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 225,000 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, Spain, France, Italy, the UK, and Ireland. Covid-19 was found to be strongly correlated with non-communicable respiratory diseases and Cancer with correlation coefficients 0.73 and 0.70 respectively. The severity of Covid-19 in the 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, March, April

Introduction

Covid-19 has crossed a three million mark causing more than 225000 deaths worldwide in over three 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. Italy, the United Kingdom (UK), Spain, and France together and the USA alone have lost more than 100,000 and 55,000 lives in less than two 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 1st 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 100,000 population. The given mortality rate was divided by 100,000 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-

19 caused deaths for February, March, and April 2020 were calculated. The increase of Covid-19 deaths in April in comparison to March 2020 was 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 April 2020 - number of deaths by Covid-19 in March 2020)/ number of deaths by Covid-19 in March 2020]*100. Further, deaths occurred in April 2020 were compared 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 reported more than 100 deaths by Covid-19 by April 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.

Results

France showed the highest mortality rate (Covid-19 caused deaths out of Covid-19 positive cases per 1000) at 190, which was followed by Belgium, UK, and Italy 157, 156, and 136 respectively (Figure1). The mortality rate in Brazil, Canada, and the USA was at 70, 59, and 53 respectively (Figure1). Japan, Norway, the Republic of Korea, Chile, and Israel were in the bottom place with a mortality rate at 30, 26, 23, 14, and 14 respectively (Figure1).
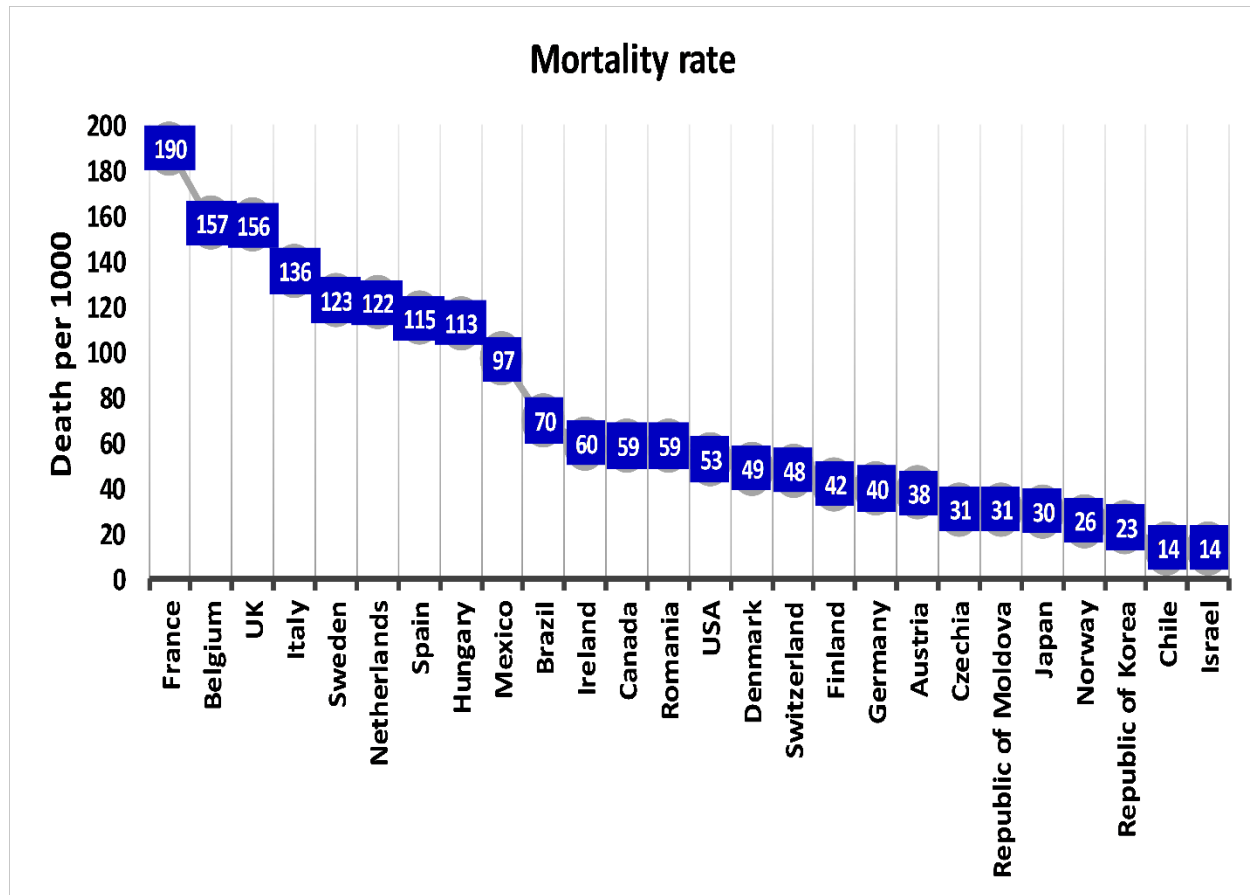
Figure1: Mortality Rate of Covid-19
Mortality rate of Covid-19 was calculated as deaths caused by Covid-19 per 1000 Covid-19 affected people; UK: The United Kingdom; USA: The United States of America

