ClinicSearch

International Journal of Clinical Research and Reports

Jose Luis Turabian *

Open Access

Research Article

Risk factors and Incidence Rate of Complications Originated as a Consequence of the Acute sars-cov-2 Infection or the Treatments Performed. A Longitudinal Study in General Medicine from march 15, 2020 to october 31, 2022 in toledo, Spain

Jose Luis Turabian *

Health Center Santa Maria de Benquerencia. Regional Health Service of Castilla la Mancha (SESCAM), Toledo, Spain.

***Correspondence Author:** Jose Luis Turabian, Health Center Santa Maria de Benquerencia. Regional Health Service of Castilla la Mancha (SESCAM), Toledo, Spain.

Received Date: February 02, 2023 | Accepted Date: February 21, 2023 | Published Date: March 01, 2023

Citation: Jose L. Turabian (2023), Consequence of the Acute sars-cov-2 Infection or the Treatments Performed. A Longitudinal Study in General Medicine from march 15, 2020 to october 31, 2022 in toledo, Spain, *International Journal of Clinical Research and Reports*. 2(2); **DOI:**10.31579/2835-785X/016

Abstract

Background

The epidemiological data on complications originated as a consequence of the acute infection of covid-19 or the treatments performed are not well known.

Objectives

To estimate the incidence rate and the risk factors of complications originated as a consequence of the acute infection of covid-19 or the treatments performed in general practitioner consultation

Methodology

An observational, longitudinal and prospective study of patients with covid-19 to detect complications originated as a consequence of the acute infection of covid-19 or the treatments performed in a general practice setting in Toledo, Spain, from March 15, 2020 to October 31, 2022

Results

687 positive cases of acute covid-19 were diagnosed in the general medicine consultation under study. Of these, 36 (36% were women and 39% had >=65 years old) presented complications originated as a consequence of the acute infection of covid-19 or the treatments performed, which represents a gross incidence rate of 5% cases x March 15, 2020 to October 31, 2022. In >=65 years old, incidence rate was of 23 %. The incidence rate of complications was much higher in 2020 vs. 2021 and 2022 (21%, 5% and 1% cases, respectively). The only statistically significant risk factors for complications originated as a consequence of acute infection of covid-19 or the treatments performed were aged > = 65 years (RR= 2.46), having presented moderate-severe severity of primary infection (RR= 14.54), having chronic diseases (RR= 3.11), and specifically of circulatory system (RR= 1.98).

Conclusion

In the context of general medicine in Toledo (Spain) incidence rate of complications originated as a consequence of acute infection of covid-19 or the treatments performed, was higher in cases with acute infection in 2020, and in >=65 years old, and are risk factors having presented moderate-severe severity of primary infection, having chronic diseases, and specifically of circulatory system, and being >= 65 years old.

Keywords: covid-19; complications; epidemiology; public health; general practice

Introduction

Clinical evolution of infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (covid-19), is highly variable, and can cover a wide clinical spectrum, from being asymptomatic or mild symptoms to severe respiratory failure requiring supplemental oxygen and/or mechanical ventilation and even fatal respiratory failure (1).

Although most people recover well, but in addition to its possible severity, there is a wide range of covid-19-related illnesses and organ damage, creating a complex prognostic picture (2). In severe cases of patients hospitalized with covid-19, high mortality rates are experienced, ranging from 10% to 30% (3). And of the patients discharged from the hospital, more than one in 10 will die within six months (4).

Typical coronavirus symptoms, at least in the early stage of the pandemic, included fever, cough, and shortness of breath. Less known are the complications of the disease. The vast majority of these complications appear to stem from pneumonia caused by damage to the lungs. This causes respiratory malfunction and the entry of other pathogens that aggravate pneumonia. There may be chronification of pneumonia. Also, pneumonia can continue with sepsis. Problems can occur in other organs affected by the virus, including other infectious complications, lipid disorders and diabetes, obesity, thromboembolism, bleeding and coagulation disorders. Covid-19 may also lead to septic shock associated with low blood pressure and decreased urine output with acute renal failure and chronic kidney disease, muscular atrophy secondary to assisted ventilation and prolonged hospitalization and cardiac problems such as heart failure, cardiac arrest, ventricular fibrillation, acute myocardial infarction, myocarditis, pericarditis and hypertension; Significant neurological damage has even been recorded. This has a great weight not only when overcoming the disease, but also once the patient has left the hospital (5-12).

