Hospitalization, Recovery, Death, incubation period and Severity of COVID-19: A Systematic Review

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Abstract

Background: The novel coronavirus SARS-CoV-2 disease, named "COVID-19" by the WHO, was declared Public Health Emergency Concern globally January 2020. As of 01 February, 2021, the virus already visited more than 200 countries across the globe, with a total of over 103 million confirmed cases, over 2 million deaths and over 76 million recoveries.

COVID-19 first appeared in the African continent on 15th February 2020 in Egypt. Back in April 2020, only a few African countries reported 1, 2 or 3 confirmed cases with no death; but as of 07 June the virus visited over 45 African countries already with a total of 183,474 confirmed cases, 81,367 recovered and 5,041 deaths. Moreover, country context evidence is important at least to reduce the impact of COVID 19 in Africa region.

Objective: The objective is to get cohesive understanding on hospitalization, recovery, death, incubation period and severity of COVID-19.

Methods: Systematic Review was carried out to synthesis cohesive information on hospitalization, recovery, death, incubation period and severity of the disease. This review includes a systematic literature search of PubMed and other sources like Google Scholar and Research Gate.

Results: Hospitalization rate for young is as low as 1%, while it ranged from 20.7% to 31.4% for older people. Hospitalization rate was high among patients with obesity (Body Mass Index>40), and heart failure. Recovery rate ranged from 30% in China to over 70% in South Korea. Overall case fatality rate from different studies ranged from 0.1% to 6%. But this value increases to as much as over 45% for those over 75 years old. The median incubation period ranged from 4 days to 5.1 days but showed increment for the older ages. Proportion of critically ill patients ranged from 0.026% to 23%. More severe cases were seen among males than females.

Conclusion: This systematic review in-sight the variation in hospitalization, recovery, death, incubation period and severity of COVID-19 pertaining to patients' characteristics. [*Ethiop. J. Health Dev.* 2021; 35(SI-1):76-81]

Key words: Hospitalization, Recovery, Death, incubation period severity, COVID-19, systematic review

Introduction

An outbreak of "pneumonia of unknown etiology" in Wuhan, Hubei Province, China in early December 2019 has spiralled into an epidemic that ravaged China and eventually developed to a pandemic state (1). The causative agent was argued to be a new beta-corona-virus related to the Middle East Respiratory Syndrome virus (MERS-CoV) and the Severe Acute Respiratory Syndrome virus (SARS-CoV). The novel coronavirus SARS-CoV-2 disease, named "COVID-19" by the World Health Organization (WHO), was declared as Public Health Emergency Concern globally January 2020 (2).

In the beginning, China's government lockdown Wuhan and suspended all public transport, flights and trains; by late January 2020, there were about 40,000 confirmed cases and 909 deaths (2.2%) as reported by the National Health Commission of China. During this period, 319 cases and one death were reported in 24 other countries (3).

The novel virus is transmitted from person to person by respiratory droplets and related routes, causing symptoms, among other things, like fever, cough, and shortness of breath after a period believed to range from 2 to 14 days following infection (1, 4, 5). Preliminary studies suggest that old people with co-morbidities might be at higher risk for severe illness from COVID-19 (4, 6, 7); but, exact virologic and epidemiological characteristics of this zoonotic human coronavirus are still the source of controversy.

Methodology

The review started by identifying PICOS (participants, interventions, comparators, outcomes, and study design) structure. It followed the five-step principle to conduct the systematic review, namely, i) *Framing questions for a review, ii) Identifying relevant work, ii) Assessing the quality of studies, iV) Summarizing the evidence, and v) Interpreting the findings.*

Our protocol follows recommendations set out in the Statement of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)(8) (Figure 1).

