Title: A normalized mortality rate showed the diverse severity of Covid-19 and its association

with other chronic diseases

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Abstract

Covid-19 has given a halt to all the activities in the world. Europe was most affected, followed by the United States of America. It has taken more than 350000 lives until now. In this study, we have assessed the severity of Covid-19 by analyzing the mortality rate of Covid-19 and other chronic diseases. The Covid-19 data and "death rate" data caused by other diseases were downloaded from the world health organization (WHO) website. A normalized method was used to see the mortality rate of Covid-19 in comparison to other diseases. The deaths caused by Covid-19 in April 2020 have overtaken the average number of deaths caused by Cancer, Cardiovascular diseases, and other diseases in Belgium, the United Kingdom (UK), Spain, France, and Ireland. Covid-19 was found to be strongly correlated with non-communicable respiratory diseases and Cancer with correlation coefficients 0.73 and 0.67 respectively. The severity of Covid-19 in the United States of America (USA) was moderate. The severity of Covid-19 in Asian countries was found to be low. Europe showed the highest diversity in the mortality rate of Covid-19. On average, except for a few European countries, Cardiovascular diseases, cancer, and non-communicable respiratory diseases were still more lethal and caused more deaths than Covid-19.

Keywords: Covid-19, SARS-Cov-2, Mortality rate, Cancer, Cardiovascular disease, Respiratory disease, Diabetes, Kidney diseases, April, May

Introduction

Covid-19 has crossed a six million mark causing more than 350000 deaths worldwide in over five months[1]. It was originated in China and spread all over the world[2,3]. Europe and the United States of America (USA) were the worst affected by SARS-Cov-2 infection. The United Kingdom (UK), Italy, Spain, and France together and the USA alone have lost more than 125000 and 100000 lives in less than three months, respectively. It was on the increase in Europe and the United States of America as well as in other parts of the world.

Fever, cough, and shortness of breath were found to be the initial symptoms in Covid-19, which was caused by the SARS-Cov-2 virus infection[4]. Most of the countries have been under lockdown to stop the transmission of SARS-Cov-2. It is not completely known how Covid-19 was associated with other preexisting disease conditions and why the mortality rate differed in different countries and regions. It has been reported that Covid-19 mortality increased by multifold in preexisting cardiovascular diseases, cancer, diabetes mellitus, and kidney diseases[5,6].

In this study, we have analyzed the total death counts of Covid-19, cardiovascular diseases, cancer, respiratory diseases (non-communicable), respiratory infectious diseases, diabetes mellitus, and kidney disease to see the severity, diversity, and association of Covid-19 with other chronic diseases.

Materials and Methods

There was a different opinion on the incubation period of SARS-Cov-2 as it was reported from 5 to 14 days of incubation period[7-9]. In this study, the mortality rate of Covid-19 in comparison to other diseases was calculated for April 2020. One month can have 6 cycles of

incubation period with the least incubation period or 2 cycles of incubation period at a high incubation period of 14 days.

Two different datasets were used for this study. The first dataset on Covid-19 was downloaded from the Covid-19 dashboard set up by WHO[10]. Covid-19 data was updated until 31st May 2020. As the second dataset, the Global Health Estimate (GHE) 2016 summary table which was released in March 2018 by the Department of Information, Evidence, and Research, World Health Organization (WHO), Geneva, Switzerland was downloaded from the WHO website[11]. GHE code – 0, 380, 610, 800, 1100, 1170, and 1270, which contain data for all causes, respiratory infectious diseases, malignant neoplasms, diabetes mellitus, cardiovascular diseases, non-communicable respiratory diseases, and kidney diseases respectively were used for this study.

The mortality rate of Covid-19 was calculated by two methods. As the first method, the mortality rate was calculated by dividing the total deaths caused by Covid-19 by the total number of positive Covid-19 cases. The ratio was multiplied by 1000 to get the number of Covid-19 caused deaths per 1000 covid-19 positive cases. This method was used to see the death rate of Covid-19 among SARS-Cov-2 infected people.