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. Mexico found to be at the top with 1.86 fold change in Covid-19 caused deaths,

followed by the Republic of Moldova, Canada, Brazil, and Chile (Figure 3). The USA and other

European countries where the mortality rate was higher showed a moderate increase in fold change

(Figure 3). Spain and Italy were found to have a low fold change increase in Covid-19 caused

deaths irrespective of the very high number of deaths occurred due to Covid-19 (Figure 3). The

only country (in this study), the Republic of Korea showed a negative fold change (Figure 3).
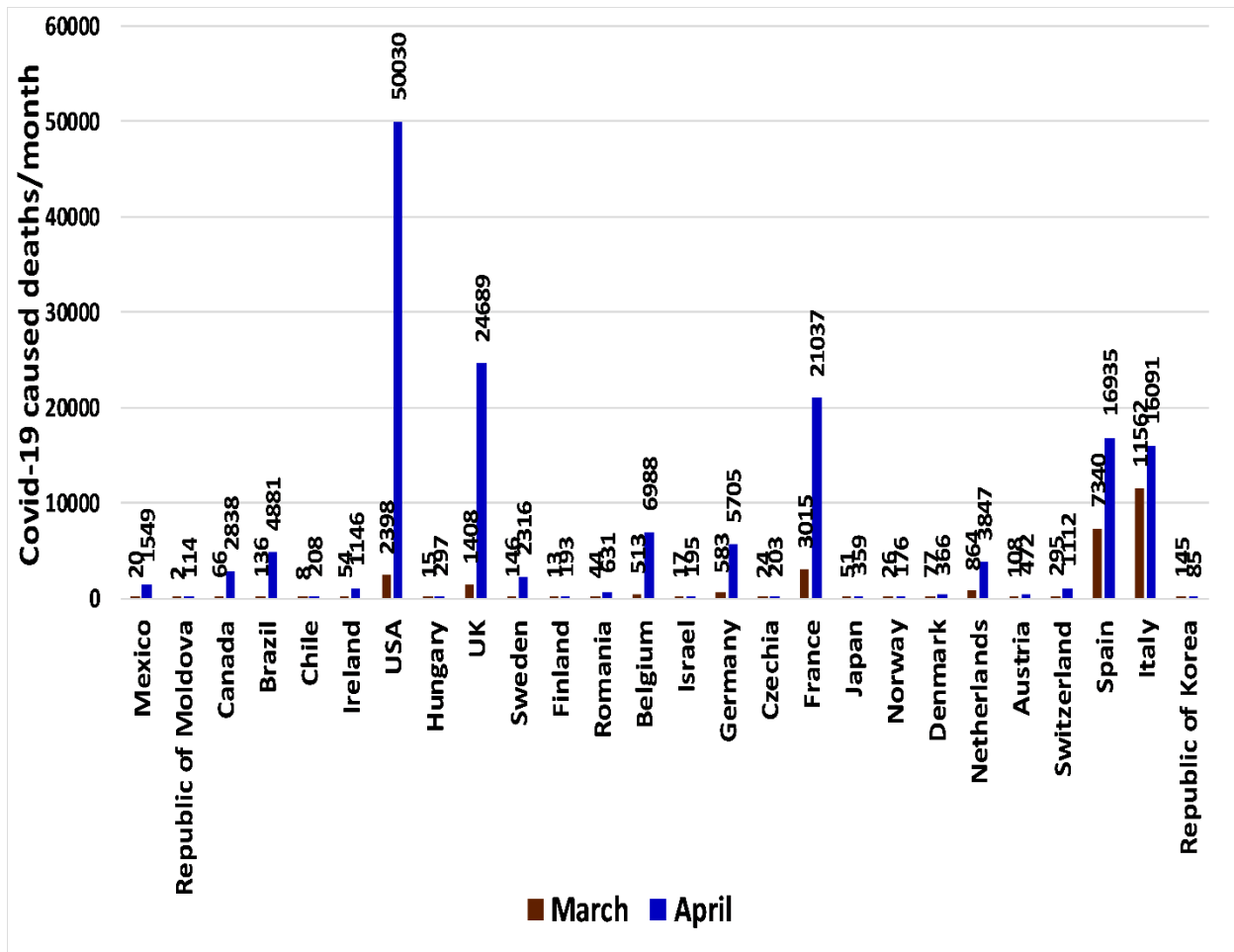
Figure2: Deaths Caused by Covid-19 per Month
X-axis denotes the country; Y-axis denotes the number of deaths/month
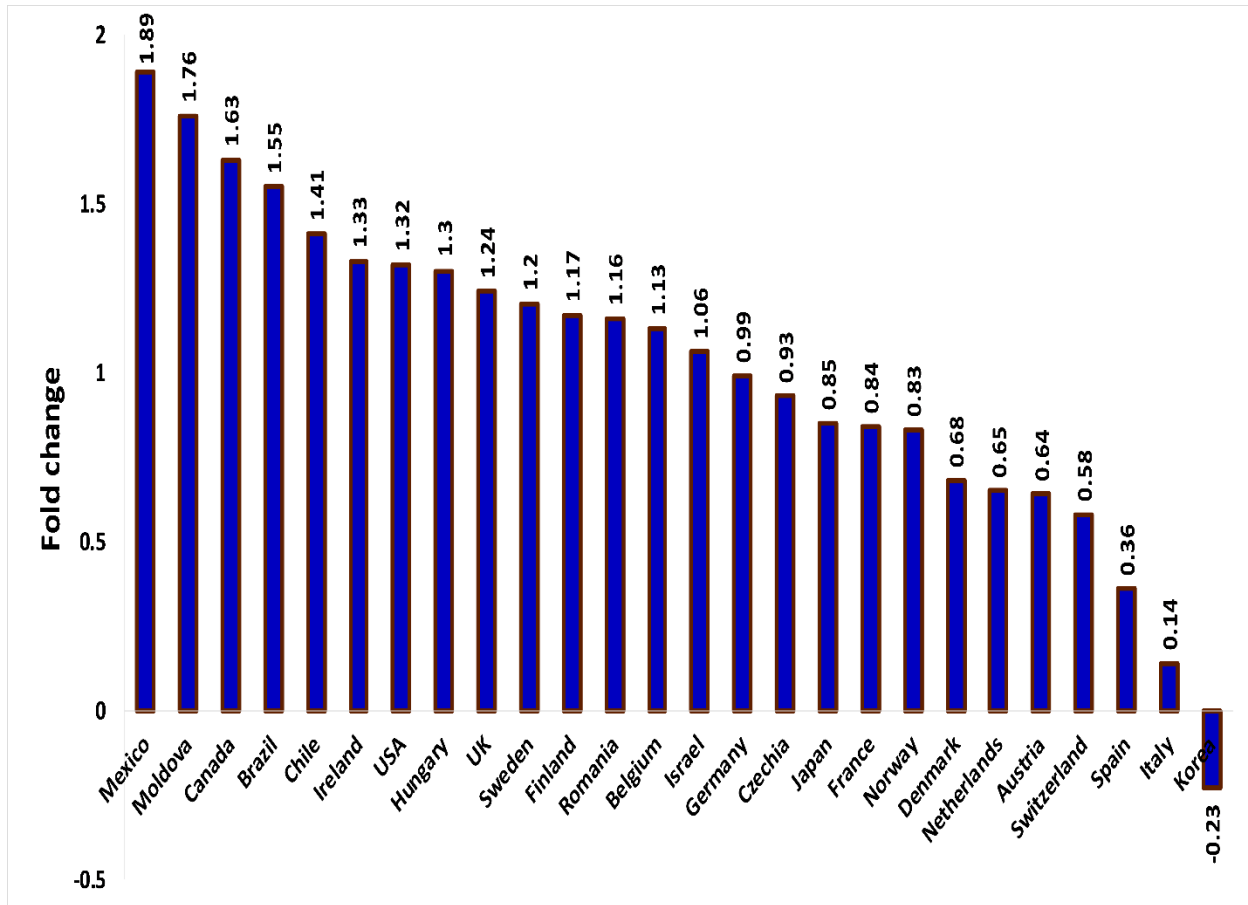
Figure3: Fold Change in Covid-19 Cases