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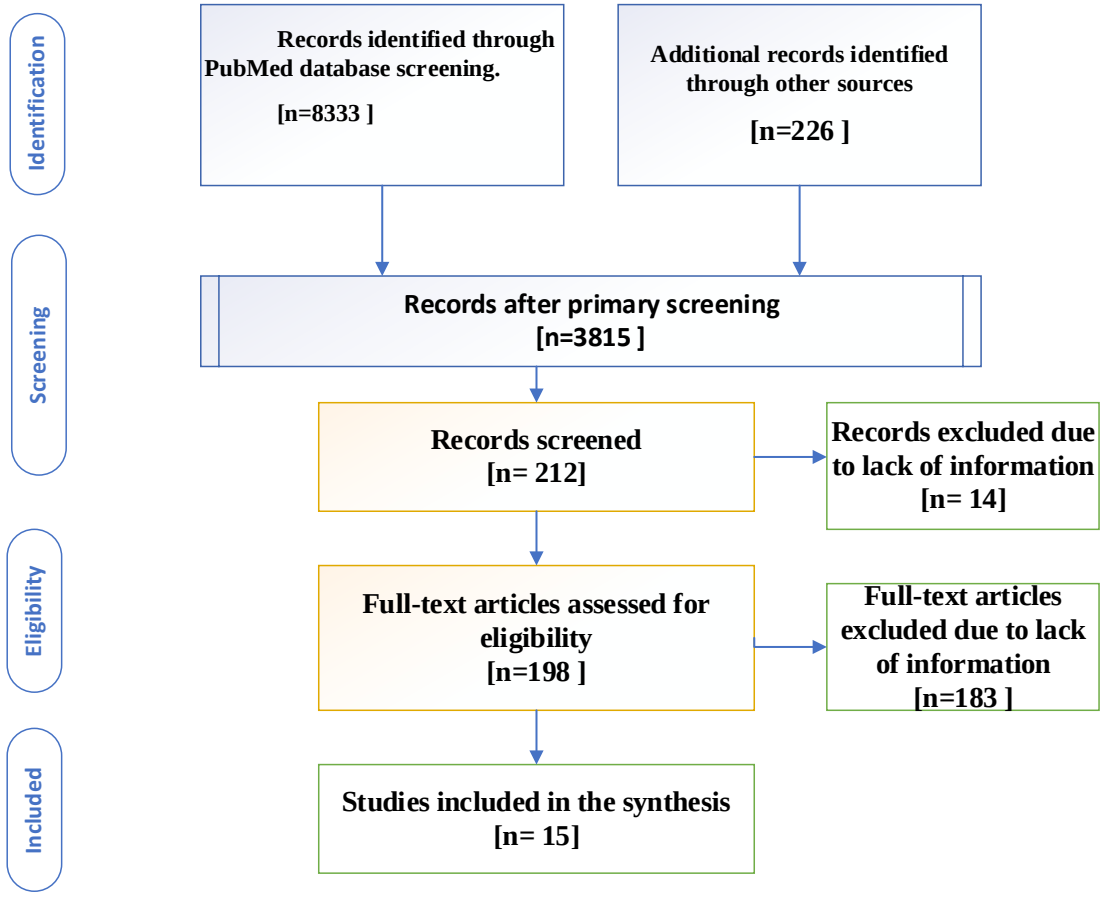

Figure 1. **PRISMA (preferred reporting items for systematic reviews and meta-analyses) flowchart of study inclusions and exclusions.**

We included peer-reviewed and pre-print articles that reported hospitalization cases, case fatality rate, recovery rate, rate of infection, and COVID 19 severity. The article's language was English, and publications from January 1, to June 24, 2020 were included. Systematic reviews and meta-analysis studies, opinion articles and letters not presenting original data, as well as studies reporting cases with incomplete information were excluded.

For the inclusion and exclusion criteria the full texts of the relevant articles were examined based on the PRISMA framework. The initial selection of search outcomes were first assessed by title and abstract. The researchers independently evaluated the search results by title and abstract based on the set eligibility criteria. The disagreement between the researchers were resolved by discussion.

The searching strategy for PubMed was prepared using keywords from the study topic and searched by combining with Boolean operator OR/AND (Table 1).

