada, SK. COVID-19 and non-communicable diseases. *Postgrad Med J*. 2020, 96 (1137): 429-430 doi: 10.1136/

13. 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) : 497-506. . doi :https://doi.org/10.1016/S0140-6736(20)30183-5.

14. 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) : 425-434 . doi:https://doi.org/10.1016/S1473-3099(20)30086-4

15. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. *Clin Immunol.*. 2020, 20 (108427) : 1 – 7 doi: 10.1016/j.clim.2020.108427

16. CSO Statistical Year Book 2004; Ministry of Planning and International Cooperation: Sana'a, Republic of Yemen, 2005

17. CSO Statistical Year Book 2006; Ministry of Planning and International Cooperation: Sana'a, Republic of Yemen, 2007

18. CSO Statistical Year Book 2010; Ministry of Planning and International Cooperation: Sana'a, Republic of Yemen, 2011

19. 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]

20. 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]

21. 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) .

22. 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, 58(7): 1063–1069 doi: 10.1515/cclm-2020-0240

23. 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. *Radiology*. 2020, 296(2): E97–E104 doi: 10.1148/radiol.2020201473

24. Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. *BMJ* .2020, 368 (1198): 1 - 8 doi: 10.1136/bmj.m1198

25. 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) :846-848 . doi:https://doi.org/10.1016/S0140-6736(20)30526-2

26. 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, 8(152):1 – 6 doi.org/10.3389/fpubh.2020.00152

27. 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): 1175–1177 doi:https://doi.org/10.1016/S0140-6736(20)30801-1

28. Wenham C, Smith J, Morgan R. COVID-19: the gendered impacts of the outbreak. *The Lancet*. 2020. 395 (10227): 846-848. doi:https://doi.org/10.1016/S0140-6736(20)30526-2

29. 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]

30. Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA* . 2020, 323 (14):1335 . doi: 10.1001/jama.2020.4344.

31. Guan W- jie, Ni Z- yi, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* 2020, 382 (18) :1708-1720. doi: 10.1056/NEJMoa2002032

32. 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

33. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta- analysis. *Int J Infect Dis* . 2020 ; 94:91-95. doi: 10.1016/j.ijid.2020.03.017

34. Chen X, Liao B, Cheng L, Peng X , Xu X , Li Y, Hu T , Li J, Zhou X, Ren B. *Appl Microbiol Biotechnol.* 2020, 104 (18) :7777-7785. doi: 10.1007/s00253-020-10814-6.

35. 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): 2002328 doi: 10.1183/13993003.02328-2020

36. Ajay M, Kamal KS, Amos L, George A . Tuberculosis and COVID-19 Co-infection: An Updated Review . *ACTA BIOMEDICA*. 2021, 92 (1): e2021025 doi: https://doi.org/10.23750/abm.v92i1.10738

37. 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)

38. 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, 41 (4): 720-730 00:1–11.doi: https://doi.org/10.1111/liv.14774

39. 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): 8708 doi: 10.3390/ijerph17238708.

40. 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(4):373-382 . 10.1016/j.jinf.2019.07.008

41. Sangshin P, Yeonjin L, Ian C M, Young JC. Global Seasonality of Human Coronaviruses: A Systematic Review *Open Forum Infectious Diseases*.. 2020, 7(11): ofaa443 doi: https://doi.org/10.1093/ofid/ofaa443