University of Louisville Journal of Respiratory Infections

BRIEF REVIEW

Age, Comorbidities, and Mortality Correlation in COVID-19 Patients: A Review

Vidyulata Salunkhe[1], MD, MPH; Amr Aboelnasr[1], MD; Parul Pahal[1], MD; Nida Qadir[1], MD; Simra Kiran[1], MD; Balaji Sekaran[1], MD; Omar Fahmy[1], MD; Farah Daas[1], MD; Syed Shah[1], MD*

[1]Center of Excellence for Research in Infectious Diseases (CERID), Division of Infectious Diseases, University of Louisville School of Medicine, Louisville, KY USA

*vidyulata.salunkhe@louisville.edu

Abstract

Background: The risk of death due to COVID-19 among hospitalized patients is known to be higher in older adults and those with underlying health conditions. Understanding the percentage of patients who are at increased risk of death due COVID-19 and how this varies between age groups will inform the healthcare community how to evaluate the risk of COVID-19, and better design healthcare and economic policies.

Methods: We conducted a literature search for studies published between December 2019 until May 16, 2020 in PubMed, Embase, and Cochrane (CENTRAL). Descriptive statistics were performed.

Results: We reviewed 14 studies of which 13 were retrospective and one was prospective. Eleven studies were conducted in Wuhan, China. A grand total of 11,938 COVID-19 confirmed patients were reviewed. Among these patients, 7637 (64%) were males. Our review reported hypertension (41%), diabetes (21%), cardiac diseases (14%), COPD (8%), chronic kidney disease (4%) and cerebrovascular disease (10%) as the most common underlying diseases among patients who died during hospitalization due to COVID-19. The total number of patients died in the hospital was 1744 (15%). Among patients who died in the hospital, 1% patients were 30-39 years, 16% patients were 40-59 years and 83% patients were more than 60 years of age.

Conclusions: Older patients with underlying diseases appear to be at higher risk of mortality from COVID-19. Comorbidities are significant predictors of mortality in COVID-19 patients. There is an urgent need to know the epidemiology of the novel virus and characterize its potential impact.

Recommended Citation:
Salunkhe, Vidyulata; Aboelnasr, Amr; Pahal, Parul; Qadir, Nida; Kiran, Simra; Sekaran, Balaji; Fahmy, Omar; Daas, Farah; Shah, Syed (2020). "Age, Comorbidities, and Mortality Correlation in COVID-19 Patients: A Review," *The University of Louisville Journal of Respiratory Infections*: Vol. 4, Iss. 1, Article 69.

Received Date: September 16, 2020

Accepted Date: November 4, 2020

Published Date: November 23, 2020

Funding Source: The author(s) received no specific funding for this work.

Conflict of Interest: All authors declared no conflict of interest in relation to the main objective of this work.

Introduction

The first case of Severe Acute Respiratory Syndrome-related Coronavirus-2 (SARS-CoV-2) was reported in Wuhan, China in December 2019. The World Health Organization (WHO) recognized this virus as a global pandemic on March 11, 2020. [1] It is caused by a positive–sense RNA virus. It is a highly infectious virus, and has been reported to have 1-5% mortality rate or more. [2] Individuals from all age groups are susceptible to SARS-CoV-2 infection. Coronavirus disease-2019 (COVID-19) is the syndrome caused by this virus, and is associated with higher mortality than influenza. [3] It is difficult to estimate the COVID-19 global mortality, given the high variability in testing and management strategies adopted in different countries. The COVID-19 mortality rate is calculated as the number of deaths due to COVID-19 divided by the total COVID-19 cases. The total cases available to count are those who are evaluated either test positive or are clinically diagnosed despite a negative test. However, it's a challenge to capture the total cases of COVID-19, because it is difficult to trace asymptomatic cases, especially with limited resources and inadequate testing in some parts of the world. [4] The mortality rate due to COVID-19 varies among different age groups in different countries. [5]

The age-related mortality risk cannot be estimated accurately with the current limited information regarding prevalence, mortality and overall epidemiology of COVID-19. [6]

There is an urgent need to know the epidemiology of the novel virus and characterize its potential impact. This information is essential for the healthcare community to evaluate the risk of COVID-19 in patients, and design health and economic policies. We will describe the mortality in COVID-19 patients as they relate to different age groups and comorbidities in this review.

