Outbreak Investigation: First Ten COVID – 19 Infection Related Deaths in Hodeidah, Yemen

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Authors' contributions

This work was carried out in collaboration among all authors. Author MAAK wrote, revised and edited the final manuscript and responsible for summarizing all epidemiological and clinical data. Author IA contributed to data analysis and writing of manuscript. Author ABG contributed to data analysis and revision of manuscript. Authors KS and AM collected the epidemiological and clinical data. Authors AZ and EA supported outbreak investigation. All authors read and approved the final manuscript.

Short Communication

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ABSTRACT

Background: Many acute respiratory syndrome coronavirus 2 (SARS-CoV-2) related deaths were reported in Yemen. The question is about what risk factors contribute to this excess death. Hodeidah governorate in the Western part of Yemen is exposed to the COVID-19 pandemic like other governorates in Yemen, adding to the current chronic problems. No study till now documented the SARS-CoV-2 pandemic process in Hodeidah, Yemen, especially deaths.

Objective: The aim of this short report is to explore more data about the first ten SARS-CoV-2-related deaths in Hodeidah. Yemen.

Methods: An outbreak investigation was carried out directly with patients before death and their families based on world health organization (WHO) guideline and Center for Disease Control and Prevention -US (CDC-US) guideline. On the other hand, the medical reports of patients were investigated in the triage area of the Center of Tropical Medicine and Infectious Diseases (CTMID), AL-Thawrah Public Hospital Authority, Hodeidah, Yemen from 24th to 31st May 2020.

Results: The first ten death patients at the same time were investigated, the age ranging from 25-65 years with a median age of 57 years, seven deaths (70%) were at age over 50 years while males are more exposed to deaths (eight cases; 80%). The deaths are more in residents of urban (eight cases; 80%) than in rural areas (20%). Co-infections with other communicable diseases were reported in 3 dead patients (30%); tuberculosis, dengue, and hepatitis B (HVB). While six died patients (60%) had non-communicable diseases namely diabetes mellitus, heart disease, hypertension, chronic asthma, and chronic renal failure uncontrolled. One death (10%) of medication error in the private sector (non–isolation center facilities ; sub-standard management)

Conclusion: Old age and co-morbidity with non-communicable diseases may be contributing factors to excess deaths among SARS-CoV-2 patients. Co-infections with other infections like dengue is of high concern in Hodeidah, Yemen. The post-epidemiological investigation, the control and prevention measures were implemented by local authorities in collaboration with the private sector and non-governmental organizations namely re-habitation of SARS-CoV-2 isolation centers to reduce the mortality rate, also different practices and knowledge to reduce the morbidity rate.

1. INTRODUCTION

Acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a respiratory disease that is caused by a novel single-stranded positive-sense RNA virus (nCoV-19) that was first isolated on 31 December 2019 when emerged in Wuhan, Hubei Province, China [1,2]. The resulting disease so called SARS-CoV-2 then emerged worldwide and caused mortality globally at the rate of 3.7% till the 12th of March 2020 when declared by the World Health Organization (WHO) as a pandemic [3]. The emergence of SARS-CoV-2 expanded to 216 countries causing 356,254 deaths and 5,657,529 confirmed cases all over the world till May 29, 2020 [4]. However, chronic pulmonary diseases and lower respiratory infections are two of the top ten global causes of death [5]. Disease severity is ranging from mild non-fatal respiratory illness to more serious complications that may lead to death while associated with chronic diseases or other communicable diseases [6,7]. Mainly the more susceptible patients for mortality were those who experienced SARS-CoV-2 and a co-morbidity, with diabetes and hypertension being the most common co-morbid followed by coronary heart disease and older aged patients [8-12]. Clinical features of SARS-CoV-2 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 on April 10, 2020 in Hadhramout then emerged to other parts of the country [16-17]. Many of deaths were reported in Yemen raising the question about what risk factors contributed to this excess death. No study till now documented the SARS-CoV-2 pandemic process in Hodeidah, Yemen especially deaths. Therefore , the aim of this short communication is to explore more data about the first ten SARS-CoV-2 related deaths in Hodeidah , Yemen in May 2020.