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 April 2020 - number of deaths by Covid-19 in March 2020)/ number of deaths by Covid-19 in March 2020]*100; Moldova: The Republic of Moldova; Korea: The 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, Spain, France, Italy, UK, Ireland, Netherlands, Sweden, and the USA 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 for April 2020, except Sweden and the USA, where cardiovascular diseases caused deaths on average were higher (Figure4, Table1). The second group comprised of Switzerland, Canada, Denmark, Germany, Austria, Brazil, Israel, Norway, and Finland. 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 Brazil, Israel, and Norway (Figure 5, Table 2).
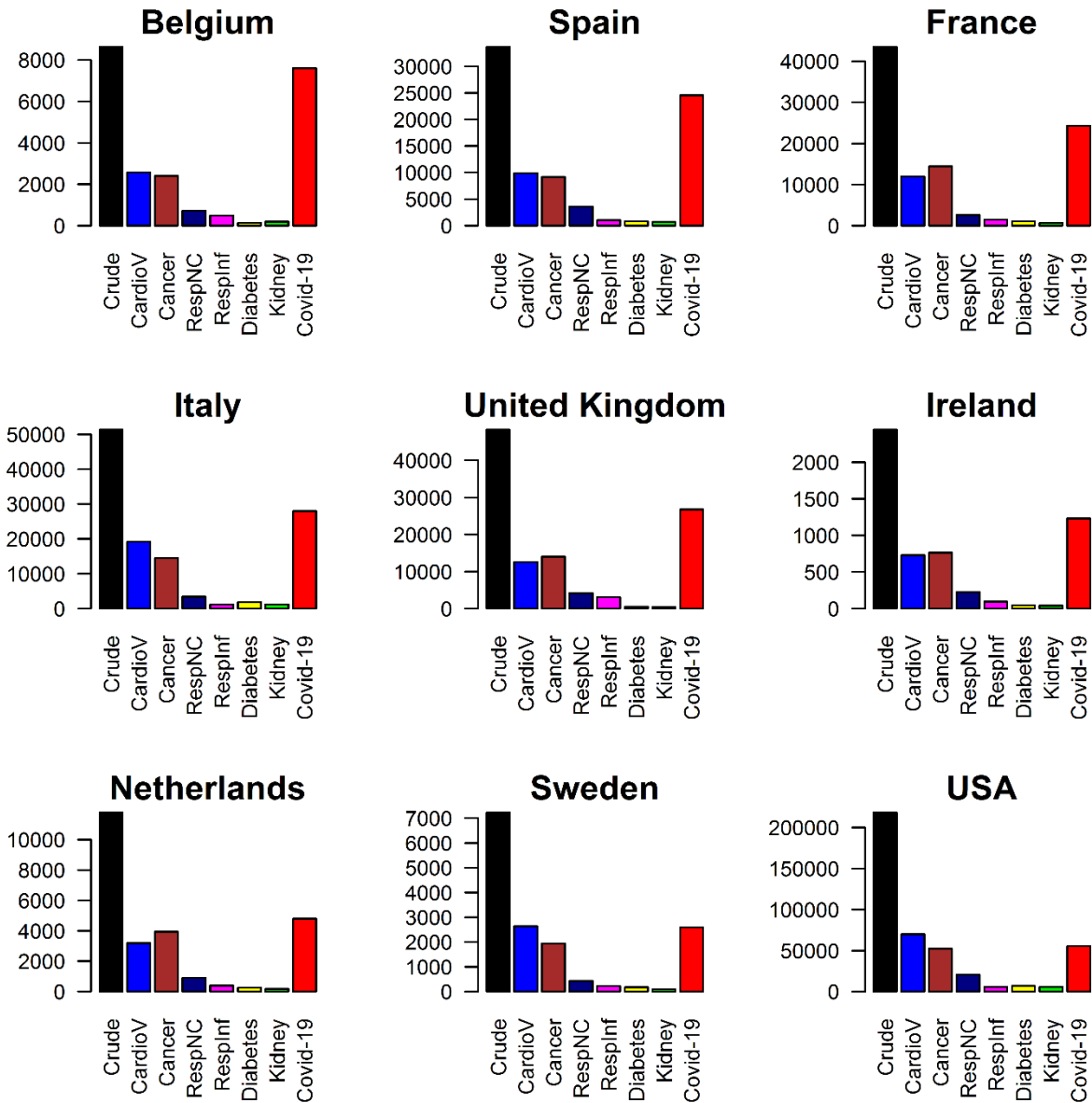
Figure-4: Deaths Caused by Covid-19 and Other Diseases (High risk group)