Table 1: **PubMed search result**

Search No	Search query	Result
# 1	"COVID-19" [All Fields] OR "COVID" [All Fields] OR " Coronavirus" [All Fields] OR "SARS-CoV-2" [All Fields] OR "severe acute respiratory syndrome" [All Fields] Filters: from 2020/1/1 - 2020/6/30	32,600
# 2	severity [All Fields] Filters: from 2020/1/1 - 2020/6/30	63,042
#3	"hospitalization rate" [All Fields] Filters: from 2020/1/1 - 2020/6/30	127
#4	"death rate" OR "fatality rate" [All Fields] Filters: from 2020/1/1 - 2020/6/30	898
#1 AND #2 AND #3 AND #4	((("COVID-19" [All Fields] OR "COVID" [All Fields] OR " Coronavirus" [All Fields] OR "SARS-CoV-2" [All Fields] OR "severe acute respiratory syndrome" [All Fields] AND (2020/1/1:2020/6/30[pdat])) AND (severity [All Fields] AND (2020/1/1:2020/6/30[pdat]))) OR ("hospitalization rate" [All Fields] AND (2020/1/1:2020/6/30[pdat]))) OR ("death rate" OR "fatality rate" [All Fields] AND (2020/1/1:2020/6/30[pdat])) Filters: from 2020/1/1 - 2020/6/30	8,333

The quality of the articles included in the review was checked and rated with Critical Appraisal Checklist for Cross-Sectional Study by the team of the review to reduce the risk of bias(9).

Basic characteristics of articles such as authors, name of publishing journal, time of publication, country of the study, study design, sample size, and quality score of the article were included. The extraction was performed by two reviewers and a third reviewer checked the accuracy of the extracted data. A principal investigator checked the articles list and data extractions to ensure the overall relevance of the included articles and the quality.

Initially, when search was conducted using keywords by applying the OR/AND Boolean operators, a total of 8,333 search results were found from PubMed (Table 1). After filtering these result by article types, publication status (preprint/published), and language (English) a total of 3815 articles remained. We screened and filtered the articles further by reading the title and abstract where 212 articles were selected for full-text assessment. Of these, 10 articles which fulfilled the inclusion criteria and contained relevant information were selected. We also identified 3 articles from the ResearchGate and 2 articles from Google Scholar that fulfilled the inclusion criteria. So, a total of 15 articles were included for the final systematic review of qualitative synthesis.

Results

Studies search and characteristics

Among these 15 studies, majority of them 8 were from China, 4 were from the USA and the remaining were one each from Brazil, Italy and South Korea (Table 2). The study subjects included a total of 114,018 cases ranging from 99 to 72,314 cases. The study designs of the included studies were record review 4, cross-sectional 3, cohort 3, surveillance 1, report 1, case series 1 and others didn't report the study design (Table 2).

Table 2: **Characteristics of the included studies**

Author	Journal	Time	Country	Study design	Sample size (N)	Quality score	Reference
CDC COVID-19 Response Team	NA	2020	USA	Report		Fair	24
Chen N et al	Lancet	2020	China	Retrospective single centered study	99	Fair	28
Garg S et al	Preprint	2020	USA	Surveillance	1482	fair	25
Guan W et al	engl j med	2020	China	Cross-sectional	1099	Good	34
Lauer SA et al	Ann Intern Med	2020	China	Not reported	181	Fair	33
Li R et al	Preprint	2020	USA	Cross-sectional	19425	V.Good	37
Petrilli CM	Preprint	2020	USA	Cross-sectional	4103	V.Good	23
Ricardo A et al	Brasília	2020	Brazil	Not reported		Fair	27
Wu Z et al	JAMA	2020	China	Case series	72,314	Good	31
Giacomelli A et al	Pharmacological Research	2020	Italy	Prospective cohort	233	Good	29
Li X et al	Article in press (J ALLERGY CLIN IMMUNOL)	2020	China	Retrospective cohort	548	V.Good	26
Shim E et al	Intern. Journal of Infectious Diseases	2020	S.Korea	Record review	6284	Fair	30
Ye Q. et al	J Med Virol	2020	China	Record review	1099	Good	32
Nie X et al	JID	2020	China	Retrospective record review	7015	Good	35
Kong T-k	Aging Medicine	2020	China	Record review	136	Fair	36

From the articles reported sex, 53.98% were male with variations from 50.49% in USA to 69.1% in Italy. The median age across the studies were 52.13 years old, ranging from 47 years in China to 61 years in Italy.