It is currently known that covid-19 is a multisystemic disease, which can occur with complications at the time of presentation or developing during the acute phase of the disease. These complications can be respiratory, cardiovascular, renal, gastrohepatic, thromboembolic, neurological, cerebrovascular and autoimmune, among others (13-15).

Since the outbreak of the covid-19 pandemic, great efforts have been made to identify the possible determinants of increased risk of contracting the infection and developing its serious clinical manifestations within various demographic factors and medical conditions (16). Initial data seemed to indicate that 81% of cases are mild, 14% severe and 5% critical, with a 15% risk of death in people over 80 and 8% in people of more than 70 years (17). On the other hand, age and underlying pathologies seem to be the most established risk factors (18, 19). Also, a history of geriatric disease, obesity, and chronic disease are classified as risk factors for adverse outcomes of covid-19 (20).

However, some time after the covid-19 pandemic began in 2019, little is known about the complications of SARS-CoV-2 infection, which appear to be common in hospitalized patients, but the spectrum of symptoms in milder cases need further investigation (21). Thus, overall, the data on the risk of presenting complications from covid-19 are limited, as well as the importance of comorbidities in covid-19 with serious complications (20).

In this context, we present an observational, longitudinal and prospective study of patients with complications originated as a consequence of the acute infection of covid-19 or the treatments performed, whose objectives were: 1. Estimate incidence rate (IR) of complications originated as a consequence of the acute infection of covid-19 or the treatments performed; and 2. Identify the risk factors for complications originated as a consequence of the acute infection of covid-19.

Material and Methods

Design and emplacement

An observational, longitudinal and prospective study of patients with complications originated as a consequence of the acute infection of covid-19 or the treatments performed was carried out from March 15, 2020 to October 31, 2022, in a family medicine office at the Health Center Santa Maria de Benquerencia, Toledo (Spain), which has a list of 2,000 patients > 14 years of age (in Spain, the general practitioners [GPs] care for people > 14 years of age, except for exceptions requested by the child's family and accepted by the GP).

Objectives

1. Estimate IR of complications originated as a consequence of the acute infection of covid-19 or the treatments performed in GP consultation. IR was calculated by dividing the number of cases of complications originated as a consequence of the acute infection of covid-19 by the primoinfections of covid-19 in the follow-up time (from March 15, 2020 to October 31, 2022) (22). Similarly, the data on the incidence of complications originated as a consequence of the acute infection of covid-19 were extrapolated to the entire population attended in the consultation (N=2,000 people) (23).

2. Identify the risk factors for complications originated as a consequence of the acute infection of covid-19. In this sense, the variables collected were compared by calculating the relative risk (RR) as the incidence of risk factors in those exposed to complications originated as a consequence of the acute infection of covid-19 / incidence of risk factors in those not exposed to complications originated as a consequence of the acute infection of covid-19. The RR was interpreted as follows (24): From 0 to 0.5: protection factor effectively; from 0.6 to 0.8: true benefits; from 0.9 to 1.1: not significant; from 1.2 to 1.6: weak risk; from 1.7 to 2.5: moderate risk; more than 2.5: strong risk.

Inclusion criteria

The inclusion and exclusion criteria in this study have already been previously published (25). Complications were considered health problems that originated as a result of acute covid-19 infection or the treatments performed. Complications due to covid-19 were defined as those cases presenting acute respiratory infection, dyspnea (oxygen saturation less than or equal to 92%), tachypnea, clinical and/or radiological signs of pneumonia. In addition, those who required hospitalization (including admission to the intensive care unit) and death from covid-19 (26) were considered. Specific sequelae of acute covid-19 infection were excluded: when there were persistent symptoms or pathologies during acute infection or after apparent recovery from acute covid-19 infection, which are not part of acute covid-19 infection (27).