Methods

Data sources and search strategy

We conducted a literature search for articles published (including ahead of print) until May 16, 2020 in PubMed, Embase, and Cochrane (CENTRAL). The search was conducted on May 14, 2020. Articles reporting mortality rates from COVID-19 were included in the review. We searched articles by using keywords with combinations of "COVID-19" AND "mortality", "coronavirus" AND "mortality", "SARS-CoV-2" AND "mortality". Studies that did not report data about mortality or death rate due to COVID-19 were excluded from this review. Studies conducted in hospital, outpatient, or intensive care unit (ICU) were included. Duplicate publications, reviews, editorials, case reports, letters, surveillance, non-English and articles predicting mortality were not included. A flow diagram of literature search is shown in **Figure 1**.

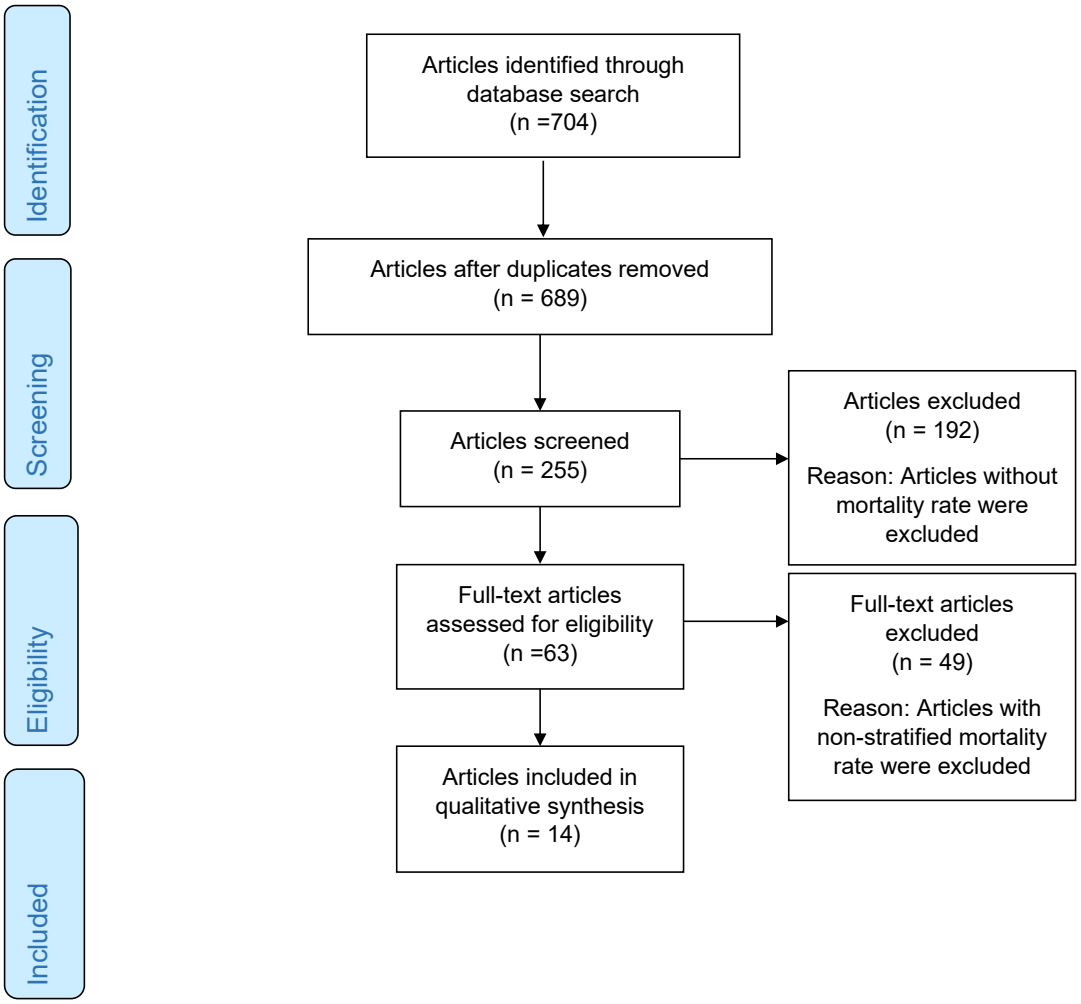

Figure 1. Flow Diagram

Data extraction

Two authors independently reviewed each article by reviewing title and abstract using Rayyan. [7] The full text of included articles was reviewed. Any conflict between two authors for selecting studies for this review were resolved through discussion and review by a third author. The following variables were extracted: author, study type, date, age, gender, total number of participants, comorbidities, mortality rate.

We identified a total of 704 articles. After removing duplicates, the authors checked the title, abstract and full articles of included studies. The primary outcome of our analysis was in-hospital mortality. Studies that reported mortality rate not stratified by comorbidities or by age group were excluded. Out of these, we found fourteen studies where mortality rate was stratified by comorbidities or by age groups. These studies were included into this review.