The second method was based on the total number of deaths caused by Covid-19 and other diseases in a month to compare the severity of Covid-19 with other diseases. The deaths caused by injuries were subtracted from the total death counts to consider the deaths that caused by diseases only. The mortality rate caused by different diseases and reasons was converted into deaths per month. The downloaded data was in the unit of mortality per 100000 population. The given mortality rate was divided by 100000 and then multiplied by the population of that country which gave the number of deaths from various causes per year. It further divided by 12, which gave an average death occurred per month by the specific disease for the respective country. Covid-

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19 caused deaths for February, March, April, and May 2020 were calculated. The increase of Covid-19 deaths in May in comparison to April 2020 and in April in comparison to March 2020 were calculated in percentage. There was a great percentage increase and variation (in hundreds to thousands) in the number of Covid-19 deaths, so the percentage was converted into log10 value for fold change analysis. Fold change was calculated as log10(x), where x = [(number of deaths by Covid-19 in May or April 2020 - number of deaths by Covid-19 in April or March 2020)/ number of deaths by Covid-19 in April or March 2020]*100. Covid-19 caused deaths for the months of February, March, April, and May were calculated and the highest number of deaths (irrespective of month) was taken to compare with the deaths caused by cardiovascular diseases, cancer, non-communicable respiratory diseases, respiratory infectious diseases, diabetes mellitus, and kidney diseases on a monthly average. All countries who have more than 10000 SARS-Cov-2 positive patients and 100 deaths by Covid-19 by May 2020 were included in the preliminary label. Only those countries were selected for the final study where high completeness and quality of cause of death assignment was available (according to WHO norms)[12]. All death counts and percentages were rounded off to the nearest value. All the calculations performed and graphs were drawn in R version 3.6.2 and Microsoft Excel[13,14]. Shapiro Wilk normality test performed to see the normality distribution. Spearman's rank correlation analysis performed to see the association of Covid-19 with other diseases. This study did not require any ethical approval.

Results

France showed the highest mortality rate (Covid-19 caused deaths out of Covid-19 positive cases per 1000) at 193, which was followed by Belgium, UK, Italy, and the UK at 162, 143, and 141 respectively (Figure1). The mortality rate in Canada, Brazil, and the USA was at 78, 60, and

59 respectively (Figure1). Norway, the Republic of Korea, Israel, and Chile were in the bottom

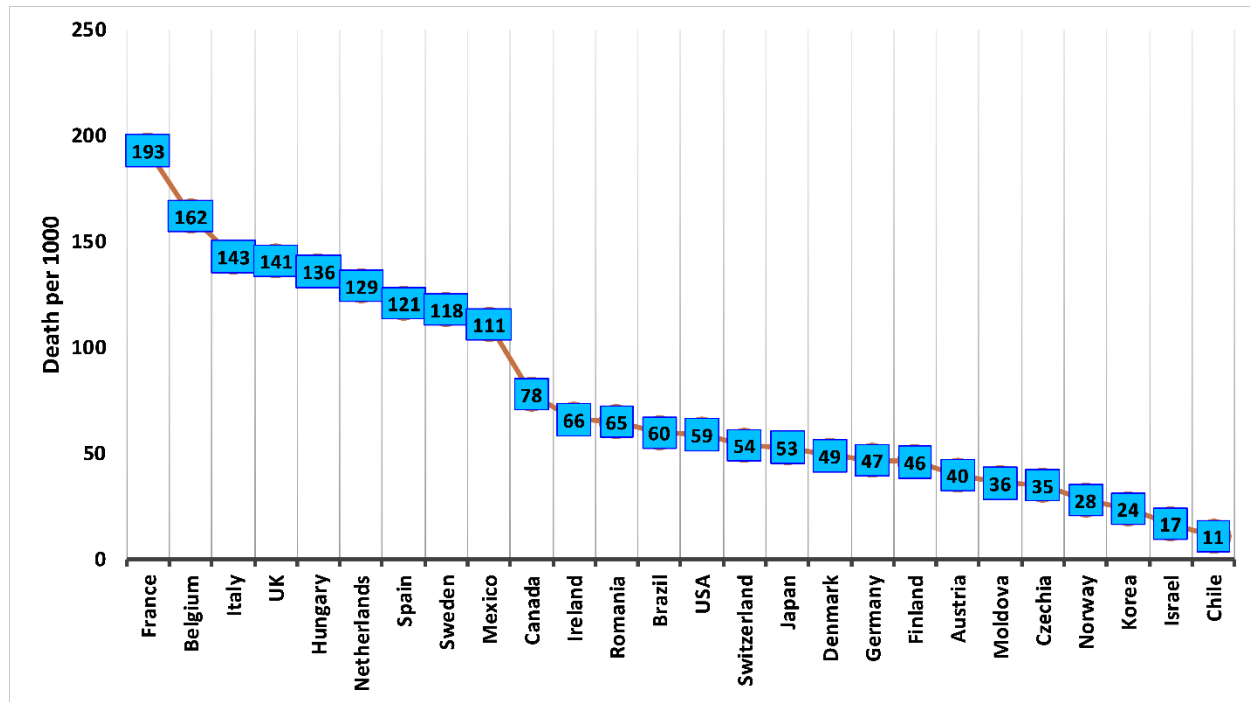place with a mortality rate at 28, 24, 17, and 11 respectively (Figure1).

