

COVID-19 Pandemic Waves in Italy: An Epidemiological Overview about Infections, Swabs and Death Rates

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Abstract

Introduction: On March 11, 2020, the World Health Organization (WHO) declared that the entire World was overrun by a pandemic. Science has managed, in a short time, to characterize a new disease, sequence a new viral genome, develop diagnostics, produce treatment protocols and establish the efficacy of drugs and vaccines in randomized controlled trials. In this paper we have dealt with different topics regarding the pandemic linked to COVID-19. Objectives: Aim of this paper is to compare the number of deaths attributable to COVID-19, that occurred in the different Italian macro-areas, in the different pandemic waves; we studied the trend of the curves relating to the proportion of deaths to the number of infected in the Italian macro-areas for the pandemic waves and analysed the mortality data, focusing on the Italian context and comparing it with other foreign countries. We examined the data regarding swabs, hospitalizations, home isolation, admissions to intensive care and deaths registered in pandemic period. Results: Geographically, Italy was differently affected by the pandemic. Northern Italy was the most affected area. In comparison with some foreign countries, Italy is one of the nations that paid the most in terms of deaths, due to: delays in understanding the seriousness of the emergency; the slow management in the tracking systems of contagions; the high number of hospitalizations; a corporate organizational system poorly planned. Conclusion: The years 2020 and 2021 have been dramatic and unprecedented. The year 2021 was the year of redemption, where, despite social, economic and health difficulties, thanks to mass vaccination, we were able to give a real strong response to the pandemic. Trust in science has led to a drastic decrease in mortality throughout the world.

Keywords

Statistical Analysis, Comparisons, Swabs, Hospitalizations, Death Rates

1. Introduction

On March 11, 2020, the World Health Organization (WHO) declared that the entire World was overrun by a pandemic. As of January 4, 2020, there are approximately 300 million confirmed cases and nearly 5.5 million deaths due to COVID-19. The global epi-demiology of the disease suggests that infections and transmission of the virus vary by geographic region in which one lives, due to demographic, genetic, environmental and behavioural differences in the population, as well as socioeconomic conditions, age and associated comorbidities [1]. Coronavirus penetrates the human respiratory system and then passes from one individual to another when people sneeze, cough and talk. Peak infectivity is reached about a day before the onset of symptoms and declines within a week of the onset of symptoms. As it is now well known, SARS-COV-2 virus has, among the worst complications that of evolving into an infectious viral pneumonia of interstitial type, with symptoms related to Acute Respiratory Distress (ARDS). After the discovery of COVID-19, several vaccines have been licensed, which in the space of a few months have lowered the infection curve. Certainly, the creation of vaccines in a very short time was a rarity as well as a record. Science has managed, in a short time, to characterize a new disease, sequence a new viral genome, develop diagnostics, produce treatment protocols and establish the efficacy of drugs and vaccines in randomized controlled trials.

2. Methods

The examined data were provided by the Higher Health Institute (HHI) and refer to swabs performed (molecular and antigenic), hospitalizations, home isolation, admissions to intensive care and subsequent deaths. In this study there are no applicable criteria for the inclusion/exclusion of patients, because the data are taken from official administrative sources relating to the totality of the Italian population affected by COVID-19.

In our epidemiological study, the pandemic data are classified into 4 pandemic waves:

- the first from February 2020 until June 2020;
- the second from July 2020 to February 2021;
- the third from March 2021 until August 2021;
- the fourth and last one, from September 2021 to December 31, 2021.

As established by the World Health Organization, to decree the presence of a pandemic wave the virus must lead to a peak of infections followed by a substantial reduction phase. This situation occurred in Italy four times, albeit with peaks of different intensity (https://univadis.it/diewarticle/covid-19).

With reference to *statistical methods*, we applied:

- z test in order to perform comparison of proportions in death rates (ratio between the number of deaths attributable to COVID-19 and the infected people) between Italian macroareas (North vs Center, North vs South, Center vs South), occurred in the different pandemic waves (from February 2020 to December 31, 2021);
- Cox and Stuart test, in order to assess whether there is a significant increase or decrease in the trend of curves relating to the proportion of death rates in the Italian macro-areas during the pandemic period [2];
- z test in order to perform comparison of proportions in death rates occurred in Italy compared to some European and non-European countries, trying to individuate similarities and differences in the mortality rates.

