# Journal of Current Trends in Infectious Diseases Research and Treatment





Research Article

# Comparison of Chronic Diseases in Cases of Covid-19 Between 2020, 2021, 2022, 2023 and 2024

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#### **Abstract**

# **Background**

It is not clear how chronic have varied comorbidities in patients with covid-19h in the community throughout the pandemic and endemic time.

#### **Objective**

To compare chronic diseases in cases of covid-19 during 2020, 2021, 2022, 2023 and 2024 years in the same population in general medicine.

#### Methodology

Comparison of secondary data among covid-19 cases in 2020, 2021, 2022, 2023 and 2024 years of previous studies, all of them carried out in the same population of patients treated in a general medicine office in Toledo, Spain.

#### **Results**

100 covid-19 cases were included in 2020, 42 in 2021, 46 in 2022, 76 in 2023 and 54 in 2024. The frequency of covid-19 cases with chronic diseases increased significantly from 2020 to 2024, as did the age of cases. By chronic disease groups, these tended to increase in Neoplasms, Mental and Nervous and Senses, and to decrease in Endocrine, Circulatory system and Respiratory system. However, no statistically significant differences were found in the evolution of the presence of chronic disease groups in covid-19 cases in 2020, 2021, 2022, 2023 and 2024, except in the Musculoskeletal disease group which showed irregular percentages. and whose frequency was significantly higher in 2021.

#### **Conclusions**

In the context of general medicine in Toledo (Spain), from 2020 to 2024, the trend is observed that cases of covid-19 are more frequently over 65 years of age and with more comorbidity, than tends to modify the pattern of the pandemic start and be lower in Endocrine, Circulatory system and Respiratory system, and higher in Neoplasms, Mental and Nervous and Senses, in 2024.

**Keywords:** COVID-19, SARS-CoV-2, Chronic Conditions, Comorbidity, Epidemiological Characteristic, Secondary Analysis, General Practice

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Received Date: 13-Nov-2024 Accepted Date: 18-Nov-2024 Published Date: 25-Nov-2024

# Introduction

It is well known that coronavirus disease 2019 (covid-19) shows greater severity if there are comorbidities, particularly severe comorbidities and multimorbidity, that reduce organ reserve, impair the emergency immune/hematopoiesis response and serve as general markers of aging [1-5].

So, covid-19 Patients at risk are people who suffer from multiple diseases, or are immunocompromised. The association of infection with comorbidities as diabetes mellitus, arterial hypertension, obesity, chronic kidney disease and chronic obstructive pulmonary disease, darkens the prognosis and causes complications [6-10].

Thus, it is evident that identifying comorbidities that can be risk factors for severe cases and also in community mild-moderate cases can be useful to guide public health interventions to protect the most vulnerable groups of the population against covid-19. For example, information on risk comorbidities for covid-19 can be used to design risk stratification tools and clinical pathways, thereby establishing more

effective early intervention strategies and resource allocation policies [11].

However, establishing causality and determining underlying mechanisms and clinical implications has been challenging, due to the multitude of confounding factors and patient variability. Several distinct pathological mechanisms, which are not active in all patients, determine health outcomes in the three different phases of covid-19, from the initial phase of viral replication to inflammatory lung injury and post-acute sequelae. Specific comorbidities (and general multimorbidity) may exacerbate these pathological mechanisms or reduce patient tolerance to organ injury [12].

In addition, the organ involvement of severe acute respiratory syndrome coronavirus (SARS-CoV-2) has varied since 2020 as a consequence of changes in the virus and hybrid immunity, moving from a severe multiorgan disease, predominantly with lower respiratory tract involvement, to a milder disease with common cold or flu-like symptoms, and predominantly upper respiratory tract involvement [13,14].

Consequently, the frequency and importance of chronic diseases associated with covid-19 may have changed from the beginning of the pandemic in 2020 to the endemic phase of 2024. However, the evolution of the frequency of chronic diseases/comorbidities of covid-19 cases during the pandemic and subsequently in the endemic phase is unknown, and data is especially lacking in non-hospitalized (community) patients and even more its evolution over time in specific geographic areas [15].

In this context, we present a comparative study based on previously published data, to evaluate the frequency and variation of chronic diseases/comorbidities of covid-19 cases in 2020 (without vaccination), 2021 (with 1 or 2 dose vaccination), 2022 (with first booster), 2023 (with second booster) and 2024 (with third booster), from the same population attended in a general medicine consultation in these time periods.