Table 1. Studies characteristics included in analysis.

	Study	Study Design	City, Country	Hospital Setting	Total patients	Males, N (%)	Median age[years] (IQR)
1.	Fei Zhou et al [8]	Retrospective, multicenter cohort study	Wuhan, China	Inpatients	191	119(62)	56·0 (46·0–67·0)
2.	Xiaobo Yang et al [9]	Retrospective observational	Wuhan, China	Intensive care unit	52	35(67)	59·7 (13·3)
3.	Mingli Yuan et al [10]	Retrospective	Wuhan, China	Inpatient	27	12(45)	60 (47–69)
4.	Giacomo Grasselli et al [11]	Retrospective case series	72 hospitals, Lombard, Italy	Intensive care unit	1591	1304 (82)	63 (56-70)
5.	Jianlei Cao et al [12]	Retrospective cohort	Wuhan, China	Inpatient	102	54(52)	54 (37-67)
6.	Tao Chen et al [13]	Retrospective case series	Wuhan, China	Inpatients	274	171 (62)	62.0 (44.0-70.0)
7.	Xun Li et al [14]	Retrospective	Wuhan, China	Inpatients	25	10(40)	71.48* ± 12.42
8.	Nikpouraghdam M et al [15]	Retrospective	Tehran, Iran	Inpatients	2968	1958(66)	56(46-65)
9.	Safiya Richardson [16]	Retrospective	12 hospitals, New York, USA	Inpatients	5700	3437(60)	63(52-75)
10.	Bicheng Zhang [17]	Retrospective	Wuhan, China	Inpatients	82	54 (66)	72.5 (65.0-80.0)
11.	Lin Fu et al [18]	Retrospective	Wuhan, China	Inpatients	200	99 (49)	NA
12.	TieLong Chen et al [19]	Retrospective	Wuhan, China	Inpatients	203	108 (53)	54 (41–68)
13.	Yang Wang [20]	Retrospective	Wuhan, China	Intensive care unit	344	179 (52)	64 (52-72)
14.	Rong-Hui Du [21]	Prospective	Wuhan, China	Inpatients	179	97 (54)	57.6*±13.7
Total					**11938**	**7637**	

*= Mean age
NA=Not available

Table 2. Mortality reported in studies stratified by comorbidities.

Risk Factor	Mortality (%)
Hypertension	41
Diabetes	21
Chronic cardiac diseases	14
Smoking	13
Cerebrovascular disease	10
Chronic obstructive pulmonary disease (COPD)	8
Chronic kidney disease	4

Table 3. Mortality reported in studies stratified by age.