In the comparison between Italy and other European countries, the inclusion criteria of these states refer to the identification of neighboring states to Italy with a similar socio-economic context, such as France, Germany, Spain, The United Kingdom.

In the comparison, however, between Italy and non-European countries, the choice of the same was aimed at considering different socio-economic realities.

The data on COVID mortality in Italy, used in the present work, come from the HHI and from Italian National Institute of Statistics (ISTAT). Deaths due to COVID-19 are counted as deaths due to infection, confirmed by means of molecular swab, and reported daily to the Regional Surveillance System. These data refer to the period from February 2020 to December 2021 and have been detected through criteria indicated by the European Center for Disease Prevention and Control (E.C.D.C.) and World Health Organization (WHO).

The criteria, in addition to confirmed positivity with molecular test, include:

- the presence of a clinical and instrumental picture indicative of COVID-19;
- the absence of a clear cause of death other than COVID-19;
- the absence of a period of complete clinical recovery between illness and death.

The significance level for all statistical analyses was 0.05; all significant p-values (P < 0.050) were highlighted in bold. The statistical analyses were performed using SPSS for Windows package, version 22.0.

3. Results

3.1. Epidemic Curves

The epidemic curve, *i.e.* the graph showing the number of new cases of a disease as a function of time, is one of the most common forms of displaying the trend of a disease in a population. It and its shape provide valuable information about the course of an epidemic and can help answer important questions regarding the type of exposure, the route of spread of the disease, when exposure to the disease agent occurred, what the incubation period was, etc. [3] [4] [5]. **Figure 1** shows the trend in the rate of SARS-COV-2 infections for the period February

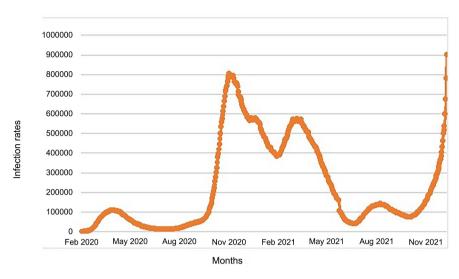


Figure 1. SARS-COV-2 infection rate (calculated as ratio between COVID-19 positive subjects and total population) during two years of pandemic in Italy.

2020-December 2021 in the Italian territory. The first phase of the epidemic was characterized by a highly localized transmission, thanks also to the preventive public health measures of "social distancing", initially limited to some restricted areas and gradually extended to the whole of Italy since March 11, 2020 ("lock-down"). On the other hand, the second phase of the epidemic involves a longer period and a higher rate of positive people, reaching a significant decrease in June 2021. The phenomena resume sudden growth in the autumn months reaching an unprecedented peak in December 2021.

An important role in the case of a pandemic is played by the "Surveillance System", whose purpose is to keep under control all the information necessary for public health, in order to decide the actions to control the problems that a disease may cause on the health of citizens. This is a crucial and delicate phase, the consequences of which have repercussions both on the mobilization of public health resources and on other public institutions and on the whole community.

3.2. The Health Crisis and the Organization of Care in Italy

Behind the social and economic crisis, the Italian National Health System (NHS) collapsed because of the exponential increase of hospitalized patients [6] [7]. It is quite evident, however, how the pandemic showed the limited economic resources made available by the NHS, which had to deal with the excessive burden placed on the shoulders of health workers (from doctors to nurses and other professional figures) in terms of working conditions [8] [9]. If we consider the data at the national level starting from February 2020 (Figure 1), we can clearly observe a trend of the epidemic based on four main peaks, in correspondence to the four pandemic waves. The first wave, unexpected and dramatic in many Italian realities, mostly affected Northern Italy and its intensity waned with the measures adopted to contain the epidemic and with the arrival of the summer

period [10]. The second wave, which exploded at the end of September, had a considerably larger size and a national spread, arriving, in mid-December, with values that were slightly decreasing but returned to rise in January and February, remaining however higher than those reached in the first wave. The second wave was also biphasic, with a slight decrease in the first months of 2021 and then a new increase in the spring of 2021. During November and December 2021, there is an increase in positivity due to the Omicron variant. **Figure 2** shows the trend of Intensive Care Unit (ICU) admissions in Italy during the four main pandemic waves. It shows the presence of spikes in ICU admissions at the start of the pandemic, then in autumn 2020 and spring 2021.