Diagnosis of covid-19

The diagnosis was performed with reverse transcriptase polymerase chain reaction (PCR) oropharyngeal swab tests or antigen testing. Spain had not initially devised an intensive testing strategy for suspected cases of covid-19 infections (28); since the beginning of the pandemic in mid-March 2020, PCR tests were only performed in the hospital context until mid-May 2020, date when they began to be performed in general medicine as well. In mid-December 2020, rapid antigen tests began for symptomatic patients with less than 5 days of evolution. The PCR tests were performed both in symptomatic patients and in asymptomatic contacts. A symptomatic confirmed case with active infection was considered to be any person with a clinical picture of sudden onset acute respiratory infection of any severity that occurs, among others, with fever, cough or feeling of shortness of breath. Other symptoms such as odynophagia, anosmia, ageusia, muscle pain, diarrhoea, chest pain or headache, among others, were also considered symptoms of suspected SARS-CoV-2 infection according to clinical criteria; plus a positive PCR or rapid antigen test positive (29).

In Spain, since April 28, 2022 there was a new "Surveillance and Control Strategy Against Covid-19" that included the non-performance of diagnostic tests, which were focused only on those over 60 years of age, immunosuppressed and pregnant women, health wokers and serious cases, as well as elimination of contact tracing (30).

Definition of cases and controls

Patients with complications originated as a consequence of the acute infection of covid-19 or the treatments performed were considered “cases.” "Control" patients were those with acute covid-19 without complications originated as a consequence of the acute infection of covid-19 or the treatments performed. Control data were obtained from previous studies in the same consultation, with the same population attended, and carried out by the same researcher (31-34).

Collected variables

The variables collected and their definitions and criteria have been previously published (25). These variables were: Age; sex; if the patient was a healthcare professional, acute covid-19 infection date; complications originated as a consequence of the acute infection of covid-19 or the treatments performed (as defined above), chronic diseases (defined as "any alteration or deviation from normal that has one or more of the following characteristics: is permanent, leaves residual impairment, is caused by a non-reversible pathological alteration, requires special training of the patient for rehabilitation, and / or can be expected to require a long period of control, observation or treatment” (35), classified according to the International Statistical Classification of Diseases and Health-Related Problems, CD-10 Version: 2019 (36); vaccination status against covid-19 at the date of acute infection; and severity of the disease (mild cases: clinical symptoms are mild and no manifestation of pneumonia can be found on images; moderate cases: with symptoms such as fever and respiratory tract symptoms, and the manifestation of pneumonia can be seen on the imaging tests; and severe cases: respiratory distress, respiratory rate ≥ 30 breaths / min., pulse oxygen saturation ≤ 93% with room air at rest, arterial partial pressure of oxygen / oxygen concentration ration ≤ 300 mmHg.) (37). To simplify comparison, moderate and severe cases were counted together.

Statistical analysis

The bivariate comparisons were performed using the Chi Square test (X2) with Yates correction or Fisher Exact Test when necessary, (according to the number the expected cell totals) for percentages.

Results

687 positive cases of acute covid-19 were diagnosed in the general medicine consultation. Of these, 36 cases (36% were women and 39% had >=65 years old) presented complications originated as a consequence of the acute infection of covid-19 or the treatments performed, which represents a gross IR of 5% cases x March 15, 2020 to October 31, 2022. In >=65 years old, IR was of 23 % cases x March 15, 2020 to October 31, 2022. IR of complications with respect to covid-19 cases was much higher in 2020 (21% cases) versus in 2021 and 2022 (5% and 1% cases, respectively) (**TABLE 1**). IR of complications originated as a consequence of the acute infection of covid-19 or the treatments performed with respect to the total population attended in that office (N= 2,000), from March 15, 2020 to October 31, 2022, was 1.8 %. The only statistically significant risk factors for complications originated as a consequence of the acute infection of covid-19 or the treatments performed were aged >= 65 years [RR= 2.46 (95% CI: 1.3, 4.67). Moderate risk; X2= 8.8539. p= .002925], having presented moderate-severe severity of primary infection [RR= 14.54 (95% CI: 8.68, 24.37). Strong risk; X2= 108.4104. p < 0.00001], having chronic diseases [RR= 3.11 (95% CI: 1.38, 7). Strong risk; X2= 8.5601. p= .003436], and specifically having chronic disease of circulatory system [RR= 1.98 (95% CI: 1.29, 3.05). Moderate risk; X2= 10.7329. p= .001052] (**TABLE 2, TABLE 3**).

Discussion

Main findings

The main results of our study were:

1. The incidence rate of complications originated as a consequence of the acute infection of covid-19 or the treatments performed was high or very high in >=65 years old (23% cases x March 15, 2020 to October 31, 2022). On the other hand, the IR of complications was much higher in 2020 versus 2021 and 2022 (21%, 5% and 1% cases, respectively).