Age group	Mortality (%)
0-19 years	0%
20-29 years	0.3%
30-39 years	1%
40-59 years	16%
≥60 years	82%

Results

We reviewed 14 studies, which included 13 retrospective and one prospective study. Eleven studies were conducted in Wuhan, China. A total of 11,938 confirmed COVID-19 patients were included in the review. Among these total patients, 7637 (64%) were males. All patients included in the review were hospitalized patients with confirmed diagnosis of COVID-19. The diagnostic test used for confirmation was reverse transcriptase-polymerase chain reaction assay of nasal or pharyngeal swabs.

Our review reported hypertension, diabetes, cardiac diseases as the most common underlying diseases among patients who died during hospitalization due to COVID-19. Chronic cardiac diseases included chronic heart disease and coronary heart disease. Social history of current smoking was present in 13% of patients.

The total number of patients who died in the hospital was 1744 (15%). Among the patients who died in the hospital, 1% were 30-39 years old, 16% were 40-59 years and 82% were more than 60 years of age.

Discussion

The analysis from this manuscript demonstrates that age and presence of underlying diseases correlate with risk of death from COVID-19. The severity of disease presentation increases with age. The most common co-morbidity was hypertension among hospitalized patients who died from SARS-CoV2. Patients with cardiovascular disease and diabetes were also at high risk of death from this pathogen. Interestingly, our data also demonstrates that male sex was associated with higher mortality.

Multiple studies have corroborated our findings that elderly patients are at a higher risk of mortality from COVID-19. [22] Approximately 80% of deaths occurred among adults over the age of 60-years. One mechanism of this phenomenon is that older age can lead to defects in T cell and B cell function, causing an excess inflammatory response contributing to worse outcomes. [8] Furthermore, several studies have demonstrated that hypertension and cardiovascular disease portends poor prognosis. [23] Patients with a history of hypertension have 2.5-fold higher risk of fatal COVID-19, especially older age groups when compared to patients without hypertension. [24] Another study demonstrates that the presence of cardiovascular risk factors does not increase the likelihood of developing the infection but are associated with an increased COVID-19-related mortality. [2,23] One potential mechanism of cardiovascular events from SARS-CoV-2 is from the release of cytokines and chemokines that can precipitate vascular inflammation, plaque instability and myocardial inflammation. [25] A recent study reported myocardial injury in 20% of patients confirmed with COVID-19, and who were associated with a higher mortality rate. [26]

Our data suggest that diabetes is a prominent co-morbid condition that increases the risk of COVID-19 related morbidity. Diabetic patients are more likely to be older than non-diabetes patients, whereas older age is also associated with higher mortality due to COVID-19. [27] Previous studies have also reported an association of diabetes with poor prognosis in other viral infections like seasonal influenza, H1N1 influenza, and Severe Acute Respiratory Syndrome (SARS). [28,29,30] There is scarce data about glucose metabolism and the development of acute complications of diabetes like ketoacidosis in patients with COVID-19. Infection due to SARS-CoV-2 in patients with diabetes possibly triggers higher stress conditions by releasing hyperglycemic hormones like glucocorticoids and catecholamines that can lead to increased blood glucose levels. [31] In diabetic patients, COVID-19 can progress rapidly to acute respiratory distress syndrome, septic shock and organ failure. [31] Diabetes causes impaired neutrophil chemotaxis and phagocytosis which predisposes diabetic patients to infections in general. [32]

Our study also demonstrates that male sex was associated with higher mortality. A recent case study conducted at a hospital in Wuhan, China also showed a higher percentage of males died compared to females. This study showed that men were approximately two times more likely than females to die from COVID-19, and that sex is an independent risk

factor for severity and mortality in COVID-19 patients. [22]

Our review has few limitations. As most of the studies are from China and may present a location bias in the results. Furthermore, not all case studies reported co-morbid conditions related to COVID-19 mortality. Our study only utilized descriptive statistics and did not calculate if co-morbid conditions or age were independent predictors of outcomes. Because of the descriptive nature of these data, attack rates among patients with and without underlying health conditions could not be compared, and thus the risk difference of severe disease with COVID-19 between these groups could not be estimated. However, this is one of the few studies to review the risk of age and co-morbidities from COVID-19. Future prospective studies will be essential to corroborate these findings.

