American Journal of Biomedical Sciences
ISSN: 1937-9080
nwpii.com/ajbms

The Development of Ogunlade COVID-19 Diagnostic Criteria (OCDC) and OCRAS for Management of Coronavirus Disease 2019 (COVID-19) Pandemic

***Oluwadare Ogunlade, MB.CH.B., M.Sc., PhD., FWACP.**

Department of Physiological Sciences,College of Health Sciences,Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria
***Corresponding Author**
Department of Physiological Sciences,
College of Health Sciences,
Obafemi Awolowo University, Ile-Ife, Osun State
Nigeria
Email:ogunladeomotomilayo@gmail.com

Received:19 May 2020; | Revised:09 June 2020; | Accepted:11 September 2020

Abstract

Objective: To develop clinical diagnostic criteria and a risk assessment score for management of COVID-19 suspected cases or contacts.

Methods: Literature on the manifestations, risk factors and co-morbidities of Coronavirus disease (COVID-19) were reviewed extensively to identify the key variables useful for the disease diagnosis and risk profiling. The variables were sub-classified into major and minor criteria for synthesis into clinical diagnostic criteria. The variables closely related to COVID-19 were allocated graded score points which were summed up to form Ogunlade COVID-19 Risk Assessment Score (OCRAS) for risk profiling. The total score was stratified into four levels of risk and presented in a coloured-coded risk stratification chart. In order to allow for daily monitoring of the risk level per time, new chart was developed to incorporate inputs of OCRAS on daily basis.

Results: This study evolved Ogunlade COVID-19 Diagnostic Criteria(OCDC) and Ogunlade COVID-19 Risk Assessment Score (OCRAS) as clinical diagnostic and risk profiling tools respectively. OCDC were made up of 5 major and 12 minor criteria. Using OCDC, the diagnosis of COVID-19 should be made clinically in the presence of at least 4 (3 *major plus 1 minor or 1 major plus 3 minor*) criteria. The minimum and maximum values of OCRAS were 24 and 72 respectively. The individual's OCRAS should be stratified into four levels of risk using the COVID-19 Risk Stratification Chart (CRSC). The COVID-19 Risk Monitoring Chart (CRMC) was generated for daily monitoring of the OCRAS values for 14 days.

Conclusion: The paper reported the development of a simple-to-use clinical diagnostic criteria and a unique risk assessment score for clinical decision making in the management of COVID-19. Nations with less developed health system or serious health infrastructure deficit will find the innovations helpful to break the chains of community transmission of COVID-19.

Keywords: Development, Ogunlade, Diagnostic Criteria, OCRAS, COVID-19, Pandemic

1. Introduction

Consequential to the Ebola epidemic in 2015, the World Health Organization (WHO) coordinated global experts to develop Research and Development (R&D) Blueprint aiming at emergency preparedness against outbreak of pandemic [1]. This blueprint was endorsed by the World Health Assembly in May 2016. In February 2018, WHO unveiled a list of prioritized diseases for research and development in emergency context [2,3]. The prioritized diseases were; Middle East Respiratory Syndrome (MERS), Severe Acute Respiratory Syndrome (SARS) and Disease X [2]. The 'Disease X' was defined by WHO as 'a new disease with an epidemic or pandemic potential caused by an unknown pathogen' [3]. Leveraging on this, a group of scientists working at Key Laboratory of Medical Molecular Virology, School of Basic Medical Sciences in China, New York Blood Centre, The Lindsley F. Kimball Research Institute, New York, United States of America (USA) and CAS Key Laboratory of Special Pathogens, Wuhan Institute of Virology, Center for Biosafety Mega-Science, Chinese Academy of Science, Wuhan, China explored this research opportunity and funding to focus on Severe Acute Respiratory Syndrome-related coronavirus (SARSr-CoV) isolated from bat feacal samples in Vero E6 cells[4]. SARSr-CoV was identified as potentially dangerous virus because it could utilize angiotensin converting enzyme II as receptor for infecting human, civet and Chinese horseshoe bat [4,5]. Laboratory explorations to get the in vitro inhibitor of the SARSr-CoV and possible vaccine are still on-going [6]. On November 17, 2019, a confirmed case of a strange disease linked with coronavirus was reported in Wuhan [7]. Another case of unknown disease was reported in Wuhan on December 1, 2019 [8,9]. On December 2, 2019, a 51year old Dongguan doctor developed cough and fever and was the first hospitalized case of the unknown disease [10]. On December 10, 2019, a 57year old seafood merchant in Wuhan was identified as manifesting features of the unknown disease [11]. On December 12, 2019, there was a news on the occurrence of clusters of cases of unknown pneumonia among traders in local Huanan China Seafood Market in Wuhan, Hubei Province, China [12,13]. The causative agent of the new disease was identified and reported to be homologous to SARSr-CoV [13]. Hence, the Scientist wanted the disease to be considered by WHO as the first Disease X [6]. On December 31, WHO was formerly notified by the Chinese authority of the outbreak of a new disease [13]. On February 11, 2020, the name, coronavirus disease 2019 (COVID-19) was given to the new disease by WHO [14-16] while the group of scientists who were involved in the gene sequencing of the causative agent referred to it as '2019 novel Coronavirus (2019-nCoV)' on January 7[17]. The Coronaviridae Study Group (CSG) of the International Committee on Taxonomy of Viruses (ICTV) renamed the causative agent of the disease as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [17].