Hospitalization, recovery and death rates

Research in New York showed 48.7% of COVID-19 patients had been hospitalized among 4,103 cases (Table 3). The highest hospitalization rate was seen among patients aged 65-74 (OR of 10.9, and aged ≥75 years (OR of 66.8); with an odds ratio of 6.2, and 4.3 among patients with obesity (BMI>40) and heart failure respectively (10). A CDC COVID-19 response team reported that hospitalization rate ranges from 20.7% to 31.4% among 2,449 patients in USA; less than 1% of hospitalizations, among people aged 19 years, from 2%-3% among people aged about 19 -60 years and about 31% among adults aged about 85 years (11).

Table 3**: Characteristics of the studies**

Author	Time	Sample size (N)	Age (median)	Sex (male %)	Hospitalization (%)	Recovery (%)	Death (%)	Severity (mild/sever/critical) %	Incubation period (median days)
Chen N et al	2020	99	55	67.7		31	11		
Garg S et al	2020	1482	NR	54	0.0046				
Guan W et al	2020	1099	47	58.1			1.4	-/5/2.3	4
Lauer SA et al	2020	181	44.5	59.7					5.1
Li R et al	2020	19425			0.25			-/0.12/0.026	
Petrilli CM	2020	4103	52	50.49	48.7	49.1	14.6		
Wu Z et al	2020	72,314	NR	NR			2.3	81/14/5	
Giacomelli A et al	2020	233	61	69.1		69.5	20.6		
Li X et al	2020	548	60	50.9				-/49.1/-	
Shim E et al	2020	6284				1.72	0.7		
Ye Q. et al	2020	1099	47	58.2			4	-/-/23.4	5.2
Nie X et al	2020	7015	44.24 mean	54.12					5
Kong T-k	2020	136	50.5	53					8.3

The discharge rate among hospitalized patients in New York City, Italy, China and South Korea were 49.1% (10), 31% (12), 69.5 percent(13), and 72% (14) respectively.

The overall death rate among the 1,999 hospitalized patients in New York City was 14.6%; and 36.4% among ventilated patients (10). However, the case-specific fatality rates were 8.0% among patients aged 70 to 79, 14.8% aged over 80, and 49.0% in critical cases (15).

The case-fatality ratio in Wuhan was 4.5% while for those outside was 3.2% (16). Death ratio was 4.2, 20.6 and 0.7% in Wuhan's, in the rest of China(17), in Italy (13), and in South Korean (14) respectively. This study indicated the crude case fatality rate for males (1.1%) and females (0.4%) (14). More than 80% of those died were over 60 years old and more than 75% of the deaths had underlying diseases.

Incubation period

A study conducted in 181 confirmed cases in China showed an estimated median incubation period of 5.1 days and 97.5% of them developed symptoms within 11.5 days of infection(18); another study from 1099 patients showed the median incubation period of 4 days (interquartile range, 2 to 7)(19) (Table 3). For 1 case the longest period of incubation was 24 days. The incubation period was less than 13 days for more than 95% of COVID-19 cases (20). However, the incubation period varied by age (21).

Severity of Disease

A report from the USA CDC indicated that 31% of cases, 45% of hospitalizations, 53% of ICU admissions, and 80% of deaths associated with COVID-19 were among adults aged ≥65 years(Table 3). The highest percentage of severe outcomes were observed among persons aged ≥85 years (11). The strongest critical illness risks were observed among patients with admission of oxygen saturation <88% (OR 6.99, d-dimer>2500 (OR 6.9), ferritin >2500 (OR 6.9), and C-reactive protein (CRP) >200 (OR 5.78) (10).