Figure1: Mortality Rate of Covid-19
Mortality rate of Covid-19 was calculated as deaths caused by Covid-19 per 1000 SARS-Cov-2
affected people; UK: The United Kingdom; USA: The United States of America; Moldova:
Republic of Moldova; Korea: Republic of Korea

France, Italy, Japan, and the Republic of Korea reported 2, 29, 5, and 17 deaths caused by

Covid-19 in February 2020. There was no death reported due to Covid-19 in other countries (in

this study) in February 2020. All the countries (in this study) reported Covid-19 caused deaths in

March 2020 (Figure 2). The lowest number of death due to Covid-19 in March 2020 was seen in

the Republic of Moldova while the highest death reported from Italy (Figure 2). The month of

April 2020 saw the highest number of Covid-19 caused deaths worldwide (Figure 2). The increase

in the number of deaths due to Covid-19 in April 2020 in comparison to March 2020 was calculated

as a fold change and the same way for the month of May 2020. Mexico found to be at the top with

3.88 and 2.61 fold change in Covid-19 caused deaths for April and May 2020, respectively (Figure 3). The Republic of Moldova, Canada, Brazil, and Chile recorded 3.75 and 1.75, 3.62 and 1.65, 3.54 and 2.57, and 3.40 and 2.44 for April and May 2020, respectively (Figure 3). Other countries in the study, except the above mentioned, recorded a negative fold change for May 2020 that showed a decrease in Covid-19 mortality. The USA and other European countries where the mortality rate was higher showed a moderate increase in fold change in March but decreased in May 2020 (Figure 3). Spain, the Republic of Korea, and Italy were found to have a low positive fold change and a negative and least fold change in Covid-19 caused deaths in April and May 2020, respectively irrespective of the very high number of deaths occurred due to Covid-19 in Spain and Italy (Figure 3).
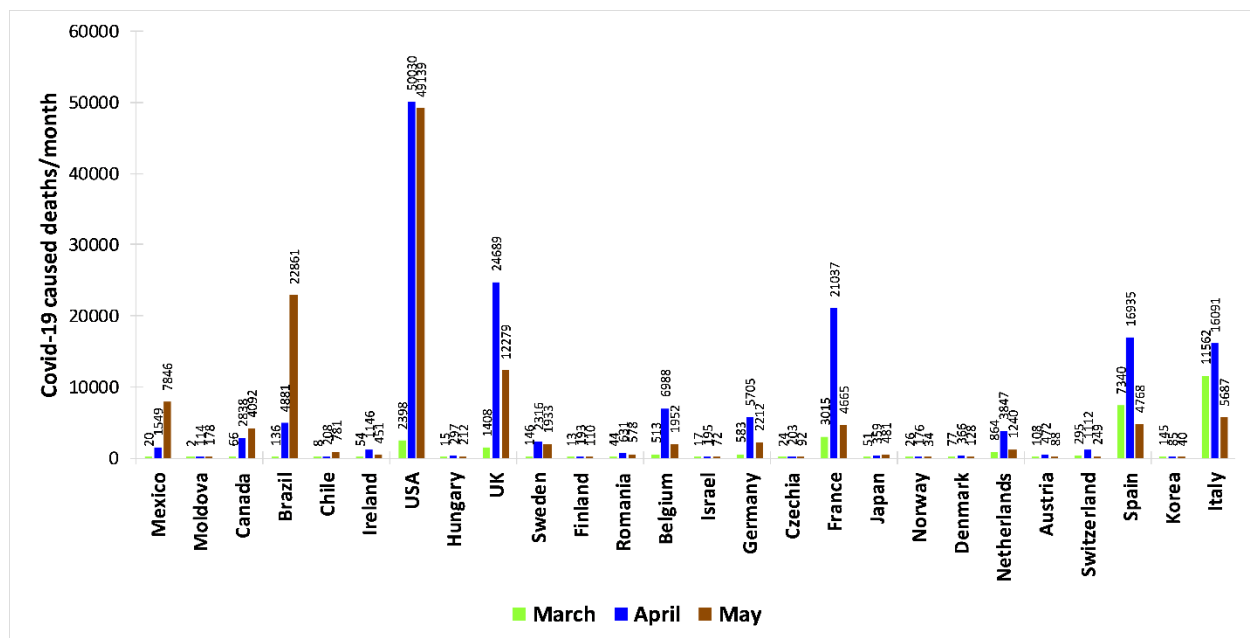