WHO declared COVID-19 a pandemic on the March 11th, 2020[18,19]. Since onset, COVID-19 pandemic has resulted in deaths, enormous health and socioeconomic challenges globally. In the mid of this pandemic, WHO updated the R&D Blueprint list of prioritized diseases to include; COVID-19, Crimean-Congo haemorrhagic fever, Ebola virus disease, Marburg virus disease, Lassa fever, Middle East respiratory syndrome coronavirus (MERS-CoV), Severe Acute Respiratory Syndrome (SARS), Nipah and henipaviral diseases, Rift Valley fever, Zika and "Disease X" [20] while most nations struggle to contain the spread of the disease.

The major manifestations of COVID-19 include fever, dry cough, shortness of breath and fatigue. Other manifestations include sneezing, sore throat, runny or stuffy nose, body aches, back pain, headache, hyposmia or anosmia, hypogeusia or ageusia, nausea and or vomiting, loss of appetite, diarrhea, abdominal discomfort and or pain [21-24]. The features of severe COVID-19 were respiratory failure, oxygen desaturation, bilateral pulmonary infiltrates and lymphopaenia. The onset of the symptoms of COVID-19 is gradual after an initial incubation period of 2-14 days [25]. The predisposing factors were recent travel, close contact with infected individuals, male sex, blood group type A, older age groups (⩾ 60years) and

pre-existing co-morbidities such as heart, lung, and kidney diseases. Male pattern of baldness had been identified as an important predictor of severity of COVID-19[26].

The diagnosis of COVID-19 could be made from clinical manifestations, history of travel, antigen-based test, reversed transcriptase polymerase chain reaction test and or antibodies testing [27]. Testing kits and facilities are very scarce globally especially in developing countries. Little is known about clinical profiling as a tool for risk stratification, diagnosis, monitoring and surveillance. A host risk score was established in China to assess risk of susceptibility [28]. This piece is about the development of Ogunlade COVID-19 Risk Assessment Score to assist in the war against the virus.

Table 1: Ogunlade COVID-19 Diagnostic Criteria (OCDC)

Major Criteria

1. Fever
2. Cough (*usually dry, no phlegm*)
3. Fatigue *(easy tiredness)*
4. Shortness of Breath
5. Travel or contact history;
    a. Recent travel to high risk nation/state/town
    b. Contact with returnee from COVID-19 high risk nation/state/town
    c. Contact with suspected/confirmed/treated cases of COVID-19
    d. Living in same abode with suspected, confirmed/treated case of COVID-19