During 2020, variants of the original Wuhan virus predominated in Spain (38). In the period from March to April, 2020, in Spain the A lineage of the coronavirus predominated, especially the SEC7 and SEC8, and from summer to December, 2020, the 20E (EU1) variant (39, 40). In the period from January 2021 the alpha variant predominated, and from the summer-autumn of 2021 the delta variant (41, 42). From January 2022 to October 2022, the omicron variant predominated (43-45).

Therefore, the data used in our study, which included information on the different epidemiological waves of the pandemic during 2020, 2021 and 2022, yield results that suggest that the Asian original virus strains are a much higher cause of serious complications than other later variants. Although it can also be influenced by the vaccination rate; it must be remembered that vaccination began in 2021. In any case, this data coincides with other publications that indicate that in 2022 cases rose 230%, but deaths barely 20% (46).

On the other hand, it must be taken into account that the "denominator" of the IR [the total number of covid-19 cases in the consultation (687 positive cases)] is probably underestimated. In Spain, since April 28, 2022 there was a new "Surveillance and Control Strategy Against Covid-19" that included the non-performance of diagnostic tests, that focused only on those over 60 years of age, immunosuppressed and pregnant women, vulnerable areas (socio-health workers) and serious cases, and the elimination of contact tracing (30). Therefore, since that date, patients carried out self-diagnosis with antigen tests purchased at a pharmacy, although they usually informed the GP of their result if it was positive. In contrast, the IR “numerator” (cases with complications originated as a consequence of the acute infection of covid-19 or the treatments performed) are probably valid, due to the characteristics of the complications itself, which requires assistance from the GP.

Consequently, it is possible that the IR of complications for the entire pandemic period is overestimated, but at the expense of the calculation for 2022 (when tests in general medicine were no longer carried out); Being so, this bias would not affect the years 2020 and 2021, dates where the cases with complications are concentrated, especially in the year 2020.

2. In our study, the following risk factors were statistically significant:

- Aged >= 65 years (Moderate risk)

- Moderate-severe severity of primary infection (Strong risk)

- Chronic diseases (Strong risk)

- Chronic disease of the circulatory system (Moderate risk)

Comparison with other studies

A fact to take into account is the difficulty of comparison due to the fact that most researchers do not differentiate the terms of "persistent symptoms", "sequels" and "complications" of covid-19, using these words as interchangeable , when in reality they are different concepts (26, 27, 47-50). In any case, excessive risks for complications have been observed preferentially in critically ill hospitalized patients (5). In agreement with this data, we found that having presented moderate-severe severity of primary infection supposes a strong risk factor.

On the other hand, age over 65 years has been repeatedly pointed out as an important factor that contributes to the risk of hospitalization, pneumonia, and death from covid-19. Relative risks for complications from covid-19

have been reported according to age in > 30 years of 1.28 (95%: 0.6 to 2.75), and in > 60 years 2.04 (95%: 0.88 to 4.74). Although some studies have indicated that arrhythmias, gastrointestinal bleeding and sepsis were more common in younger patients (59). We found that being >= 65 years is a moderate risk factor.

Another established risk factor is the presence of chronic diseases: cardiovascular diseases and arterial hypertension, diabetes, chronic obstructive pulmonary disease, cancer, immunosuppression, other chronic diseases, smoking and obesity. A relative risk for complications from covid-19 in the presence of comorbidity of 2.94 (95%: 1.95 to 4.42) has been reported (7-10, 26, 51, 52, 60-66). However, other studies have reported a relatively poor correlation between pre-existing risk factors and complications (59). In our study we found that presenting chronic diseases entails a strong risk, and specifically having chronic circulatory system disease a moderate risk. It has been reported that underlying heart disease can worsen the severity of any infection, including covid-19 (16, 63). In this sense, covid-19 is actually a multi-organ disease and several possible mechanisms underlying cardiac muscle injury have been proposed: direct cytotoxic damage, dysregulation of the renin-angiotensin-aldosterone system, endothelial inflammation, and dysregulation of the immune response (67).

Study limitations and strengths

1. Infections were not genetically sequenced; Thus, complications cannot be accurately ascribed to a certain variant of SARS-CoV-2.