3.3. The Curves of Contagions in Italy

The trend of contagions has been monitored, especially by calculating the incidence and prevalence of cases, thanks to the data published daily by Civil Protection.

Among the factors that certainly influence the reading of numbers, so much higher than in the first wave, certainly include the spread of the epidemic throughout the Italian territory and the increased diagnostic capacity of the health service: in December 2021 values of over 1.5 million swabs per day were reached.

Figure 3 shows the trend of daily variations in the number of infected people (in brown) and in the number of swabs (in orange) performed in Italy in the period between February 2020 and December 2021; we emphasize that since January 2021 the molecular swabs have been added for SARS-COV-2 infection diagnosis.

The pandemic trend can also be reconstructed with the time series of patients in home isolation (**Figure 4**), patients admitted to ICU and hospitalized in Italy (**Figure 5**). These figures show that the number of patients in home isolation is significantly higher than those admitted to intensive care. The figures show that the number of patients in home isolation is significantly higher than those admitted to intensive care. Specifically, the comparison between the epidemic waves highlights that the first phase has seen the maximum peak of the number of patients hospitalized in intensive care, against a relatively small number of cases in home isolation. On the other hand, in the second wave an inversion of the trend of the curves was observed: although reaching very high values in hospitalizations, due to the national distribution of admissions, an increase in the values of home isolates is noted.

This trend is also observed in the third wave, which retraces the anterior phase of the pandemic. The period of spring 2021, turns out to be a pivotal point for the analysis of the fourth wave that we are still living. In fact, starting in January 2021, the mass vaccination campaign began, as well as restrictive measures for the community. From this moment on, in fact, we can observe a sudden decrease in admissions to ICUs and wards dedicated to COVID-19 patients. Only

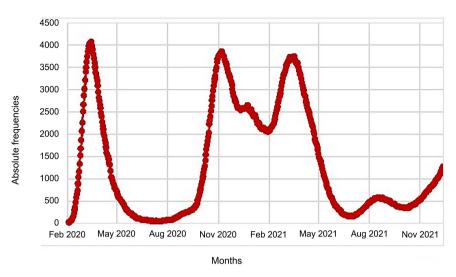


Figure 2. Trend of intensive care admissions of COVID-19 subjects in two years of pandemic in Italy.

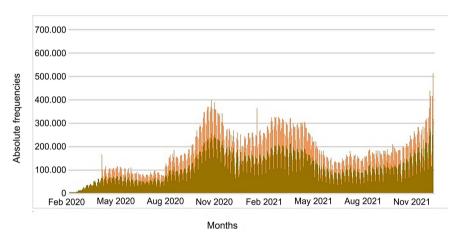


Figure 3. Trend of daily variations in the number of infected (in brown) and in the number of performed swabs (in orange) in Italy.

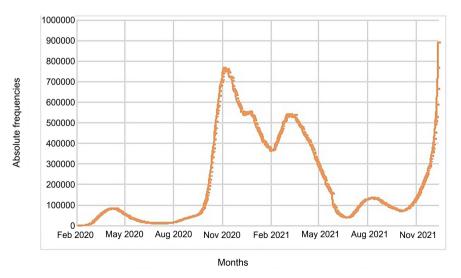


Figure 4. Trend of COVID-19 patients in home isolation in Italy.

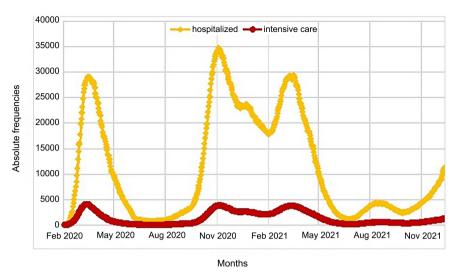


Figure 5. Trend of COVID-19 patients admitted to Intensive Care Unit and hospitalized in Italy.

with the arrival of the Omicron variant, we can speak of a real fourth wave. Admissions in ordinary hospitalization go up, even if halved compared to previous waves, but the number of positive patients in home isolation increases, a sign that, thanks to mass vaccination, hospitalization has been reduced.