Figure2: Deaths Caused by Covid-19 per Month
X-axis denotes the country; Y-axis denotes the number of deaths/month; UK: The United Kingdom; USA: The United States of America, Moldova: Republic of Moldova; Korea: Republic of Korea
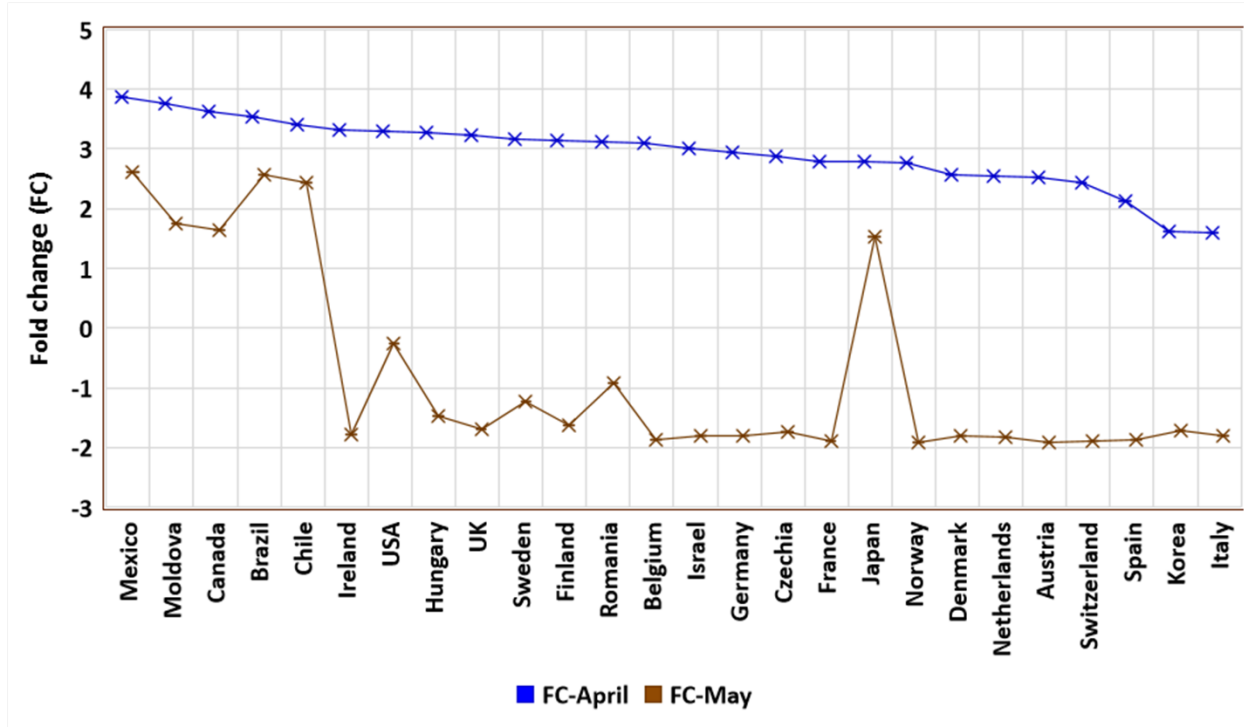
Figure3: Fold Change in Covid-19 Cases
X-axis denotes the country; Y-axis denotes the fold change; Fold change was calculated as $\log10(x)$, where x = [(number of deaths by Covid-19 in May or April 2020 - number of deaths by Covid-19 in April or March 2020)/ number of deaths by Covid-19 in April or March 2020]*100; UK: The United Kingdom; USA: The United States of America, Moldova: Republic of Moldova; Korea: Republic of Korea