2. MATERIALS AND METHODS

2.1 Study Area

Hodeidah governorate in the Western part of Yemen is exposed to severe acute respiratory

infection (SARI) like other governorates in Yemen, adding to the current chronic problems. 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 ongoing armed conflicts since 2015 [18].

2.2 Outbreak Investigation

An outbreak investigation was carried out directly with patients before death and their families based on world health organization (WHO) guideline and Center for Disease Control and Prevention -US (CDC-US) guideline. On the other hand, the medical reports of patients. The steps listed were presented in conceptual order; in practice, however, ten steps may be done at the same time:

1) **Prepare for field work:** The team included professors and consultants in epidemiology, pharmacology of infectious diseases, radiology, internal medicines. Also specialists in public health and microbiologist (virologist). The appropriate supplies and equipment were prepared to carry out the investigation before departing for the field.

2) **Establish the existence of an outbreak:** From 24th May to 31st May 2021. Patients with SARI in Hodeidah, Yemen were investigated.

3) **Verify the diagnosis:** Reference hospital supported the clinical, radiological, hematological and biochemical finding. Also two laboratories namely CTMID laboratory in Hodeidah and the National Center of Public Health Laboratories (NCPHL) in Sana'a confirmed the cases. On the other mean, the nasopharyngeal swabs were collected from cases and confirmed by Real-Time - Polymerase Chain Reaction (RT-PCR).

4) **Construct a working case definition:** National case definition that was extracted from WHO guidelines and used to screen and triage the cases epidemiologically (suspected, probable and confirmed) and clinically (mild, moderate, severe and critical cases).

5) **Find cases systematically and record information:** The general information (name, address, and telephone number. Also, the demographic information (age, sex, residence). The clinical information (symptoms, signs, date of onset, duration of illness and whether hospitalization or death occurred). Risk factors information (specific disease and other infection). In addition, other information (source of the report, usually a physician, clinic, hospital, or laboratory) was reported.

6) **Perform descriptive epidemiology:** The data were summarized to provide a comprehensive characterization of the outbreak - trends over time, geographic distribution (place), and the populations (persons) affected by the disease and at risk for the disease. The etiological, source, and modes of transmission were hypotheses. Data after being collected were checked for completeness, entered into Excel format then analyzed using tables, graphs, average, median, ranges, frequencies and percentages were the main descriptive tools.

7) **Evaluate hypotheses epidemiologically:** The descriptive study (case series) was chosen in this analysis.

8) **Implement control and prevention measures:** The control and prevention measures were implemented. CTMID continued to monitor. COVID -19 isolation department was built.

9) **Communicate findings:** Oral and written reports were presented for local authorities namely AL Thawrah Public Hospital of Hodeidah, Epidemiological Surveillance and Control Diseases Administration - Office of Public Health and Population. Also for the Governorate of Hodeidah, Yemen and non-governmental organizations.

10) **Initiate or maintain surveillance:** The surveillance was implemented namely active and passive [19-21].

3. RESULTS

3.1 Socio-demographic Factors

During the study period, the analysis of first 10 dead patients in the same time was reported at the triage area of CTMID, AL-Thawrah Public Hospital Authority, Hodeidah, Yemen. All cases had Acute Respiratory Distress Syndrome (ARDS) for a period of two weeks before hospitalization. All the ten deaths were confirmed having SARS-CoV-2 infection by using the RT-PCR technique. The general characteristics of patients were shown in Table 1, their age ranging was from 25-65 years with a median age of 57 years, seven deaths (70%)

were at age over 50 years while males were more exposed to eight cases (80%) and deaths were more in residents of urban (eight cases; 80%) than rural areas (two cases; 20%) (Table 1).