### Material and Methods

# **Design and Emplacement**

TThis study compares data from previous observational, longitudinal and prospective studies of covid-19 infections from March, 2020 to October, 2024, already published [16-18]. All studies were conducted on the same population: patients saw in a general medicine office in Toledo, Spain, which has a list of 2,000 patients > 14 years of age (in Spain, general

practitioner (GP) care for people > 14 years of age, except for exceptions). The GPs in Spain work within the National Health System, which is public in nature, and are the gateway for all patients to the system, and each person is assigned a GP. The methodology of all studies has been previously published and here only the main elements will be repeated for the current study.

# **Outcome of Interest**

Evaluation of variation of chronic diseases of covid-19 cases in 2020, 2021, 2022, 2023 and 2024.

#### **Definition of Chronic Diseases**

It was 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, and they were classified according to the International Statistical Classification of Diseases and Health-Related Problems, CD-10 Version: 2019 [19-22].

#### **Statistical Analysis**

The comparisons were performed using the Chi Square test (X2) or test of Kruskal-Wallis, both with degrees freedom= 4.

#### **Ethical Issues**

No personal data of the patients were used, but only group results, which were taken from the clinical history.

#### **Results**

100 covid-19 cases were included in 2020, 42 in 2021, 46 in 2022, 76 in 2023 and 54 in 2024. The frequency of covid-19 cases with chronic diseases increased significantly from 2020 to 2024 [X2 (df=4)= 19.478. p= .000633], as well as the age of the cases [X2 (df=4)= 12.7967. p= .012313] (TABLE 1, FIGURE 1). By chronic disease groups, they tended to increase in Neoplasms, Mental, and Nervous and Senses, and decrease in Endocrine, Circulatory system, and Respiratory system. However, no statistically significant differences were found in the evolution of the presence of chronic disease groups in covid-19 cases in 2020, 2021, 2022, 2023 and 2024 (% of chronic disease groups for the total in each year), except in the Musculoskeletal disease group which showed irregular

TABLE 1 : COMPARISON OF SELECTED VARIABLES AMONG COVID-19 CASES FOR EACH YEAR (2020, 2021, 2022, 2023 AND 2024)

| VARIABLES                 | COVID-19<br>CASES IN 2020<br>N=100 | COVID-19<br>CASES IN 2021<br>N=42 | COVID-19<br>CASES IN 2022<br>N=46 | COVID-19<br>CASES IN 2023<br>N=76 | COVID-19<br>CASES IN 2024<br>N=54 | STATISTICAL<br>SIGNIFICANCE                                   |
|---------------------------|------------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|---|
| > = 65 years              | 10 (10)                            | 9 (21)                            | 13 (28)                           | 21 (28)                           | 16 (30)                           | X2 (df=4)= 12.7967. p=<br>.012313. Significant at<br>p < .05. |
| Women                     | 54 (54)                            | 20 (48)                           | 27 (59)                           | 48 (63)                           | 30 (56)                           | X2 (df=4)= 3.0736. p=<br>.545593. NS                          |
| Chronic diseases presence | 51 (51)                            | 22 (53)                           | 35 (76)                           | 48 (63)                           | 44 (81)                           | X2 (df=4)= 19.478. p=<br>.000633. Significant at<br>p < .05.  |

(): Denotes percentages; NS: Not significant at p<.05; df= Degrees freedom

TABLE 2: CHRONIC DISEASES IN CASES OF COVID-19 FOR EACH YEAR (2020, 2021, 2022, 2023 AND 2024)