The Chinese CDC report from 72, 314 cases showed the severity condition of COVID-19 cases as 81% mild, 14% severe and 5% critical (15); with 23.7 percent having at least one coexisting disease.

During the peak epidemic in Wuhan, 0.122% of patients were in severe condition, and 0.026% needed critical care per day(16). Severe cases were higher in males than females (56.9% vs 45.2%; P =.006) (22).

Discussion

Since the first case reported on March 13, 2020, there are 5,689 confirmed cases, 2,132 recovered cases and 98 deaths in Ethiopia as of June 24, 2020 (23). The COVID-19 pandemic is currently affecting the health, social and economic affair of many countries. Ethiopia is striving to fight the disease using policy measures including state emergency, community mobilization, and clinical and epidemiological interventions. Understanding the clinical and epidemiological characteristics of the disease is crucial to mitigate its catastrophic effect by prevention and control. In this regard, the current systematic review is helpful to learn lesson and understand the characteristics of the disease associated with its spread and severity. This review focused on hospitalization, recovery and death rates as well as the incubation and severity of the disease.

Hospitalization rate varied by geospatial conditions and by demographic characteristics of patients (10, 11, 24). The possible reasons for the variation from place to place might be due to the governments measure like national and local lockdown, school and public places closure, enforcement of physical distancing and facemask use. Most studies consistently reported the older ages and males have a higher risk of hospitalization. Understanding these concepts are

important for early preparedness and planning (28-32). The proportion of recovery or discharge of patients was different in different studies (10, 12-14).

Most of the studies calculated the death rate of COVID-19 from reported confirmed cases rather than the actual cases which are typically larger than the reported confirmed cases (25). This may overestimate the death rate in most instances as most of asymptomatic and mild cases remain undetected. The studies showed the death rate widely ranged with different characteristics of patients (10, 11, 13-17). In most of the studies, the overall mortality rate was relatively low compared with age, sex, level of severity and underlying disease-specific mortality. Patients who were critically ill, under mechanical ventilation, and in ICU were at the highest rate of death. Patients over 60 were at a higher risk of death compared with younger age patients.

The overall median incubation period of COVID-19 was a little bit varying among several studies (18-21). However, there were instances that the incubation period specifically longer than the majority group in some cases (20). The incubation period also varied by age that patients with older age had a longer incubation period (21). Knowing the incubation period of COVID-19 is important for disease surveillance, prevention and control measures of the disease. Although most studies suggested the 14 days incubation period, there are evidences that the incubation period extends to 24 days.

Most studies indicated that severity of COVID-19 is associated with factors like age, sex, chronic underlying illness, co-infection of bacteria and fungi and clinical factors like d-dimer, ferritin, C-reactive protein and leukocytosis (10-12, 16, 17, 19). The studies also indicated the proportion of mild, moderate and critical cases of the disease (15).

Conclusion

The proportion of hospitalization is significantly higher in older age and male patients globally. The recovery or discharge rate of hospitalized patients varied from place to place. The older age, male, critically ill and chronic disease patients were at higher risk of death. Patients with older age have a prolonged incubation period. The important predictors of COVID-19 severity were age, sex, presence of chronic illness, and clinical factors like d-dimer, ferritin, C-reactive protein and leukocytosis.

Recommendations

The Federal Ministry of Health and Addis Ababa City Administration should strengthen the intervention measures to contain the spread of the disease in Addis Ababa and to limit its spread to other regions of the country.

Health care facilities should give special focus for people of older ages, having underlying and chronic disease in prevention and clinical interventions.

Limitation of the study

This review didn't include studies from Africa and Ethiopia since we cannot find published or preprint study at the time of our review. This review is a qualitative synthesis that cannot show the statistical significance of the issues described.

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