3.4. Healthcare Workers: Contagion and Emotional Burden

The battle between Italian health workers and COVID-19 was characterized by moments of great criticality and resulted in a high number of infections and deaths [11].

According to data reported by HHI, since the beginning of the pandemic, the infection of healthcare personnel is about 182,000. Figure 6 highlights that the rate of infection among health workers is in line with the increase of contagions of the entire population in all pandemic waves, although the highest percentage of deaths (40%) was recorded in the first pandemic wave and, precisely, in the interval March 2020-April 2020, a period in which health workers, faced with a completely unexpected event, found themselves unprepared and also suffered from the organization and management of protections, often following guide-lines dictated by the WHO that were unclear and continuously changing.

On the other hand, the second pandemic wave was characterized by an increase in infections, which reached 25.3%, but also by a significant decrease in deaths (below 10%). These data highlight how the reshaping of healthcare management strategies has led to better preparation for the pandemic wave on the part of healthcare workers. The third and fourth wave, despite numbers of infections significantly higher than the first (only in the last weeks of December, the reports of health workers tested positive to COVID-19 are more than 15,000), have seen a complete cessation of deaths, all thanks to well-defined protocols against contagion and to vaccinations with "booster" dose. Growing fear of the possibility of contagion and illness marked, in a distinct way, the mind of

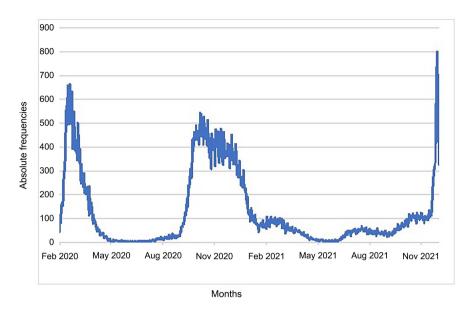


Figure 6. Trend of positive healthcare workers in two years of pandemic in Italy.

healthcare workers, showing a real challenge on their psychological and mental health impact [12]. This situation created many difficulties in balancing work, private and family life. For these reasons, the HHI has dictated some practical indications, drawn from the analysis of the literature, on the prevention of emotional stress in health workers [13] [14].

3.5. COVID-19 Mortality Analysis: Comparison between Italian Geographical Areas

We focused our attention on the mortality data, firstly analysing the Italian context and, then, comparing it with other foreign countries. In **Figure 7** and **Figure 8** we considered the total trend of deaths and deaths rates, respectively, recorded in Italy in the period ranged from February 2020 and December 2021 divided into the three geographical areas (as provided by ISTAT):

- NORTH (Lombardy, Piedmont, Liguria, Valle d'Aosta, Emilia Romagna, Friuli Venezia Giulia, Trento, Bolzano, Veneto);
- CENTER (Latium, Marche, Tuscany, Umbria);
- SOUTH (Abruzzo, Basilicata, Calabria, Campania, Molise, Puglia and the islands Sicily and Sardinia).

The North come out the most affected geographic extension, while the regions of Central and Southern Italy (although in the first pandemic wave they did not record a large incidence of mortality) since the fall of 2020 have totalled tens of thousands of deaths, due to the spread of the virus throughout the Peninsula.

As of December 31, 2021, the total number of deaths in Italy is 137,247 people.

In particular, analysing the curve in **Figure 7**, we can see that the epidemic diffusion during the first phase was characterized by an increase in deaths, mainly in the North of the country, with about 30 thousand deaths, against the few thousand that occurred in the Center and in the South. In the summer months,

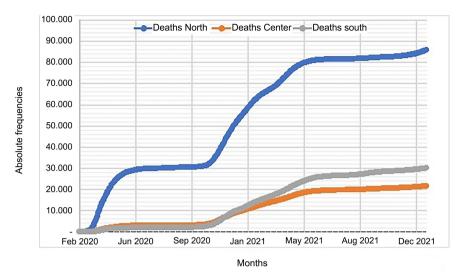


Figure 7. Trend in COVID-19 deaths in Northern, Central and Southern Italy during the pandemic.