Countries were divided into three groups based on the share of Covid-19 caused deaths out of total deaths caused by all the diseases on a monthly average. Belgium, the UK, Spain, France, Ireland, Netherlands, Sweden, Italy, and Brazil were found to be in the high risk group (Figure 4). Covid-19 caused the highest number of deaths in these countries than any other diseases on an average month , except Sweden, Italy, and Brazil where cardiovascular diseases caused deaths on average were higher and in Netherlands, cancer caused more deaths (Figure4, Table1). The second group comprised of the USA, Switzerland, Canada, Mexico, Chile, Denmark, Germany, Austria, and Norway. They were found to be in a moderate risk group where Covid-19 caused deaths were lower than cardiovascular diseases and cancer caused deaths but higher than

respiratory diseases, diabetes, and kidney diseases except Mexico, Denmark, and Norway (Figure
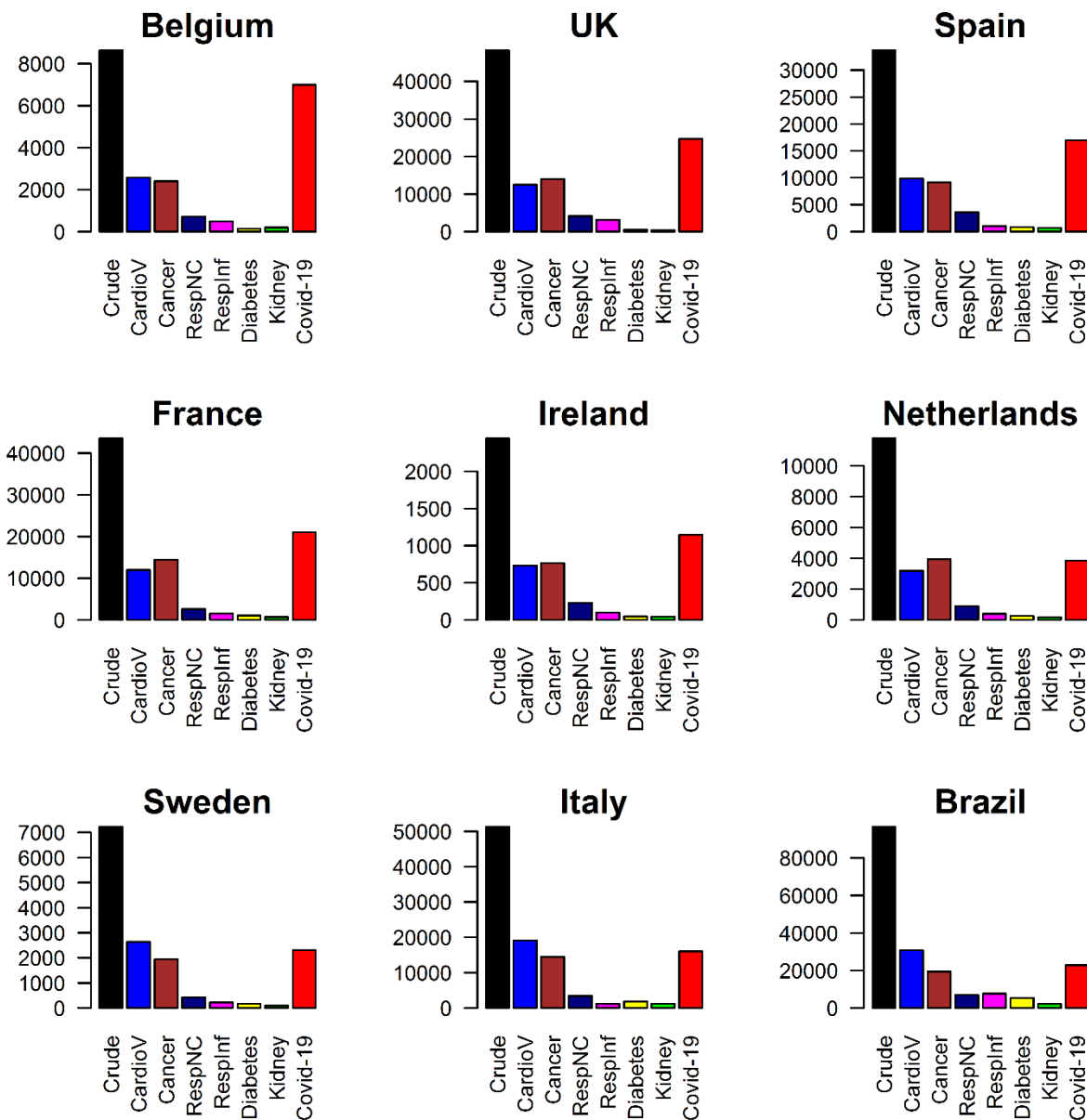
5, Table 1).