In conclusion, older patients with underlying disease appear to be at a higher risk of mortality from COVID-19. Comorbidities are significant predictors of mortality in COVID-19 patients. More studies are needed to understand underlying pathophysiological mechanisms of risk-factors and age in association with COVID-19.

Acknowledgements

The authors acknowledge the efforts of University of Louisville Pneumonia Study Group University of Louisville, Louisville, Kentucky, as well as Forest W. Arnold, DO, MSc, Associate Professor of Medicine, Division of Infectious Diseases, University of Louisville, Louisville, KY.

References

1. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed. 2020 Mar;91(1):157–60. PMID:32191675
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the chinese center for disease control and prevention. JAMA. 2020 Apr;323(13):1239–42. https://doi.org/10.1001/jama.2020.2648 PMID:32091533
3. Adams JG, Walls RM. Supporting the health care workforce during the COVID-19 global epidemic. JAMA. 2020 Apr;323(15):1439–40. https://doi.org/10.1001/jama.2020.3972 PMID:32163102
4. Zhou X, Li Y, Li T, Zhang W. Follow-up of asymptomatic patients with SARS-CoV-2 infection. Clin Microbiol Infect. 2020 Jul;26(7):957–9. https://doi.org/10.1016/j.cmi.2020.03.024 PMID:32234453
5. Rajgor DD, Lee MH, Archuleta S, Bagdasarian N, Quek SC. The many estimates of the COVID-19 case fatality rate. Lancet Infect Dis. 2020 Jul;20(7):776–7. https://doi.org/10.1016/S1473-3099(20)30244-9 PMID:32224313
6. Lipsitch M, Swerdlow DL, Finelli L. Defining the epidemiology of Covid-19 - studies needed. N Engl J Med. 2020 Mar;382(13):1194–6. https://doi.org/10.1056/NEJMp2002125 PMID:32074416
7. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016 Dec;5(1):210. https://doi.org/10.1186/s13643-016-0384-4 PMID:27919275
8. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 Mar;395(10229):1054–62. https://doi.org/10.1016/S0140-6736(20)30566-3 PMID:32171076
9. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020 May;8(5):475–81. https://doi.org/10.1016/S2213-2600(20)30079-5 PMID:32105632
10. Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. PLoS One. 2020 Mar;15(3):e0230548. https://doi.org/10.1371/journal.pone.0230548 PMID:32191764
11. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the lombardy region, Italy. JAMA. 2020 Apr;323(16):1574–81. https://doi.org/10.1001/jama.2020.5394 PMID:32250385
12. Cao J, Tu WJ, Cheng W, Yu L, Lei Y, Lui YK, et al. Clinical features and short-term outcomes of 102 patients with coronavirus disease 2019 in Wuhan, China. Clin Infect Dis. 2020 Mar;71(15):748-755.
13. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020;368:m1295. doi: https://doi.org/10.1136/bmj.m1295
14. Li X, Wang L, Yan S, Yang F, Xiang L, Zhu J, et al. Clinical characteristics of 25 death cases with COVID-19: a retrospective review of medical records in a single medical center, Wuhan, China. In J Infect Dis. 2020 Apr 3.
15. Nikpouraghdam M, Farahani AJ, Alishiri G, Heydari S, Ebrahimnia M, Samadinia H, et al. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: a single center study. J Clin Virol. 2020 Apr 21.
16. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al.; the Northwell COVID-19 Research Consortium. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the new york city Area. JAMA. 2020 May;323(20):2052–9. https://doi.org/10.1001/