Minor Criteria

1. Runny or Stuffy nose
2. Sneezing
3. Sore throat
4. Body pains/backpain/headache
5. Recent change in smell (*hyposmia or anosmia*)
6. Recent change in taste (*hypogeusia or ageusia*)
7. Nausea and or vomiting
8. Abdominal discomfort or pain
9. Diarrhoea (*loose or watery stool more than 3 times a day*)
10. Altered level of consciousness
11. Pre-existing health state such as pregnancy
12. Pre-existing ill-health such as
    a. Airway/lung disease
    b. Heart disease
    c. Kidney disease
    d. Diabetes mellitus
    e. Cancer
    f. Other chronic illnesses

COVID-19: *Coronavirus Disease 2019*

The diagnosis of COVID-19 is made clinically with at least 4 (*3 major plus 1minor criteria or1major plus 3 minor*) criteria

2. Materials and Methods

Literature on the manifestations, risk factors and co-morbidities of COVID-19 were reviewed extensively to identify the key variables useful for its diagnosis and risk profiling. The clinical and epidemiological variables of the new disease were selected and sub-classified into major and minor criteria. These criteria were synthesized creatively to develop unique clinical diagnostic criteria. A total of 16 criteria were considered for development of the Ogunlade COVID-19 Diagnostic Criteria. In order to allow for progressive risk assessment and monitoring, the variables closely related to COVID-19 either clinically or epidemiologically were allocated score of 1, 2 or 3. In all, 24 variables were scored. The total score, which was the sum of the points obtained across the 24 variables was designated Ogunlade COVID-19 Risk Assessment Score (OCRAS). This score was also stratified into four levels of risk (Low, Medium, High and Very High) and presented in a coloured-coded risk stratification chart. In order to allow for daily monitoring of the risk level per time, another chart was developed to incorporate inputs of OCRAS on daily basis.

3. Results

This study unveiled the newly developed Ogunlade COVID-19 Diagnostic Criteria (OCDC) and Ogunlade COVID-19 Risk Assessment Score (OCRAS). OCDC was made up of 5 major criteria (fever, cough, fatigue, shortness of breath and history of travel or contact with returnee from high risk area or contact with suspected/confirmed/treated cases of COVID-19) and 12 minor criteria (runny nose, sneezing, body pains/backpain/headache, altered smell, altered taste, nausea and/vomiting, abdominal discomfort or pain, diarrhea, altered level of consciousness, health state such as pregnancy and ill-health such as chronic illnesses [Table 1]. Using OCDC, the clinical diagnosis of COVID-19 was articulated to be made with the presence of at least 4 (3 major and 1 minor or 1 major and 3 minor) criteria [Table 1]. The risk assessment score generated from the graded point score is known as Ogunlade COVID-19 Risk Assessment Score (OCRAS). The minimum score was 24 while the maximum Score was 72 (Table 2). The 24 items included in OCRAS development were; age, sex, ABO blood Group, fever, cough, shortness of breath, fatigue, runny or stuffy nose, sneezing, sore throat, body ache/back pain/headache, altered smell, altered taste, nausea and/vomiting, abdominal discomfort/pain, diarrhea and altered sensorium. Other variables within OCRAS were; nature of onset of symptoms, presence of COVID-19 case at abode, recent travel history, close contact with returnees or cases, baldness, health state such as pregnancy and ill-health such as airway/lung, heart or kidney diseases, stroke, diabetes mellitus, cancer or other chronic illnesses. The total value of OCRAS was stratified using a coloured chart called COVID-19 Risk Stratification Chart (CRSC). The risk strata were; Low (24-32), Medium (33-42), High (43-52) and Very High (53-72) denoted by green, yellow, orange and red respectively [Table 3]. In order to monitor individual's risk of contracting COVID-19 with time, special charts called COVID-19 Risk Monitoring Charts (CRMC) were designed for quarantine and isolation services (Tables 4 & 5). These were made for the purpose of input of OCRAS values on daily basis

Table 2: Ogunlade COVID-19 Risk Assessment Score (OCRAS)