| CHRONIC<br>DISEASES<br>ACCORDING TO<br>WHO,<br>ICD-10 GROUPS* | COVID-19<br>CASES IN 2020<br>N=100 | COVID-19<br>CASES IN 2021<br>N=42 | COVID-19<br>CASES IN 2022<br>N=46 | COVID-19<br>CASES IN 2023<br>N=76 | COVID-19<br>CASES IN 2024<br>N=54 | STATISTICAL<br>SIGNIFICANCE                                  |
|---|------------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|--|
| -I Infectious   | 0                                  | 0                                 | 0                                 | 1 (1)                             | 2 (1)                             | Kruskal-Wallis (df=4):<br>H= 1.8281, p= .767. NS             |
| -II Neoplasms   | 3 (3)                              | 1 (1)                             | 5 (3)                             | 4 (2)                             | 14 (7)                            | Kruskal-Wallis (df=4):<br>H= 2.07. p= .722. NS               |
| -III Diseases of the blood                                    | 1 (1)                              | 3 (3)                             | 1 (1)                             | 3 (2)                             | 6 (3)                             | Kruskal-Wallis (df=4):<br>H= 1.6. p= .809. NS                |
| -IV Endocrine   | 26 (23)                            | 15 (17)                           | 24 (16)                           | 28 (18)                           | 29 (15)                           | X2 (df=4)= 3.6192. p=<br>.45999. NS                          |
| -V Mental   | 11 (10)                            | 5 (6)                             | 8 (6)                             | 15 (10)                           | 23 (12)                           | X2 (df=)= 5.2558. p=<br>.262045. NS                          |
| -VI-VIII Nervous and Senses                                   | 9 (8)                              | 11 (13)                           | 14 (10)                           | 13 (8)                            | 25 (13)                           | X2 (df=4)= 3.0978. p=<br>.541597. NS                         |
| -IX Circulatory<br>system                                     | 16 (14)                            | 10 (11)                           | 18 (12)                           | 30 (19)                           | 18 (9)                            | X2 (df=4)= 7.2432. p=<br>.123579. NS                         |
| -X Respiratory<br>system                                      | 12 (10)                            | 3 (3)                             | 8 (6)                             | 6 (4)                             | 9 (4)                             | X2 (df=4)= 7.8232. p=<br>.098275. NS                         |
| -XI Digestive<br>system                                       | 11 (10)                            | 14 (16)                           | 18 (12)                           | 22 (14)                           | 21 (11)                           | X2 (df=4)= 2.5817. p=<br>.630068. NS                         |
| -XII Diseases of<br>the skin                                  | 3 (3)                              | 0                                 | 8 (6)                             | 3 (2)                             | 4 (2)                             | Kruskal-Wallis (df=4):<br>H= 1.73. p= .786. NS               |
| -XIII Musculo-<br>skeletal                                    | 10 (9)                             | 19 (22)                           | 17 (12)                           | 8 (5)                             | 29 (15)                           | X2 (df=4)= 17.3186. p=<br>.001676. Significant at<br>p < .05 |
| -XIV<br>Genitourinary   | 10 (9)                             | 7 (8)                             | 23 (16)                           | 24 (15)                           | 16 (8)                            | X2 (df=4)= 9.0153. p=<br>.060718. NS                         |
| TOTAL*  | 112 (100)                          | 88 (100)                          | 144 (100)                         | 157 (100)                         | 196 (100)                         |  |

<sup>( ):</sup> Denotes percentages; \*Patients could have more than one chronic disease. The percentages are over the total of chronic diseases; NS: Not significant at p< .05. df=Degrees freedom

FIGURE 1: FREQUENCY OF COVID-19 CASES WITH CHRONIC DISEASES

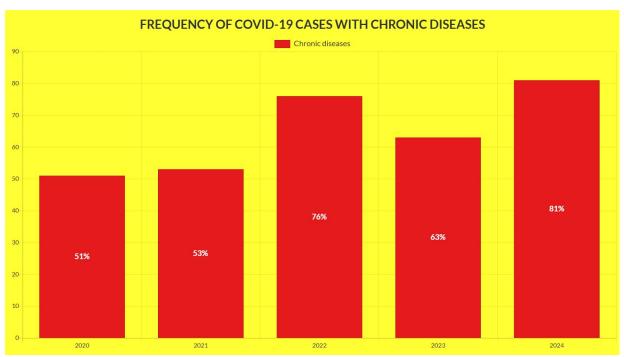


FIGURE 2: % CHRONIC DISEASES IN CASES OF COVID-19 FOR EACH YEAR (2020, 2021, 2022, 2023 AND 2024)

percentages and whose frequency was significantly higher in 2021 [X2 (4) = 17.3186. p = .001676] (TABLE 2, FIGURE 2).

# **Discussion**

# I. Main Findings

Our main findings were:

- 1. The overall frequency of cases of covid-19 with comorbidity tends to increase from 2020 to 2024, associated with the increase in cases in people over 65 years of age.
- No statistically significant differences are found by disease groups, although there is a tendency to modify the pattern accepted at the beginning of the pandemic of predominating comorbidity of Endocrine, Circulatory and Respiratory system, which decrease, while Neoplasms, Mental and Nervous and Senses increase in 2024.

Two fundamental factors must be taken into account to correctly evaluate our data: the local evolution of SARS-CoV variants and the local degree of vaccination.

Since the start of the pandemic, SARS-CoV-2 has been mutating [23]. In the period from March to April 2020, the A lineage of the coronavirus predominated in Spain, especially SEC7 and SEC8, and from summer to December 2020, the 20E (EU1) variant [24]. During 2021, the dominant variant in Spain was first delta and finally omicrom [25]. The predominant variants in Spain during 2023 were those of the XBB family [26-31]. In January 2024 in Spain, XBB.1.5-like + F456L accounted for 42% and BA.2.86 for 44% of positive cases [23]. In July and August 2024, the KP.3 lineage was detected in 84% of cases [32]. In September 2024, the incidence of the XEC variant of the coronavirus, a new Omicron subvariant was increasing markedly in Spain. At that time, it was the second most common strain in cases recorded in September, although still far behind the main KP.3.3, with an incidence of 13% [33, 34].