jama.2020.6775 PMID:32320003
17. Zhang B, Zhou X, Qui Y, Song Y, Feng F, Feng J, et al. Clinical characteristics of 82 cases of death from COVID-19. PLos One. [journal on the Internet]. 2020 Jul 9;15(7):e0235458. https://doi.org/10.1371/journal.pone.0235458 PMID: 32645044
18. Fu L, Fei J, Xiang HX, Xiang Y, Tan ZX, Li MD, et al. Influence factors of death risk among COVID-19 patients in Wuhan, China: a hospital-based case-cohort study. MedRxiv. 2020 Jan 1.
19. Chen T, Dai Z, Mo P, Li X, Ma Z, Song S, et al. Clinical characteristics and outcomes of older patients with coronavirus disease 2019 (COVID-19) in Wuhan, China (2019): a single-centered, retrospective study. J Gerontol A Biol Sci Med Sci. 2020 Sep.
20. Wang Y, Lu X, Li Y, Chen H, Chen T, Su N, et al. Clinical course and outcomes of 344 intensive care patients with COVID-19. Am J Respir Crit Care Med. 2020 Jun 1;201(11):1430-4.
21. Du RH, Liang LR, Yang CQ, Wang W, Cao TZ, Li M, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J. 2020 May;55(5):2000524. https://doi.org/10.1183/13993003.00524-2020 PMID:32269088
22. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, et al. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. Front Public Health. 2020 Apr;8:152–152. https://doi.org/10.3389/fpubh.2020.00152 PMID:32411652
23. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol. 2020 May;109(5):531–8. https://doi.org/10.1007/s00392-020-01626-9 PMID:32161990
24. Lippi G, Wong J, Henry BM. Hypertension in patients with coronavirus disease 2019 (COVID-19): a pooled analysis. Pol Arch Intern Med. 2020 Apr;130(4):304–9. PMID:32231171
25. Bonow RO, Fonarow GC, O'Gara PT, Yancy CW. Association of coronavirus disease 2019 (COVID-19) with myocardial injury and mortality. JAMA Cardiol. 2020 Jul;5(7):751–3. https://doi.org/10.1001/jamacardio.2020.1105 PMID:32219362
26. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol. 2020;5:802-10.
27. Hussain A, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: knowledge in progress. Diabetes Res Clin Pract. 2020 Apr;162:108142–108142. https://doi.org/10.1016/j.diabres.2020.108142 PMID:32278764
28. Hong KW, Cheong HJ, Choi WS, Lee J, Wie SH, Baek JH, et al. Clinical courses and outcomes of hospitalized adult patients with seasonal influenza in Korea, 2011-2012: hospital-based influenza morbidity & mortality (HIMM) surveillance. J Infect Chemother. 2014 Jan;20(1):9–14. https://doi.org/10.1016/j.jiac.2013.07.001 PMID:24462445
29. Schoen K, Horvat N, Guerreiro NF, de Castro I, de Giassi KS. Spectrum of clinical and radiographic findings in patients with diagnosis of H1N1 and correlation with clinical severity. BMC Infect Dis. 2019 Nov;19(1):964. https://doi.org/10.1186/s12879-019-4592-0 PMID:31718571
30. Yang JK, Feng Y, Yuan MY, Yuan SY, Fu HJ, Wu BY, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabet Med. 2006 Jun;23(6):623–8. https://doi.org/10.1111/j.1464-5491.2006.01861.x PMID:16759303
31. Wang A, Zhao W, Xu Z, Gu J. Timely blood glucose management for the outbreak of 2019 novel coronavirus disease (COVID-19) is urgently needed. Diabetes Res Clin Pract. 2020 Apr;162:108118. https://doi.org/10.1016/j.diabres.2020.108118 PMID:32179126
32. Delamaire M, Maugendre D, Moreno M, Le Goff MC, Allannic H, Genetet B. Impaired leucocyte functions in diabetic patients. Diabet Med. 1997 Jan;14(1):29–34. https://doi.org/10.1002/(SICI)1096-9136(199701)14:13.0.CO;2-V PMID:9017350