Table 1. General socio-demographic data of COVID-19 death patients in Hodeidah, Yemen (N =10)

Variables	Number(n)	Ratio (%)
Gender		
Male	8	80
Female	2	20
Age		
<15	0	0
15-29	2	20
30 -49	1	10
50-59	3	30
60+	4	40
Residency		
Urban	8	80
Rural	2	20

Note: 50 patients were received in triage area of CTMID from 24th to 31st May, 2020. and 29 cases were died namely case fatality rate (CFR) was 29/50 cases (58%). The first ten death in the same time (the same day) were confirmed based on RT-PCR and the causes of death were investigated (Table 1). Other cases were confirmed epidemiologically (epidemiologically linked case: a case in which the patient has/has had contact with one or more persons who have/had the disease, and transmission of the agent by the usual modes of transmission is plausible. A case may be considered epidemiologically linked to a laboratory-confirmed case if at least one case in the chain of transmission is laboratory confirmed). On the other hand, the males (40 cases; 80%) were significantly ($X^2 = 18$; $p = 0.0002$) overrepresented in this group compared with females (10 cases; 20%) and the age range of patients was from 19-90 years old and the median age of subjects was 60 years. Also, we observed a statistically higher frequency of SARS-CoV-2 infection was 37 cases (82%) in older patients from 50 – 90 years old, and the lowest frequency was 13 cases (26%) in adult from 15 – 49 years old ($X^2 = 11.52$; $p = 0.00069$). In addition, regarding the area of residence, only 40 cases (80%) of COVID -19 infection were from the urban area; whereas 10 cases (20%) were from rural area. However, this difference statistically significant ($X^2 = 18$; $p = 0.0002$). Finally, as for seasonal distribution, the first cases of SARS-CoV-2 infection were detected in the spring season, May 2020

Table 2. Clinical, radiological, hematological and biochemical finding of COVID-19 death patients in Hodeidah, Yemen (N = 10)

| Criteria	Finding
Clinical	The most common clinical symptom observed in the patients with SARS-CoV-2 was difficulty breathing and hypoxia less than 75%, followed by fever, arthritis, cough, pharyngitis and chest pain. All cases had ARDS for a period of a two weeks to three weeks before hospitalization.
Radiological	2 cases (20%) of CO-RAD 4 and 8 cases (80%) of CO-RAD 5. The most patterns were 60% of ground glass opacifications (GGO), bilateral involvement, multi-lobar involvement, 40% of consolidation pattern. The lung involvement of death patients mor than 60%.
Hematological	White blood cells (WBCs) were $20 ± 5$ ($\times 10^9$/L) (leukocytosis), lymphocytes decreased (lymphopenia) with SARS-CoV-2 infection to 2% with average $5±3\%$. In addition, neutrophils increased (neutrophilia) to 98% with average $95±3\%$. On the other hand, the results showed increased in Neutrophils to Lymphocytes Ratio (NLR) that was 98/2 (49%).
Biochemical	The major changing in biochemical parameters was hyperglycemia (6 cases ; 60%) with HbA1C more than 7% (9-11%) and blood glucose more than 180 mg/dl (350 mg/dl – 550 mg/dl), hypoalbuminemia (80%) with albumin less than 3.5 g /dl (2.5 -1.5 g/dl) ; high level in creatinine more than 1 mg/dl (1 case ; 10% with 7 mg/dl of creatinine); C-Reactive Protein (CRP) more than 6 mg/L(43 mg/L to 97 mg/L).
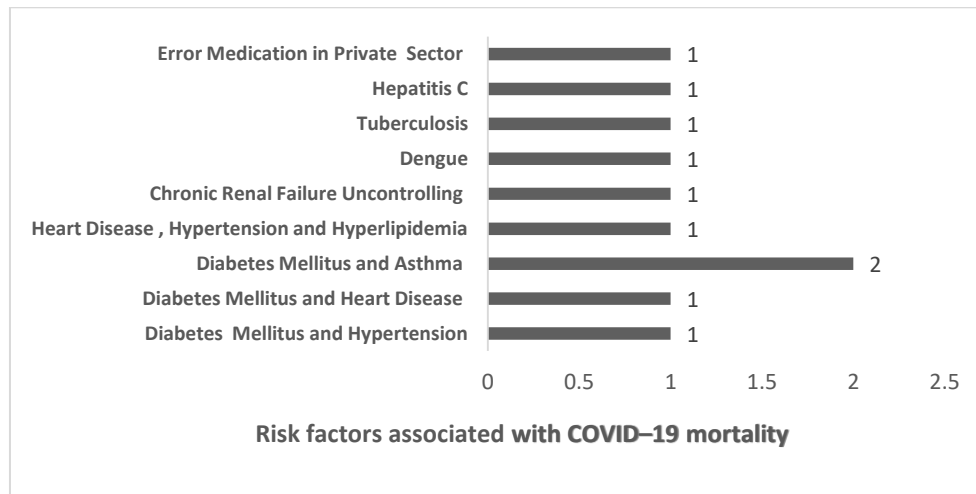
Fig. 1. Risk factors associated with SARS-CoV-2 mortality (N: 10)