Figure-4: Deaths Caused by Covid-19 and Other Diseases (High risk group)
X-axis denotes the causes of death; Y-axis denotes the number of deaths/month (average); Crude: Total deaths occurred by all the diseases; CardioV: Cardiovascular diseases; RespNC: Non-communicable respiratory diseases; RespInf: Respiratory infectious diseases; Diabetes: Diabetes mellitus; Kidney: Kidney diseases; UK: The United Kingdom
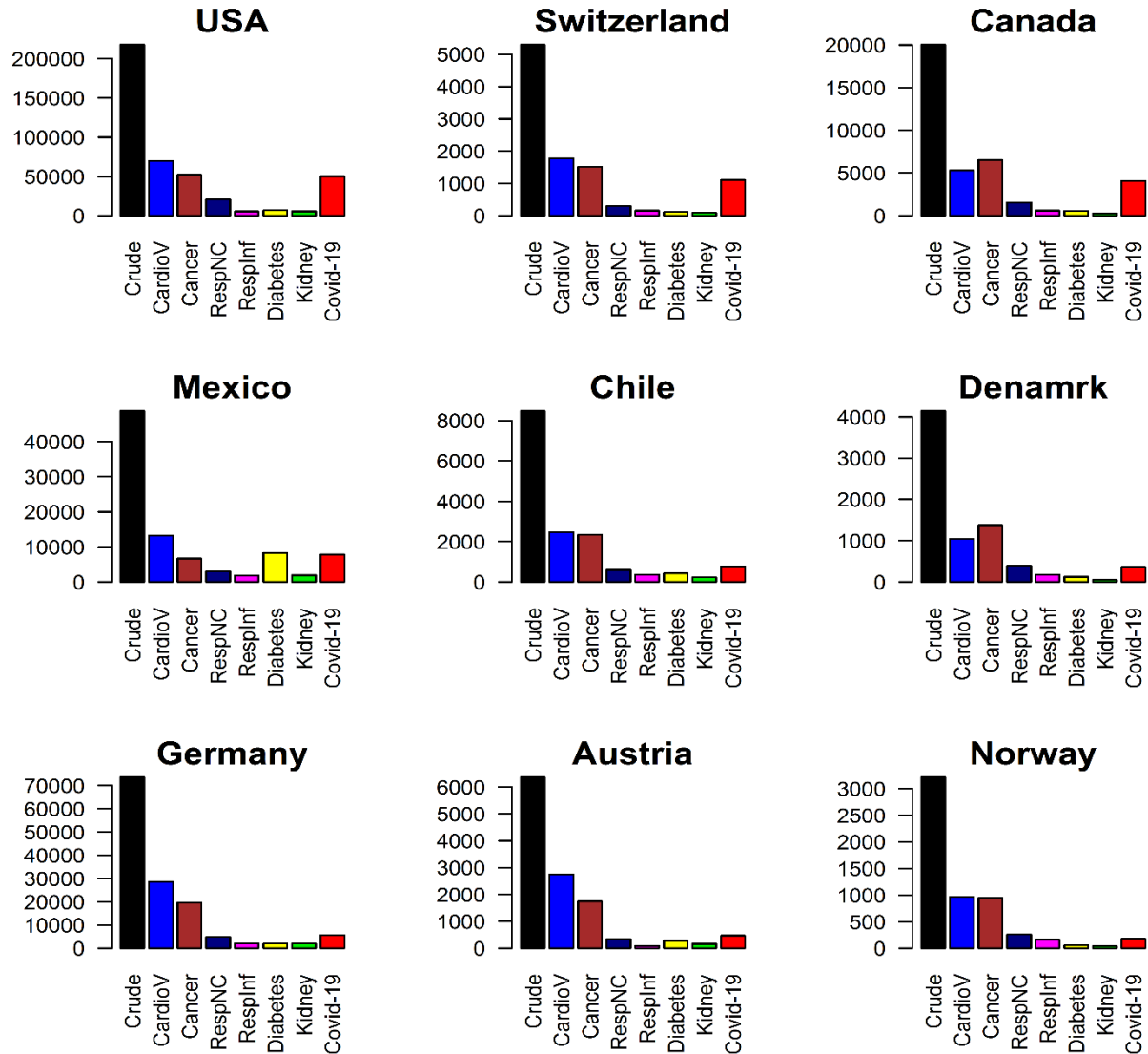
Figure-5: Deaths Caused by Covid-19 and Other Diseases (Moderate risk group)
X-axis denotes the causes of death; Y-axis denotes the number of deaths/month (average); Crude: Total deaths occurred by all the diseases; CardioV: Cardiovascular diseases; RespNC: Non-communicable respiratory diseases; RespInf: Respiratory infectious diseases; Diabetes: Diabetes mellitus; Kidney: Kidney diseases; USA: The United States of America

The third group comprised of Israel, Republic of Moldova, Finland, Romania, Romania, Hungary, Czechia, Japan, and Republic of Korea were found to be at low risk (Figure 6). Covid-19 caused

deaths in Japan and Republic of Korea were lesser than any other disease (study group diseases)

caused deaths on a month average (Figure 6, Table 1).