Variables *(Occurrence of 5-18 in the past 4 weeks)*		Score			Client's Value
		1	**2**	**3**	
1	Age (years)	< 18	18-59	≥ 60	
2	Sex	F	I	M	
3	ABO Blood Group	O	B or AB	A	
4	Baldness	No	[a]Female-pattern	[b]Male-pattern	
5	[+]**Fever**	No	Yes, *with shivering*	Yes, *without shivering*	
6	**Cough**	No	Yes, Wet (*with phlegm*)	Yes, Dry (*no phlegm*)	
7	**Shortness of breath**	No	Yes, Mild	Yes, Prominent	
8	**Fatigue** *(easy tiredness)*	No	Yes, Mild	Yes, Prominent	
9	Runny/stuffy nose	No	Yes, Moderate	Yes, Mild	
10	Sneezing	No	Yes, Moderate	Yes, Mild	
11	Sore throat	No	Yes, Moderate	Yes, Mild	
12	Body ache/ back pain/headache	No	Yes, Moderate	Yes, Mild	
13	Recent change in smell	No	Yes, *Hyposmia	Yes,**Anosmia	
14	Recent change in taste	No	Yes, [x]Hypogeusia	Yes, [xx]Ageusia	
15	Nausea and or vomiting	No	Yes, Mild	Yes, Prominent	
16	Loss of Appetite	No	Yes, Mild	Yes, Prominent	
17	Abdominal discomfort and/pain	No	Yes, Mild	Yes, Prominent	
18	Diarrhoea (loose or watery stool more than 3 times a day)	No	Yes, Mild	Yes, Prominent	
19	Onset of Symptoms	NA	Abrupt	Gradual	
20	Exposure to onset of symptoms	NA	< 7 days	≥ 7 days	
21	Presence of COVID-19 case at abode	No	Suspected case(s)	Confirmed/treated case(s)	
22	**Travel (*in the past 4 weeks*) from/to:**	No	Low risk area(s)	High risk area(s)	
23	Close contact with returnees or cases	No	Suspected case(s)	Confirmed/treated case(s)	
24	Pre-existing health state or ill-health	No	Health state such as pregnancy	Ill-health such as airway /lung, heart, kidney diseases, diabetes mellitus, stroke, cancer or any other chronic illnesses	
Total					

COVID-19 *–Coronavirus disease 2019, [+]Axillary Temperature ≥ 37.2[0]C,* ***Hyposmia**-Reduced smell, ****Anosmia**-Absence of smell, [x]**Hypogeusia**-reduced taste, [xx]**Ageusia**- loss of taste,* ***F**=Female, **I**=Intersex, **M**=Male*

*a-**Female pattern baldness**- occurs as hair thinning in the central or midline region of the scalp with preservation of the front hairline*

*b- **Male pattern baldness**-occurs as a receding hairline or loss of hair on the crown of the scalp*

***NA**: Not Applicable, **Minimum OCRAS** = 24, **Maximum OCRAS** = 72*

Table 3: COVID-19 Risk Stratification Chart (CRSC)

OCRAS	RISK	Symbol
24-32	Low	L
33-42	Medium	M
43-52	High	H
53-72	Very High	VH

COVID-19- *Coronavirus Disease 2019*
OCRAS- *Ogunlade COVID-19 Risk Assessment Score*

Table 4: COVID-19 Risk Monitoring Chart (CRMC) for Quarantine Services

Date:	Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
OCRAS															
Risk Level															

OCRAS- *Ogunlade COVID-19 Risk Assessment Score*
COVID-19- *Coronavirus Disease 2019*

Table 5: COVID-19 Risk Monitoring Chart (CRMC) for Isolation Services

Date:	Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
OCRAS															
Risk Level															

OCRAS- *Ogunlade COVID-19 Risk Assessment Score*
COVID-19- *Coronavirus Disease 2019*