X-axis denotes the causes of death; Y-axis denotes the number of deaths/month (average); Crude: Total deaths occurred by all the diseases; CardioV: Cardiovascular diseases; RespNC: Non-communicable respiratory diseases; RespInf: Respiratory infectious diseases; Diabetes: Diabetes mellitus; Kidney: Kidney diseases; USA: The United States of America
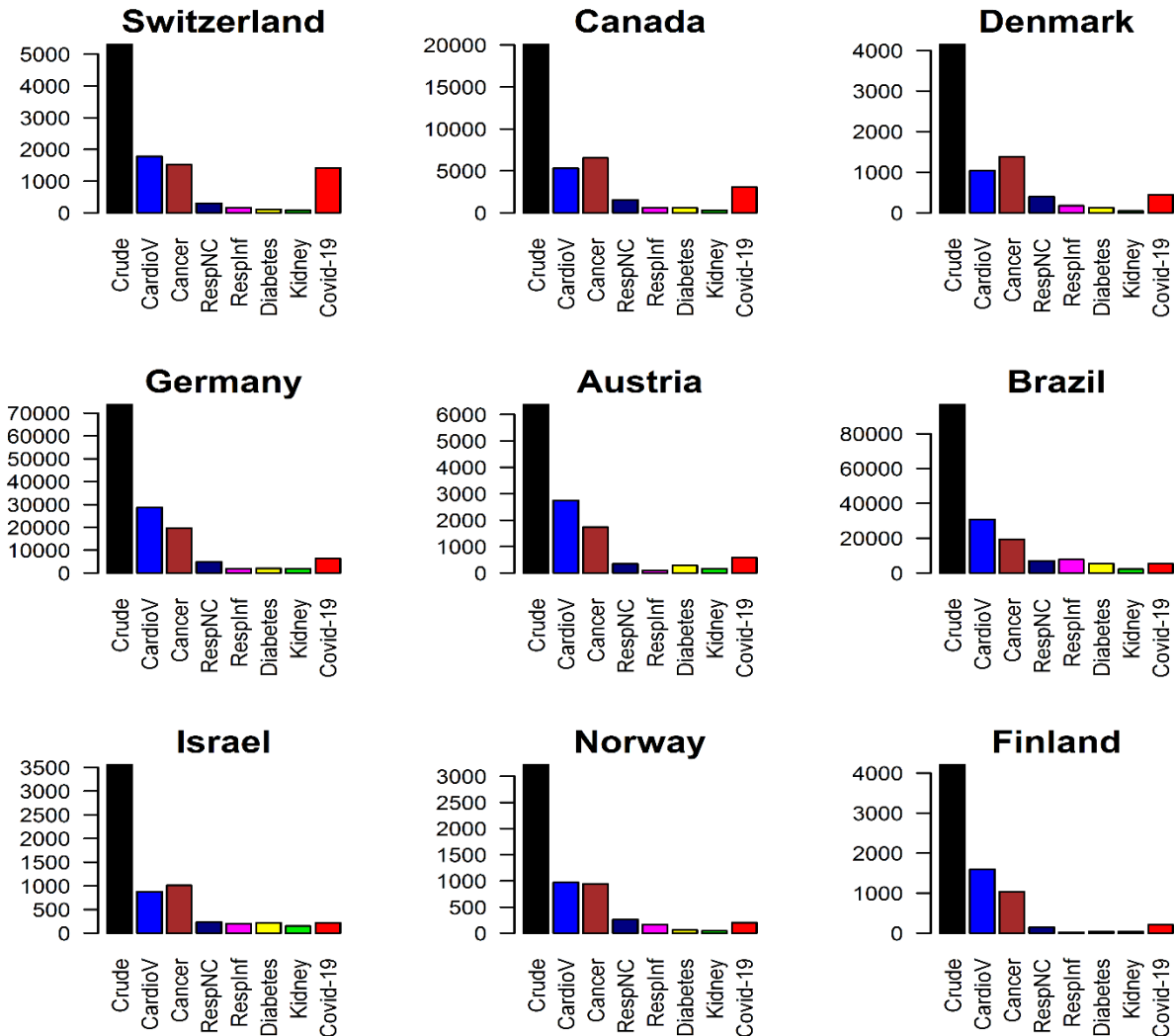
Figure-5: Deaths Caused by Covid-19 and Other Diseases (Moderate risk group)
X-axis denotes the causes of death; Y-axis denotes the number of deaths/month (average); Crude: Total deaths occurred by all the diseases; CardioV: Cardiovascular diseases; RespNC: Non-communicable respiratory diseases; RespInf: Respiratory infectious diseases; Diabetes: Diabetes mellitus; Kidney: Kidney diseases