Figure-6: Deaths Caused by Covid-19 and Other Diseases (Low risk group)
X-axis denotes the causes of death; Y-axis denotes the number of deaths/month (average); Crude: Total deaths occurred by all the diseases; CardioV: Cardiovascular diseases; RespNC: Non-communicable respiratory diseases; RespInf: Respiratory infectious diseases; Diabetes: Diabetes mellitus; Kidney: Kidney diseases; Moldova: Republic of Moldova; Korea: Republic of Korea

Table 1

Death percentage of Covid-19 in comparison to other chronic diseases and total deaths

Country	CovCrd	CovCard	CovCanc	CovRsNC	CovRsInf	CovDbt	CovKid
Belgium	80.9	270.9	291.2	969.2	1423.2	4991.4	3602.1
UK	51.1	196.9	176.1	592.2	789.0	4521.8	6187.7
Spain	50.3	171.9	184.7	470.5	1582.7	2018.5	2310.4
France	48.3	176.0	145.6	812.6	1410.0	2040.4	3062.2
Ireland	46.9	157.2	150.0	502.6	1169.4	2387.5	2728.6
Netherlands	32.7	121.1	97.6	425.6	976.4	1520.6	2249.7
Sweden	32.1	87.8	119.1	533.6	1020.3	1308.5	2463.8
Italy	31.4	84.0	111.3	467.4	1361.3	873.1	1292.4
Brazil	23.7	74.3	117.3	323.7	295.6	419.6	1043.4
USA	22.9	71.7	95.6	243.1	903.7	711.9	902.9
Switzerland	21.0	62.6	73.4	368.2	708.3	967.0	1263.6
Canada	20.4	77.1	62.7	263.8	692.4	708.0	1364
Mexico	16.1	59.1	117.6	258.0	417.3	94.5	404.6
Chile	9.2	31.6	33.5	132.6	212.8	181.2	345.6
Denmark	8.8	35.2	26.6	92.2	206.8	295.2	746.9
Germany	7.7	19.9	29.1	116.4	293.8	276.4	293.6
Austria	7.4	17.2	27.1	138.0	491.7	166.8	298.7
Norway	5.5	18.2	18.6	67.4	110.0	308.8	409.3
Israel	5.5	22.2	19.3	83.3	95.6	87.4	128.3
Moldova	4.8	7.8	30.0	211.9	195.6	445.0	395.6
Finland	4.6	12.2	18.7	133.1	772.0	459.5	551.4
Romania	3.1	5.2	14.5	81.0	110.3	280.4	118.6
Hungary	2.9	5.8	10.8	54.5	282.9	128.0	272.5
Czechia	2.4	5.1	8.8	52.1	67.7	63.8	178.1
Japan	0.5	1.6	1.4	5.0	4.1	40.0	16.2
Korea	0.4	1.6	1.2	6.1	5.5	8.5	14.7

Death count was calculated on a month average; Values are given in percent(%); Percentage was calculated as (Covid-19 caused deaths/total or chronic diseases caused deaths)*100; CovCrd: Percent of Covid-19 caused deaths with respect to (wrt) total deaths; CovCard: Percent of Covid-19 caused deaths wrt cardiovascular caused deaths; CovCanc: Percent of Covid-19 caused deaths wrt cancer caused deaths; CovRsNC: Percent of Covid-19 caused deaths wrt respiratory non-communicable diseases caused deaths; CovRsInf: Percent of Covid-19 caused deaths wrt respiratory infectious diseases caused deaths; CovDbt: Percent of Covid-19 caused deaths wrt diabetes mellitus caused deaths; CovKid: Percent of Covid-19 caused deaths wrt kidney diseases caused deaths; UK: The United Kingdom; USA: The United States of America, Moldova: Republic of Moldova; Korea: Republic of Korea