4. Discussion

As China contained the COVID-19 epidemic in her territories, the many other nations across the globe are battling with rapid spread of the new disease with its attendant morbidity and mortality [18,19]. The health systems of many advanced nations are overstretched due to increasing numbers of patients in need of admission facilities due to severe respiratory distress requiring ventilators and intensive care supports [29]. This implies that early diagnosis and prompt treatment will be of great value. Presently, there is no proven effective treatment or vaccine for the pandemic [30]. The main stake of management is symptomatic care. In developed countries, the diagnosis of COVID-19 is not posing a serious challenge because the appropriate test kits are available coupled with safe infrastructure [27]. In middle and low income countries, the use of Reverse Transcriptase Polymerase Chain Reactions (RT PCR) tests had been integrated into management of cases but the health systems are very weak. The health infrastructural deficit in most developing nations impair adequate testing. In such countries, clinical evaluation may play an important role in the assessment of COVID-19 while molecular diagnosis remains the gold standard for case identification. The OCDC, OCRAS and CRMC were developed to assist health care workers in decision making in the management of suspected cases of COVID-19. OCRAS in particular will assist in monitoring of cases. The usage of OCDC and OCRAS will complement existing management modalities. As COVID-19 spreads across many nations, it is hopeful that the OCDC and OCRAS will be put to use alongside molecular testing to break the chains of community transmission of the disease.

5. Conclusion

The paper reported the development of a simple-to-use clinical diagnostic criteria and a unique risk assessment score for clinical decision making in the management of COVID-19. Nations with less developed health system or serious health infrastructure deficit will find the innovations helpful to break the chains of community transmission of COVID-19.

References

1 Research and Development Blue Print.***World Health Organization (2015)*** http://www. who. int/csr/research-and-development/r_d_ blueprint_brochure2015.pdf?ua=1

2 List of Blueprint priority diseases.7 February. ***World Health Organization (2018)*** http:/ /origin.who.int/blueprint/priority-diseases/en/

3 2018 Annual review of diseases prioritized under the Research and Development Blueprint (PDF) (Report). Geneva, Switzerland.p. 17.Retrieved 20March 2020.***World Health Organization (2018).***

4 Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. ***Nat Rev Microbiol*** 2019; 17(3): 181-192 DOI: 10.1038/s41579-018-0118-9

5 Wang N, Li SY, Yang XL, Huang HM, Zhang YJ, Guo H, Luo CM, Miller M, Zhu G, Chmura AA, Hagan E, Zhou JH, Zhang YZ, Wang LF, Daszak P, Shi ZL. Serological Evidence of Bat SARS-Related Coronavirus Infection in Humans, ***China. Virol Sin*** 2018; 33(1): 104-107 DOI: 10.1007/s12250-018-0012-7

6 Jiang S, Shi ZL. The First Disease X is Caused by a Highly Transmissible Acute Respiratory Syndrome Coronavirus. ***Virol Sin*** 2020; 35(3): 263-265 DOI: 10.1007/s12250-020-00206-5

7 China's first confirmed Covid-19 case traced back to November 17. ***South China Morning Post.*** 13 March 2020. Archived from the original on 19 March 2020.

8 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. ***Lancet*** 2020; 395(10223): 497-506 DOI: 10.1016/S0140-6736(20)30183-5

9 Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY, Xing X, Xiang N, Wu Y, Li C, Chen Q, Li D, Liu T, Zhao J, Liu M, Tu W, Chen C, Jin L, Yang R, Wang Q, Zhou S, Wang R, Liu H, Luo Y, Liu Y, Shao G, Li H, Tao Z, Yang Y, Deng Z, Liu B, Ma Z, Zhang Y, Shi G, Lam TTY, Wu JT, Gao GF, Cowling BJ, Yang B, Leung GM, Feng Z. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. ***N Engl J Med*** 2020; 382(13): 1199-1207 DOI: 10.1056/NEJMoa2001316

10 Timeline of the 2019-20 coronavirus pandemic from November 2019 to January 2020

11 Oliveira, Nelson .Shrimp vendor identified as possible coronavirus patient zero, leaked document says. ***New York Daily News*** 27 March 2020

12 Wuhan Municipal Health Commission. Press statement related to novel corona virus infection (inChinese).http://wjw.wuhan.gov.cn/front/web/showDetail/2020023709194(2020)