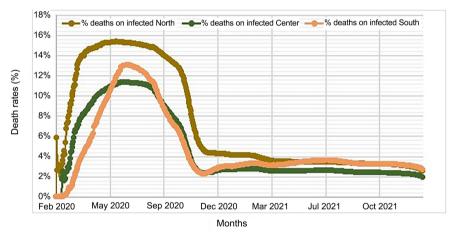


Figure 8. Trend in COVID-19 death rates (%) in Northern, Central and Southern Italy during the pandemic.

the situation was rather uniform throughout the country, while a significant worsening occurred in the second pandemic wave. In the North, the curve of deaths continued to rise, while the scenario changed in the regions of the Center and the South; in the South, there were even more deaths than in the regions of the Center. The peak of deaths, as in the previous summer, has flattened out and this trend has continued even during the fall and winter of 2021 where, despite the impressive number of positive antigenic and molecular swabs, the number of victims caused by COVID-19 are, proportionally, very few. All this thanks to the vaccination campaign promoted by the spring of 2021 that has led Italy to be an example for other nations of the world. The analysis carried out on the three Italian macro-areas has highlighted how, in reference to the number of deaths and infected, each geographical area presents a different trend than the others. Subsequently, using the data provided by HHI and ISTAT, the COVID-19 mortality rate was calculated for the entire pandemic period. Figure 8 shows that, in

all three macro-areas, the peak mortality rate reaches important numbers in the second wave, dating back to May 2020.

Focusing our attention on the data from the first pandemic wave , we can see that the North has much higher numbers of positive subjects and a higher percentage of deaths in relation to the number of infected compared to Central and Southern Italy. The Cox and Stuart test, applied to the trends of deaths recorded in the three Italian territorial divisions, allowed us to state that the trends are characterized by a significant increase (North P = 0.021; Center P = 0.035 and South P = 0.018). The comparison of proportions allowed to identify the presence of significant differences between the macro-areas; in Table 1 the results (difference, 95% confidence interval (C.I.) and p-value) show a significantly higher percentage of COVID-19 deaths in the North than in the other Italian areas (P < 0.001), while the Center and the South show similar conditions in relation to the examined variable (P = 0.222).

The same analysis was carried out for the percentage of deaths in the second pandemic wave (September 2020 and May 2021) in the three macro-areas. Italy showed a percentage decrease in the number of deaths rates (**Figure 8**). In particular, the application of Cox and Stuart test for trend provided the results: North P = 0.002; Center P = 0.008 and South P = 0.014 from which we can deduce that all decreases are statistically significant.

The results reported in Table 1 show that, in the second pandemic wave, the comparison of the death ratios significantly differs for all Italian geographical areas (P < 0.0001).

	North vs Center	North vs South	Center vs South			
	First pandemic wave					
Difference	4.38% 4.71%		0.37%			
95% C.I. *	3.9623 - 4.7877	4.2201 - 5.1843	0.2246 - 0.9586			
P-value	P < 0.0001	P < 0.0001	P = 0.222			
	S	Second pandemic wav	e			
Difference	0.20%	0.82%	1.02%			
95% C.I. *	0.1502 - 0.2493	0.7648 - 0.8757	0.9546 - 1.0854			
P-value	P < 0.0001	P < 0.0001	P < 0.0001			
		Third pandemic wave	:			
Difference	0.87%	0.02%	0.85%			
C.I. 95%. *	0.6341 - 1.1027	0.1955 - 0.2370	0.6238 - 1.0714			
P-value	P < 0.0001	P = 0.856	P < 0.0001			
		Fourth pandemic wave	e			
Difference	0.62%	0.15%	0.53%			
C.I. 95%. *	0.5422 - 0.6964	0.0669 - 0.2344	0.473 - 0.578			
P-value	P < 0.0001	P = 0.0004	P < 0.0001			

 Table 1. Results of z-test for comparison of proportions in death rates between Italian
 geographic areas in pandemic period.

*95% CI: 95% Confidence Interval. In bold, statistically significant p-value.