Table 2

Correlation of Covid-19 with chronic diseases

Covid-19		Diseases	ρ	p
Covid-19	~	RespNC	0.73	4.056 e-05
	~	Cancer	0.67	0.0002
	~	RespInf	0.65	0.0005
	~	Kidney	0.64	0.0006
	~	CardioV	0.63	0.0007
	~	Diabetes	0.61	0.001

ρ: Correlation coefficient (Spearman's rank correlation); p: probability; RespNC: Respiratory non-communicable diseases; RespInf: Respiratory infectious diseases; Kidney: Kidney diseases; CardioV: Cardiovascular diseases; Diabetes: Diabetes mellitus

Israel and Czechia recorded more Covid-19 caused deaths than the kidney diseases caused deaths and lower than the other diseases (Figure 6, Table 1). The Republic of Moldova and Finland showed the highest severity of Covid-19 in this group as the deaths caused by Covid-19 was higher than the kidney diseases, diabetes mellitus, respiratory infectious disease, and non-communicable respiratory diseases (Table 1). The Covid-19 caused deaths were lesser than cardiovascular diseases, cancer, and non-communicable diseases in Romania and Hungary (Table 1).

Covid-19 showed a statistically significant correlation with the diseases (Table 2). Covid-19 showed the strongest positive association with non-communicable respiratory diseases followed by cancer (Table 2). Respiratory infectious diseases, kidney diseases, cardiovascular diseases, and diabetes mellitus were also found to be almost equally positively associated with Covid-19 (Table 2).

Discussion

The results divided the Covid-19 affected countries into three risk groups. The highest risk group was having nine countries and all of them were from Europe except Brazil. The USA, Canada, Mexico, and Chile fell under a moderate risk group of countries with five other European countries. The third and the low risk group contained countries from Asia and Europe. European countries were found to be in all three groups. It showed that covid-19 severity was the highest and the most diverse in Europe. American countries (North America and South America) were found in the moderate risk group except Brazil. All the three Asian countries, Israel, Japan, and the Republic of Korea were in the low risk group. It showed that Covid-19 severity was diverse in the world. The Mortality rate of Covid-19 (based on total SARS-Cov-2 infected people) was the highest and most diverse in Europe, while American countries were at moderate risk. Asian countries were at low risk. It also showed that Covid-19 severity was not the same in the world.

April 2020 saw the highest number of Covid-19 deaths in the world. The Covid-19 mortality reduced in May 2020 especially in Europe and a slight decrease in the USA as well. Four American countries, Mexico, Canada, Brazil, and Chile showed an increase in Covid-19 deaths in May 2020. Japan as a surprise showed an increase in Covid-19 deaths in May 2020.

The latest reports on Covid-19 showed that a diseased condition or a person with cancer, cardiovascular, respiratory diseases, or other diseases was at higher risk of SARS-Cov-2 infection[15–17]. It was also reported that Covid-19 increased the severity of preexisting diseases[18–20]. We found that Covid-19 (SARS-Cov-2 infection) was strongly correlated with non-communicable respiratory diseases, followed by cancer, cardiovascular diseases, respiratory infectious diseases, kidney diseases, and diabetes mellitus. According to our results, SARS-Cov-2 was highly positively associated with non-communicable respiratory diseases. In this condition,

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SARS-Cov-2 infection would make the progress of the preexisting respiratory disease (non-communicable) more rapidly that can lead to mortality in a short time. The same process would apply to cancer, cardiovascular diseases, respiratory infectious diseases, kidney diseases, and diabetes mellitus also which could lead to mortality as it was also reported previously in different disease conditions [5,21–24]. The worst and the most challenging part would be to tackle the unexpected progress of the preexisting disease conditions among Covid-19 patients. It would also be possible that Covid-19 was not a life threatening disease as a single entity but helped preexisting diseases to progress rapidly towards mortality.

If we see cancer, cardiovascular diseases, kidney diseases, and other diseases then the severity of these diseases and mortality remain more or less the same (variation depends on awareness, life-style, early diagnosis, treatment, and medical care) among positive cases of these diseases irrespective of country and region. However, if we look at Covid-19 then its severity and mortality were found highly diverse. For example, Covid-19 severity and mortality were very high in Sweden, but in the neighborhood, Norway and Finland showed less severity and mortality. The same way, Covid-19 severity and mortality were different in neighbors France and Germany. These results and observations put a question mark that why SARS-Cov-2 behaves differently in different countries. How a virus can recognize a boundary?

Conclusion

The severity of Covid-19 is diverse throughout the world. Respiratory diseases (non-communicable) and cancer patients are at higher risk.

Conflict of interest

The authors declare no conflict of interest

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