3.2 Clinical, Radiological, Hematological and Biochemical Finding

The most clinical, radiological, hematological, and biochemical findings were summarized in Table 2. Clinically; the ideal clinical findings were present such as fever, dry cough, chest pain, difficulty in breathing (oxygen saturation < 75%), acute respiratory distress syndrome (ARDS), lymphopenia, and lung involvement.

3.3 Co-morbidity and Co-infection in SARS-CoV-2 Mortality

Mortality rate was high in patients that experienced SARS-CoV-2 in comorbidity with other infections as three cases (30%), mainly one case (10%) with tuberculosis, one case (10%) with dengue and one case (10%) with HBV; moreover, six cases (60%) of comorbidity with non-communicable diseases namely one case (10%) with chronic asthma, one case (10%) with chronic asthma and diabetes, two cases (20%) with heart disorders, hyperlipidemia, hypertension, and diabetes, one case (10%) with chronic renal failure uncontrolled. Finally, one case (10%) of medication error in private sector (sub-standard management).

4. DISCUSSION

Since SARS-CoV-2 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, and to die [22]. However, in this study, patients access late to hospital with a serious critical condition. Males were more susceptible to developing death severity [23] and it may due to sex-based immunological or gendered differences, such as patterns and prevalence of smoking [24]. Elderly patients are at greater risk of developing SARS-CoV-2 certainly upper than 60 years old, this was according to their underlying health condition with immune response. Krishnan et al reported that mortality from SARS-CoV-2 showed a strong relationship with age and pre-existing medical conditions, as does mortality from other causes. Older age was more strongly associated with COVID-19 death than non- SARS-CoV-2 death, as was male sex, deprivation, obesity, and some comorbidities [25]. Infection co-morbidities with SARS-CoV-2 increase the risk of mortality five times in older subjects [26]. The most commonly reported co-morbidities with SARS-CoV-2 that pose 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 make those patients more susceptible to SARS-CoV-2 complications and fatality [27]. Damien et al reported the causes of death that were categorized in four subgroups: (i) refractory respiratory failure, (ii) shock with multiorgan failure, (iii) cardiac death including proven pulmonary embolism (proximal thrombus on CT-pulmonary angiography with acute cor pulmonale on echocardiography and vasopressor requirement) and unexpected cardiac arrest (neither prior oxygen desaturation nor circulatory failure) and (iv) neurological death (ischemic/hemorrhagic stroke with brain herniation) [28].

AL Kamarany et al reported 505 cases in the first wave (June – December 2020) of SARS-CoV-2 in Hodeidah that where 9.7% needed admission to an intensive care unit (ICU) with ARDS and males were more exposed to COVID-19 namely 81.63%, 67.3% of old age. Their study reported 65.3% of ICU had chronic diseases where the most prevalent were diabetes mellitus and diabetes mellitus associated with other chronic diseases. AL Kamarany et al concluded that, old age, chronic diseases and co-infection were factors that contributed to excess morbidity and mortality among COVID-19 patients and the mortality rate was high overall, with 46.93% with severe and critical COVID19 deaths. On the other hand, radiologically, the most patterns were 85.71% of GGO, 81.63% of bilateral involvement, 83.67% of multi-lobar involvement, 75,51% of peripheral distribution, 30.61% of consolidation pattern and 6.12% of crazy paving pattern. On the other hand, in the youngest patients less than 50 year, 79% had GGO, and 21% had lung consolidations, while in the patients over 50 year, GGO were presented in 56% and consolidations in 44%. In addition, the lung involvement range of patients was from 40 to 95% and the median was 60%. The lung involvement was represented in the patients more than 50 year as 60 – 95% while in the patients less than 50 years was represented as 40 – 55%. The lung involvement of death patients was 85 to 95% of non - chronic diseases and 60 to 70% of comorbidity and coinfection [29-31]. Based on hematological parameters, the lymphopenia has good predictive values on severity and mortality [32].