The third wave, although characterised by a short period, represents the first real response to the mass vaccinations that, since the beginning of the year 2021, have involved the entire Italian territory. Specifically, the p-values obtained (P < 0.001) show a significantly higher percentage of COVID-19 deaths in the North than in the other Italian areas (**Table 1**). In fact, it is possible to observe that Central Italy maintains a lower percentage of deaths than the North (P < 0.0001) and the South (P < 0.0001); North and South show similar proportions in the third pandemic wave (P = 0.856). In the fourth wave that we are still experiencing, the trend of death rates is characterized by a decrease in all three Italian areas. Comparing the deaths ratio, we can note there were highly significant differences between North vs Center (P < 0.0001), between Center vs South (P < 0.0001) and, also, between North vs South (P = 0.0004).

3.6. COVID-19 Mortality Analysis: A Comparison between Italy and Foreign Countries

In the world the pandemic has taken on uneven distribution values, especially in terms of the increase in deaths, temporally and geographically. Very high numbers have been recorded in both infections and deaths; the lethality rate still assumes high values, being the most indicative measure of a country's ability to cure. The first wave, in Europe, mainly affected Italy and Spain, increasing deaths by 40% and 50%, respectively, in the first months of the pandemic. Specifically, analyzing some of the major European countries, we can highlight that, after a year since the start of the pandemic and different ways of dealing with the emergency from the social and health point of view, the rates of deaths and infections due to COVID-19 were still high and, unfortunately, destined to increase due to the manifestation of new variants of the virus.

This trend continues throughout the year 2021, showing a uniform growth in all the analyzed countries. As of December 31, 2021, Italy has more than 6,125,683 infected people and a total of 137,247 deaths, or 2.24%. Focusing our attention on some foreign countries, we specifically found that:

- Germany has 6,816,907 infections and a percentage of deaths on infected people of 1.59%, equal to 108,352 deaths;
- Spain has 5,534,520 infected persons and 1.60% of these infected persons have died (88,794 deaths);
- France has 8,582,736 infected and 125,533 deaths, equal to 1.46%;
- Belgium has 1,999,127 infected and 27,594 deaths, equal to 1.38%;
- Albania has 205,777 infections and 3166 deaths, equal to 1.53%;
- England has 11,361,387 infections and 147,218 deaths with a lethality rate of 1.30%;
- India has 34,746,838 infections and 477,554 deaths with a lethality rate of 1.37%;
- Iran has 6,170,979 infections and 131,083 deaths, equal to 2.12;
- USA counts 50,846,941 infected and 806,437 deaths, equal to 1.60%;
- Brazil has 617,803 deaths and 22,213,762 infected, with a rate of 2.78%.

Figure 9 and Figure10 show the trends of deaths recorded both in Italy and in the examined foreign countries. All trends show a more or less accentuated increase, the variation of which can be attributed to the different pandemic containment strategies implemented in the various nations. The application of z-test (Table 2) allows to highlight the existence of highly significant differences (P < 0.0001) between Italy and all the other States examined in this study. Specifically, Italy has a higher mortality rate than all the countries examined, with the exception of Brazil, with respect to which it has a significantly lower rate.

4. Discussion

Since February 2020, Italy has reached almost 150 thousand deaths due to

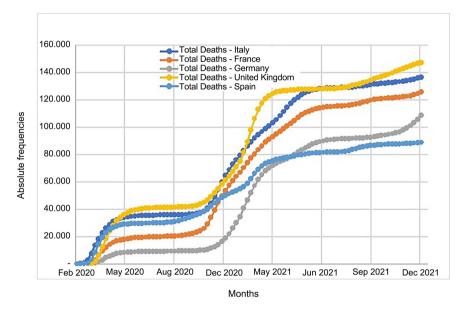


Figure 9. Trend of COVID-19 deaths during the pandemic in Italy compared to some European countries.

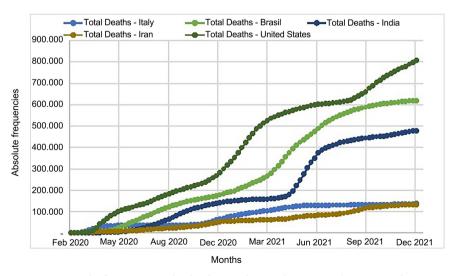


Figure 10. Trend of COVID-19 deaths during the pandemic in Italy compared to some non-European countries.