Respiratory diseases (non-communicable) and respiratory infectious diseases caused deaths were more in brazil than the Covid-19 caused deaths. Non-communicable respiratory diseases caused deaths were more in number in Israel and Norway than the Covid-19 caused deaths in the month of April 2020. The third group comprised of Mexico, Romania, Hungary, Czechia, Chile, Republic

of Moldova, Republic of Korea, and Japan were found to be at low risk (Figure 6). Covid-19

caused deaths in Mexico, Republic of Korea, and Japan was lesser than any other disease (study

group diseases) caused deaths for April 2020 (Figure 6, Table 3).
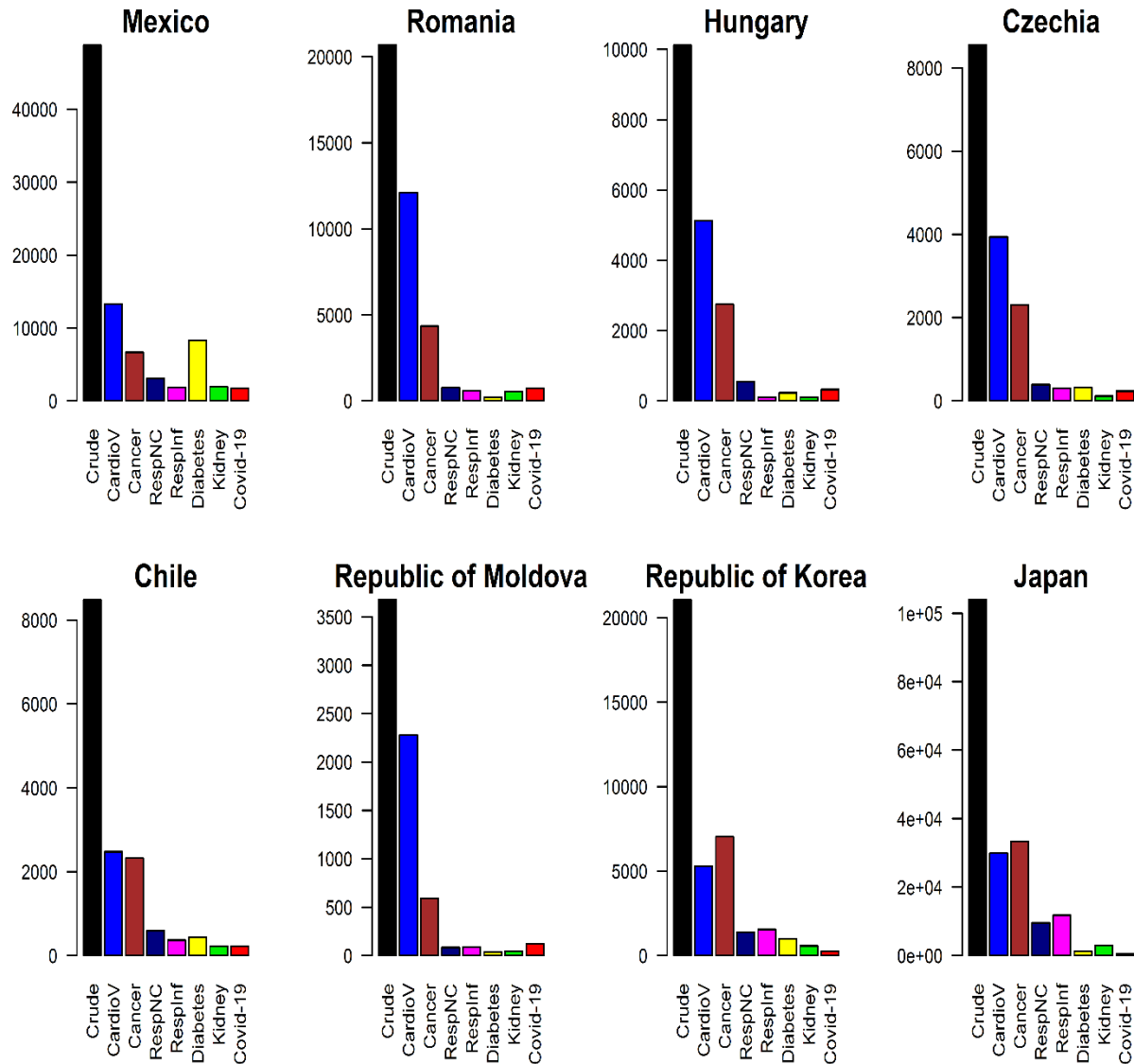
Figure-6: Deaths Caused by Covid-19 and Other Diseases (Low risk group)
X-axis denotes the causes of death; Y-axis denotes the number of deaths/month (average); Crude: Total deaths occurred by all the diseases; CardioV: Cardiovascular diseases; RespNC: Non-communicable respiratory diseases; RespInf: Respiratory infectious diseases; Diabetes: Diabetes mellitus; Kidney: Kidney diseases

Chile showed an almost equal number of deaths caused by Covid-19 and Kidney diseases and lesser than other diseases, while in Czechia Covid-19 caused deaths were more than the kidney diseases caused deaths and lower than the other diseases (Figure 6, Table 3). Covid-19 caused deaths in Romania and Hungary were more in number than the diabetes mellitus and kidney diseases caused deaths and lower than the other diseases (Table 3). The Republic of Moldova 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 3).