13 Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Si HR, Zhu Y, Li B, Huang CL, Chen HD, Chen J, Luo Y, Guo H, Jiang RD, Liu MQ, Chen Y, Shen XR, Wang X, Zheng XS, Zhao K, Chen QJ, Deng F, Liu LL, Yan B, Zhan FX, Wang YY, Xiao GF, Shi ZL. A pneumonia outbreak associated with a new coronavirus of probable bat origin. ***Nature*** 2020; 579(7798): 270-273 DOI: 10.1038/s41586-020-2012-7

14 Novel Coronavirus (2019-nCoV) Situation-22 .World Health Organization, 2020; https://www.who.in/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22-ncov.pdf

15 WHO.Novel Coronavirus-China . 2020. https: //www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/. Accessed 1 Feb 2020

16 Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W, China Novel Coronavirus I, Research T. A Novel Coronavirus from Patients with Pneumonia in China, 2019. ***N Engl J Med*** 2020; 382(8):727-733 DOI:10.1056/NEJMoa2001017

17 Coronaviridae Study Group of the International Committee on Taxonomy of V.

The species Severe acute respiratory 2019-nCoV and naming it SARS-CoV-2. ***Nat Microbiol*** 2020; 5(4): 536-544 DOI: 10.1038/s41564-020-0695-z

18 Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. ***Acta Bio Med*** 2020; 91(1):157-60.https://www.mattioli1885journals.com/index.php/actabiomedica/article/view/9397

19 WHO Director-General's opening remarks at the media briefing on COVID19 -March 2020.

20 WHO.Research and Development Blueprint. https://www.who.int/blueprint/en/2020

21 Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, Wang QZ, Sun C, Sylvia S, Rozelle S, Raat H, Zhou H. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. ***Infect Dis Poverty*** 2020; 9(1): 29 DOI: 10.1186/s40249-020-00646-x

22 Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf

23 Cascella M, Rajnik M ,Cuomo A , Dulebohn SC ,Napoli R. Features, Evaluation and Treatment Coronavirus (COVID-19) [Updated 2020 Mar 20]. In: StatPearls [Internet]. ***Treasure Island (FL): StatPearls Publishing***; 2020 Jan.https: //www.ncbi.nlm.nih. gov /books/NBK 554776/

24 Bolawale A, Abayomi A, Idris J, Omilabu S, Abdus-Salam I, Adebayo B, Opawoye F, et al. Clinical presentation, case management and outcomes for the first 32 COVID-19 patients in syndrome-related coronavirus: classifying Nigeria. ***Pan African Medial Journal*** 2020;35(2):24. DOI: 10.11604/pamj.supp.2020.35.2.2.23262

25 Shi Y, Yu X, Zhao H, Wang H, Zhao R, Sheng J. Host susceptibility to severe COVID-19 and establishment of a host risk score: findings of 487 cases outside Wuhan. ***Crit Care*** 2020; 24(1): 108 DOI: 10.1186/s13054-020-2833-7

26 Wambier CG, Vano-Galvan S, McCoy J, Gomez-Zubiaur A, Herrera S, Hermosa-Gelbard A, Moreno-Arrones OM, Jimenez-Gomez N, Gonzalez-Cantero A, Pascual PF, Segurado-Miravalles G, Shapiro J, Perez-Garcia B, Goren A. Androgenetic Alopecia Present in the Majority of Hospitalized COVID-19 Patients - the "Gabrin sign". ***J Am Acad Dermatol*** 2020 DOI: 10.1016/j.jaad.2020.05.079

27 CDC .2019 Novel Coronavirus , Wuhan , China:Symptoms. CDC.Jan 27, 2020 https://www.cdc.gov/coronavirus/2019-nCoV/about/symptoms.html.January 26,2020

28 https://www.who.int/publications-detail/covid-19-operational-guidance-for-maintaining-essential-health-services-during-an-outbreak. April 5,2020.

29 Dong L, Hu S, Gao J. Discovering drugs to treat coronavirus disease 2019 (COVID-19). ***Drug Discov Ther*** 2020; 14(1): 58-60 [PMID: 32147628 DOI: 10.5582/ddt.2020.01012]

30 Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, Shi Z, Hu Z, Zhong W, Xiao G. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. ***Cell Res*** 2020; 30(3): 269-271 DOI: 10.1038/s41422-020-0282-0