2. The number of cases with complications was small.

3. Our prospective study based on continued GP care allowed a long follow-up time.

Conclusions

In the context of general medicine in Toledo (Spain) incidence rate of complications originated as a consequence of the acute infection of covid-19 or the treatments performed, was higher in cases with acute infection in 2020, and in >=65 years old, and are risk factors having presented moderate-severe severity of primary infection, having chronic diseases, and specifically of circulatory system, and being >= 65 years old.

References

1. Mehta P, McAuley DF, Brown M, et al. (2020) COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet; 395(10229): 1033-1034.
2. Godlee F (2021) How can we manage covid fatigue? BMJ; 373: n1610.
3. Somersan-Karakaya S, Mylonakis E, Menon VP, et al. (2023) J Infect Dis; 227(1): 23–34.
4. Fraser E (2021) Persistent pulmonary disease after acute covid-19. BMJ; 373: n1565.
5. Al-Aly Z, Xie Y, Bowe B (2021) High-dimensional characterization of post-acute sequelae of COVID-19. Nature; 594: 259–264.
6. Campillo S (2020) The consequences that COVID-19 leaves in those who survive it in the ICU: kidney, neurological, cardiac and muscular damage.
7. Zhou F, Yu T, Du R, el al. (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study, Lancet; 395(10229): 1054–1062.
8. Servante J, Swallow G, Thornton JG, et al. (2021) Haemostatic and thrombo- embolic complications in pregnant women with COVID-19: a systematic review and critical analysis. BMC Pregnancy Childbirth; 21: 108.
9. Dessie ZG, Zewotir T (2021) Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients, BMC Infect Dis; 21: 855.
10. Wolff D, Nee S, Hickey NS, Marschollek M (2021) Risk factors for Covid-19 severity and fatality: a structured literature review. Infection; 49: 15–28.
11. Robitzski D (2022) Doctors and Researchers Probe How COVID-19 Attacks the Heart. Experts have a decent grasp on how COVID-19 impacts cardiovascular health in the near term. The implications of long COVID, however, remain mysterious.
12. Sarfraz Z, Sarfraz A, Barrios A, et al. (2021) Cardio-Pulmonary Sequelae in Recovered COVID-19 Patients: Considerations for Primary Care. J Prim Care Community Health
13. Aiyegbusi OL, Hughes SE, Turner G, et al. (2021) Symptoms, complications and management of long COVID: a review. J R Soc Med; 114(9): 428-429.
14. Salari N, Khodayari Y, Hosseinian-Far A, et al. (2022) Global prevalence of chronic fatigue syndrome among long COVID-19 patients: A systematic review and meta-analysis. BioPsychoSocial Med; 16: 21.
15. Gao YD, Ding M, Dong X, et al. (2021) Risk factors for severe and critically ill COVID-19 patients: A review. Allergy; 76(2): 428-455.
16. Bianconi V, Cosentini E, Mannarino MR, Pirro M (2022) Risk Factors of Developing COVID-19 and its Severe Course. In: Banach, M. (eds) Cardiovascular Complications of COVID-19. Contemporary Cardiology. Humana, Cham.
17. Wu Z, McGoogan JM (2020) 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; 323(13): 1239–1242.
18. Yang J, Zheng Y, Gou X, et al. (2020) Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis; 94:91-95.
19. Wu C, Chen X, Cai Y, et al. (2020) Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med; 180(7): 934-943.
20. Nugraha PK, Kusuma E, Sulistiawan SS, Husain TA (2021). Comorbidities as Risk Factors for Mortality in COVID-19 Acute Respiratory Distress Syndrome Adult Patients: A Single-Center Retrospective Study.
21. Blomberg B, Mohn KGI, Brokstad KA, et al. (2021) Long COVID in a prospective cohort of home-isolated patients. Nat Med; 27: 1607–13.
22. Nandí-Lozano E, Espinosa LE, Viñas-Flores L, Avila-Figueroa C (2002) [Acute respiratory infection in children who go to a child development center]. Salud Publica Mex; 44:201-206.
23. Cauthen DB (1994) Family practice incidence rates. JABFP; 7: 303-309.
24. Rey Calero J (1989) [Epidemiological method and community health]. Madrid: Interamericana. McGraw-Hill.
25. Turabian JL (2023) Complications Originated as a Consequence of the Acute Infection of COVID-19 or the Treatments Performed. Case Series in General Medicine from March 15, 2020 to October 31, 2022, in Toledo, Spain. Medp Public Health Epidemiol; 2(1): mpphe–202301001.
26. Pacheco Campos L, Dávila Aliaga C, Espinola Sánchez M (2022) Factors associated with complications from COVID-19 in hospital workers: A retrospective cohort study. Medwave.
27. Huang Y, Pinto MD, Borelli JL, et al. (2022) COVID Symptoms, Symptom Clusters, and Predictors for Becoming a Long-Hauler Looking for Clarity in the Haze of the Pandemic. Clin Nurs Res; 31(8): 1390-1398.
28. Montenegro P, Brotons C, Serrano J, et al. (2021) Community seroprevalence of COVID-19 in probable and possible cases at primary health care centres in Spain. Family Practice; 38(2): 154–159.