On the other hand, in Spain, in November 2022, more than 60% of people over 80 years of age, and 37% of people over 60 years of age, already had the second booster dose of the

covid-19 vaccine [35,36]. And 60% of the population over 80 years of age has already received the vaccine adapted against the covid-19 subvariants of the 2023/2024 campaign [37].

# 2. Comparison with other studies

Multiple studies have reported that for 2020 and 2021, in patients with SARS-CoV-2 infection, they had an average age of around 50 years, with comorbidities in 65%, and diabetes mellitus, hypertension, cardiovascular diseases, smoking, obesity and bronchial asthma were the most common underlying disorders [38-44].

It has been reported that incidence of covid-19 among patients with chronic diseases was 4.1% (74,067 cases) in 2020 and 7.3% (126,556 cases) in 2021, varying by pathology, with obesity and dementia showing the highest incidence [45].

In a meta-analysis review in the PubMed database up to 2023, it was published that it had been observed that 75% of patients hospitalized with covid-19 have, at least, one comorbidity. The most common are hypertension, diabetes, cancer, neurodegenerative diseases, cardiovascular diseases, and obesity and kidney diseases [46].

However, comorbidities associated with the disease must be put in relation to the prevalence of these pathologies in the population. It has been reported for many countries that, over time, there is a larger population with older and more chronic diseases [47]. In Spain, cardiovascular disease and diabetes mellitus are overrepresented in the cases reported to the National Surveillance Network for covid-19, with an upward gradient in the most severe cases. Chronic obstructive pulmonary disease (COPD) has an equal prevalence in the general population and covid-19 cases, while in severe cases this proportion is much higher. In cases of deaths from covid-19, a higher prevalence of cancer or neurological diseases is also observed compared to the population prevalence and non-severe cases, although the effect is less evident than in the previously described diseases. Regarding arterial hypertension, liver diseases, chronic kidney disease and immunosuppression, there does not seem to be a significant association with covid-19, according to the available data, although in other series, these conditions have been recognized as important factors associated with the poor evolution of the disease [48].

In relation to this, a study in 2022 found that, compared to the overall Medicare Fee-For-Service population, enrollees who were diagnosed with covid-19 or hospitalized for covid-19 had a higher prevalence rate across chronic conditions [49]. In another study it was estimated that compared to adults in the general population, those with covid-19 had a higher prevalence of diabetes and COPD, but a lower prevalence of cardiovascular disease [50].

In our context, a study in the same at-risk population as the current study, we found a higher prevalence of chronic diseases in the reference population in 2016 than in the covid-19 cases considered together from 2020 to 2022, and for all groups of diseases. These results suggested that, in this population, the presence of chronic comorbidities did not seem to be, in themselves, risk factors for developing covid-19 [16].

In short, the results obtained in our study show an increase in the frequency of chronic diseases (and age, with a tendency to modify the pattern of choronic diseases types accepted at the beginning of the pandemic. It can be suggested that although the presence of chronic diseases It is not by itself a risk factor for contracting covid-19, it is for the severity of the infection, and thus the identification of this variation in the comorbidities associated with the clinical presentation of covid-19 is of great importance. All this with the aim of allowing to guide the prognosis and thus carry out an early intervention, seeking to avoid severe complications and lead to the development of public health actions aimed at the prevention and protection of these vulnerable groups,

# Strengths and Weaknesses of the Study

- 1. The number of covid-19 cases were small, thus the statistical significance of some variables could be obscured.
- 2. A strength is that studies carried out on the same risk population are compared; the diagnosis of chronic disease was made with the same criteria, in the same general medicine practice, and carried out by the same researcher, which gives coherence to the results.

# **Conclusions**

In the context of general medicine in Toledo (Spain), the total frequency of cases of covid-19 with comorbidity tends to increase from 2020 to 2024, associated with the increase in cases in people over 65 years of age, but without significant differences by disease groups, although there is a tendency to modify the pattern admitted at the beginning of the pandemic of predominating comorbidity of Endocrine, Circulatory system and Respiratory system, which decrease, while Neoplasms, Mental and Nervous and Senses increase, in 2024.

In summary, In the context of general medicine in Toledo (Spain), from 2020 to 2024, there is a tendency for cases of covid-19 to be more frequently in people over 65 years of age and with more comorbidity, which tends to modify the pattern of the pandemic beginning and be lower in Endocrine, Circulatory system and Respiratory system, and higher in

Neoplasms, Mental and Nervous and Senses, in 2024. These results should be taken with caution and their direct application to other different contexts may not be appropriate.

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