	ITALY vs				
	Germany	Spain	France	England	Belgium
Difference	0.65%	0.64%	0.78%	0.94%	0.86%
C.I. 95%*	0.635 - 0.665	0.624 - 0.656	0.766 - 0.794	0.927 - 0.953	0.842 - 0.881
P-value	P < 0.0001				
	Albania	India	Iran	USA	Brazil
Difference	1.71%	0.87%	0.12%	0.64%	0.54%
C.I. 95%*	1.676 - 1.743	8.858 - 0.882	0.104 - 0.136	0.628 - 0.652	0.526 - 0.554
P-value	P < 0.0001				

Table 2. Results of z-test for comparison of proportions in death rates between Italy vs other foreign Countries in pandemic period.

*95% CI: 95% Confidence Interval. In bold, statistically significant p-value.

COVID-19 and the whole world counts almost 5.5 million. Some terms such as incidence, prevalence, mortality, lethality have entered the common language. These terms were the basis for estimates and statistics related to infections, deaths and hospitalizations from which derived government decisions to deal with the emergency that still today continues to have important repercussions on the health of citizens, both directly and indirectly.

Geographically, Italy was differently affected by the pandemic; Northern Italy was the main region to suffer the consequences. The change of course took place a few weeks after the spring peak; important social restrictions, a reorganization and an effective management in health care have favoured a change in the curve of deaths, in constant descent until the arrival of autumn. The latter period, while suffering a significantly higher hospitalization rate than the first wave, was characterized by a decline in the percentage of deaths on the total number of infected, since the beginning of the pandemic. The ability to carry out more swabs and the organization of the Health Authorities in the management of hospitalized patients have favoured a better care in the territory resulting in a significant reduction in the lethality rate in all regions of Italy.

In conclusion, evaluating the trend of the pandemic in Italy compared to the other examined countries, we can affirm that Italy has been strongly affected both in terms of epidemiological aspects and in relation to socio-economic and health aspects.

5. Conclusion

2020 and 2021 have been two dramatic and unprecedented years. We know so much more than two years ago, when suddenly we found ourselves, almost incredulous, in front of a pandemic whose causes are still unknown, but that has represented and continues to be an emergency for the entire world. Through daily bulletins, we tried to estimate, constantly, the extent of the emergency, the forecast for the future and quantify, in some way, the "human cost". The Italian

healthcare scenario has completely changed, showing an imbalance in the management of human resources. There have been logistical deficiencies that have had repercussions on the safety of health professionals, who have paid the consequences both from a psychological and physical point of view. In spite of this, with pride, difficulty, professionalism and abnegation, they have daily responded and struggled. The year 2021 was the year of redemption, where, despite multiple social, economic and health difficulties, thanks to mass vaccination, we were able to give a real strong response to the pandemic linked to COVID-19. Trust in science, the heritage of the vast majority of the country, has led to a drastic decrease in mortality throughout the world.

6. Limitation and Future Development of the Study

Among the limitations of our paper we can include some aspects:

1) with reference to health professionals, who have personally faced the COVID emergency, it would have been desirable to administer a questionnaire, designed to assess the psychological aspects linked to the workload, from a physical and emotional point of view;

2) in the comparison between Italy and other foreign countries it could be useful to consider a greater number of countries and evaluate, for each of them, the trend of positives, swabs carried out and infected health professionals, repeating the same analysis carried out on the Italian context;

3) the data are updated as of December 31, 2021, so nothing is reported for the subsequent period, in which most of the Italian population had undergone the third dose of anti-COVID vaccine.

Different strains of coronavirus have had a great impact on the epidemic, so we propose as future development of this work to analyze the consequences deriving from the spread of the different variants of the virus in each macro-areas of the Italian territory in order to identify possible differences in terms of infectivity and mortality rates.

Author Contributions

Study concept and design: AZ, AA. Acquisition of data: FL. Analysis and interpretation of data: All authors. Statistical analysis: AZ, AA. Preparation of manuscript: All authors. Review and approval of the final version of the manuscript: All authors.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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