29. Instituto de Salud Carlos III (2020) [Strategy for early detection, surveillance and control of COVID-19. Updated December 22, 2021]. Ministerio de Sanidad. España.
30. Turabian JL (2022) An ostrich strategy for covid-19 is too risky. BMJ; 377: o1112.
31. Turabian JL (2022) Covid-19 Breakthrough Infections In Vaccinated People With Vaccine Booster In 2022 Versus Covid-19 Cases In Unvaccinated People In 2020: A New Disease Whose Clinic We Should Know Or Another Cause Of The Old Symptoms Of The Common Cold? J General medicine and Clinical Practice; 5(2).
32. Turabian JL (2022) Secondary infections in the family from primary cases of covid-19 breakthrough infections in fully vaccinated or not fully vaccinated people. Two doses modestly reduce family transmission but does not eliminate it. Journal of SARS-CoV-2 Research; 2: 12-24.
33. Turabian JL (2022) Risk Factors and Incidence Rates of Covid-19 Breakthrough Infections in Vaccinated People in General Medicine Practice in Toledo (Spain). Arch Fam Med Gen Pract; 7(1):183-192.
34. Turabian JL (2022) Incidence Rates and Risk Factors of Covid-19 Reinfections from March 1, 2020 To July 1, 2022 in A General Medicine office in Toledo, Spain. Ann Community Med Prim Health Care; 1(1): 1006.
35. Strauss AL (1984) Chronic illness and the quality of life. St Louis: The C.V. Mosby Company.
36. WHO (2019) International Statistical Classification of Diseases and Health-Related Problems. ICD-10 Version
37. Mao S, Huang T, Yuan H, et al. (2020) Epidemiological analysis of 67 local COVID-19 clusters in Sichuan Province, China. BMC Public Health; 20: 1525.
38. Díez-Fuertes F, Iglesias-Caballero M, García-Pérez J, et al. (2021) A Founder Effect Led Early SARS-CoV-2 Transmission in Spain. Virol J; 96(3): e01583-20.
39. López MG, Chiner-Oms Á, García de Viedma D, et al. (2021) The first wave of the COVID-19 epidemic in Spain was associated with early introductions and fast spread of a dominating genetic variant. Nat Genet; 53: 1405–1406.
40. Hodcroft EB, Zuber M, Nadeau S, et al. (2020) Spread of a SARS-CoV-2 variant through Europe in the summer of 2020, Nature; 595: 707.
41. Centro de Coordinación de Alertas y Emergencias Sanitarias (2021) [Update on the epidemiological situation of variant B.1.1.7 of SARS-CoV-2 and other variants of interest]. Ministerio de sanidad. Gobierno de España.
42. García Marín AM, Chiner Oms A, González Candelas F, Comas Espadas I, López MG, Coscolla Devis M (2021) [What genomic epidemiology teaches us about the waves of COVID-19 in Spain (and how to avoid a new wave)]. The Conversation; 11 de Julio.
43. Evaluación rápida de riesgo (2022) [SARS-CoV-2 variants in Spain: Ómicron lineages BA.2.12.1, BA.4 and BA.5 11th update, June 28, 2022]. Centro de Coordinación de Alertas y Emergencias Sanitarias. Ministerio de sanidad. España.
44. Centro de Coordinación de Alertas y Emergencias Sanitarias (2022).[Update of the epidemiological situation of SARS-CoV-2 variants in Spain. May 17, 2022]. Ministerio de Sanidad. España.
45. Centro de Coordinación de Alertas y Emergencias Sanitarias (2022) [October 17, 2022 Update on the epidemiological situation of SARS-CoV-2 variants in Spain]. Ministerio de Sanidad. España.
46. Emergency Situational Updates (2022) Weekly epidemiological update on COVID-19 - 21 December 2022. Edition 123. WHO; 21 December 2022.
47. Greenhalgh T, Sivan M, Delaney B, Evans R, Milne R (2022) Long covid—an update for primary care. BMJ; 378: e072117.