Furthermore, this study was able to identify of co-infection between SARS-CoV-2 and dengue, the importance of this result is of high concern especially the study setting (Hodeidah) is a known place for vector – borne diseases (dengue, malaria, chikungunya and west Nile virus) endemicity in Yemen [33-38].

In most epidemiological investigations, the primary goal is control of the outbreak and prevention of additional cases. Indeed, although implementing control and prevention measures was listed after epidemiological analysis of the first 10 death related SARS-CoV-2, the local authorities CTMID in Al-Thawra Public Hospital Authority of Hodeidah,, Ministry of Public Health and Population (MOPH) first responsibility is to protect the public's health in collaboration with the private sector (Hayel Saeed Anem Companies – Hodeidah Sector), and non - governmental organizations (Save the Children International– Hodeidah Office , Yemen Country intervened in humanities emergency response project: re-habitation of SARS-CoV-2 isolation center with medical equipment for cases management and to reduce the mortality rate in Hodeidah, Yemen. On the other hand , the major recommendations of control and prevention measures in SARS-CoV-2 infection to reduce the morbidity rate that were listed in different media : i) wash your hands frequently ; ii) avoid touching your eyes , mouth and nose ; iii) cover your cough with the bend of your elbow or tissue ; iv) avoid crowded places; v) stay at home if you feel unwell even with a slight fever and cough. vi) if you have a fever , cough , and difficulty breathing, seek medical care early – but call by phone first; vii) stay away of the latest information from Ministry of Public Health and Population (MOPH) [39].

The practices control and prevention activities should be implemented as early as possible [21] but the problems with Yemen's emergency medical services are weak: the healthcare system is under-funded and under-resourced overall. In a country with scarce budget available, few resources, and poorly compensated emergency medicine staff and physicians, a depleted workforce due to mass outward migration of qualified professionals is somewhat inevitable. Systematic revisions to the health care system, rebuilding primary health care facilities, guaranteed universal insurance plans, a greater emphasis toward preventive medicine and continued training in emergency medicine, are needed to help overcome these challenges [40]. AL Thawrah Public Hospital Authority, the reference public health facility in Hodeidah city, Yemen that is still operational but threatened by fighting and rapidly moving frontlines. Airstrikes, ground attacks, military occupation and assaults on health workers are all common occurrences in Yemen. The staff who work in them are poorly equipped and underpaid: it is hardly surprising many migrate to escape such a challenging working environment. As efforts are made to improve Yemen's healthcare system, emergency care must be part of such discussions [41,40].

5. CONCLUSION

Old age and co-morbidity with non-communicable diseases may be contributing factors to excess deaths among SARS-CoV-2 patients. Co-infections with other viral infections like dengue is of high concern in Hodeidah, Yemen. Post-outbreak investigation, the control

and prevention measures were implemented by local authorities in collaboration with private sector and non-governmental organizations namely re-habitation of SARS-CoV-2 isolation center to reduce the mortality rate and different practices and knowledge to reduce the morbidity rate. The study recommended that there must be a more focused approach to preventive medicine and a better understanding of chronic disease within the Yemeni peoples to help to ensure scarce resources are allocated most effectively.

6. LIMITATIONS OF THE STUDY

There are some limitations in this study that need to be considered. The small samples size in death cases. Therefore, the study will include large sample size

CONSENT

Written informed consent for participation (family's death cases) was required for this study.

ETHICAL APPROVAL

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

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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