48. WHO (2021) A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021.
49. Frellick (2022) [When is COVID-19 not persistent, but intermediate?]. Medscape; 3 de mayo.
50. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV, on behalf of theWHO Clinical Case Definition Working Group on Post-COVID-19 Condition (2021) A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis.
51. Oliva-Sánchez PF, Vadillo-Ortega F, Bojalil-Parra R, Martínez-Kobeh JP, Pérez-Pérez JR, Pérez-Avalos JL (2022) [Risk factors for COVID-19 severe complications comparing three major epidemiological waves: An approach from primary health care in Mexico]. Aten Primaria; 54(11): 102469.
52. Mayo Clinic Staff (2022) COVID-19: Who's at higher risk of serious symptoms? Mayo Clinic; Sept. 27.
53. Reilev M, Kristensen KB, Pottegård A, et al. (2020) Characteristics and predictors of hospitalization and death in the first 11122 cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: a nationwide cohort. Int J Epidemiol; 49(5): 1468-1481.
54. Nie Y, Li J, Huang X, Guo W, et al. (2020) Epidemiological and clinical characteristics of 671 COVID-19 patients in Henan Province, China. Int J Epidemiol; 49(4): 1085-1095.
55. Ortiz-Brizuela E, Villanueva-Reza M, González-Lara MF, et al. (2020) CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF PATIENTS DIAGNOSED WITH COVID-19 IN A TERTIARY CARE CENTER IN MEXICO CITY: A PROSPECTIVE COHORT STUDY. Rev Invest Clin; 72(3): 165-177.
56. Pérez-Sastré MA, Valdés J, Ortiz-Hernández L (2020) [Clinical characteristics and severity of COVID-19 among Mexican adults]. Gac Med Mex.; 156(5): 373-381.
57. Hernández-Ávila M, Vieyra-Romero W, Gutiérrez-Díaz H, et al. (2021) [Epidemiological behavior of SARS-CoV-2 in the working population affiliated with the Mexican Social Security Institute]. Salud Publica Mex; 63(5): 607-618.
58. Ioannou GN, Locke E, Green P, et al. (2020) Risk Factors for Hospitalization, Mechanical Ventilation, or Death Among 10 131 US Veterans With SARS-CoV-2 Infection. JAMA Netw Open; 3(9): e2022310.
59. Zhang H, Wu Y, He Y, et al. (2022) Age-Related Risk Factors and Complications of Patients With COVID-19: A Population-Based Retrospective Study. Front Med (Lausanne); 8: 757459.
60. Centro de Coordinación de Alertas y Emergencias Sanitarias (2021) [SCIENTIFIC-TECHNICAL INFORMATION Coronavirus disease, COVID-19 Update, January 15, 2021]. Ministerio de Sanidad. España.
61. Anónimo (2023) [Who are the people at risk of Covid?] Redacción Médica.
62. CDC (2022) Factors That Affect Your Risk of Getting Very Sick from COVID-19. Updated Oct. 19, 2022. Last Updated Oct. 19, 2022. National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases.
63. Nania R (2020) [How chronic illnesses complicate coronavirus infections. Diabetes and heart disease increase the risk of the country's population becoming seriously ill from COVID-19]. AARP; 2 de abril.
64. Gupta A, Madhavan MV, Sehgal K, et al. (2020) Extrapulmonary manifestations of COVID-19. Nat Med; 26(7): 1017-1032.
65. Richardson S, Hirsch JS, Narasimhan M, et al. (2020) Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA; 323(20): 2052-2059.
66. Bello-Chavolla O, Bahena-López J, Antonio-Villa N, et al. (2020) Predicting Mortality Due to SARS-CoV-2: A mechanistic score relating obesity and diabetes to COVID-19 Outcomes in México. J Clin Endocrinol Metab; 105:1–10.