Table-1: Ratio of Covid-19 Caused Deaths with Other Diseases (High risk group)

Country	Cov2 /Tot	Cov2 /Card	Cov2 /Canc	Cov2 /RsNC	Cov2 /RsIn	Cov2 /Dbt	Cov2 /Kid
Belgium	88	294	316	1053	1547	5424	3914
Spain	73	249	268	682	2294	2925	3348
France	56	204	168	940	1632	2361	3543
Italy	55	146	193	812	2366	1517	2246
UK	55	214	191	642	856	4903	6710
Ireland	50	169	161	540	1257	2567	2933
Netherlands	41	151	122	53	1217	1895	2804
Sweden	36	98	133	596	1139	1461	2751
USA	25	79	106	269	1000	787	999

*Cov2: Covid-19, Tot: Total deaths caused by all the diseases; Card: Cardiovascular diseases; Canc: Cancer; RsNC: Non-communicable respiratory diseases; RsIn: Respiratory infectious diseases; Dbt: Diabetes mellitus; Kid: Kidney diseases; UK: The United Kingdom; USA: The United States of America; Values are given in percent and calculated per month as: (number of deaths caused by Covid-19/number of deaths caused by another specific diseases)*100*

Table-2: Ratio of Covid-19 Caused Deaths with Other Diseases (Moderate risk group)

Country	Cov2 /Tot	Cov2 /Card	Cov2 /Canc	Cov2 /RsNC	Cov2 /RsIn	Cov2 /Dbt	Cov2 /Kid
Switzerland	27	80	94	471	906	1237	1616
Canada	15	58	47	199	521	533	1027
Denmark	11	43	33	114	255	365	922
Germany	9	22	32	128	324	305	324
Austria	9	21	34	171	608	206	370
Brazil	6	18	28	77	71	100	249
Israel	6	25	22	95	109	100	147
Norway	6	21	22	78	128	358	474
Finland	5	13	20	146	844	502	603

Cov2: Covid-19, Tot: Total deaths caused by all the diseases; Card: Cardiovascular diseases; Canc: Cancer; RsNC: Non-communicable respiratory diseases; RsIn: Respiratory infectious diseases; Dbt: Diabetes mellitus; Kid: Kidney diseases; Values are given in percent and calculated per month as: (number of deaths caused by Covid-19/number of deaths caused by another specific diseases)*100

Table-3: Ratio of Covid-19 Caused Deaths with Other Diseases (Low risk group)

Country	Cov2 /Tot	Cov2 /Card	Cov2 /Canc	Cov2 /RsNC	Cov2 /RsIn	Cov2 /Dbt	Cov2 /Kid
Mexico	4	13	26	57	92	21	89
Romania	3	6	16	92	125	319	135
Hungary	3	6	12	59	308	139	296
Czechia	3	6	10	61	79	74	207
Chile	3	9	10	39	62	53	100
Moldova	3	5	20	142	131	298	264
Korea	1	5	4	18	16	25	43
Japan	0	1	1	5	4	36	15

Cov2: Covid-19, Tot: Total deaths caused by all the diseases; Card: Cardiovascular diseases; Canc: Cancer; RsNC: Non-communicable respiratory diseases; RsIn: Respiratory infectious diseases; Dbt: Diabetes mellitus; Kid: Kidney diseases; Values are given in percent and calculated per month as: (number of deaths caused by Covid-19/number of deaths caused by another specific diseases)*100

Table-4: Correlation of Covid-19 with Other Diseases

Covid-19	Diseases	ρ	p
Covid-19 ~	RespNC	0.73	4.367 e-05
~	Cancer	0.70	0.0001
~	CardioV	0.62	0.0008
~	RespInf	0.62	0.0008
~	Kidney	0.62	0.0008
~	Diabetes	0.57	0.002

RespNC: Noncommunicable respiratory diseases; CardioV: Cardiovascular diseases; RespInf: Respiratory infectious diseases; Kidney: Kidney diseases; Diabetes: Diabetes mellitus; ρ: Spearman's rank correlation coefficient; p: p value

Covid-19 showed a statistically significant correlation with the diseases (Table 4). Covid-19 showed the strongest positive association with non-communicable respiratory diseases followed by cancer (Table 4). Cardiovascular diseases, respiratory infectious diseases, and kidney diseases were found to be equally positively associated with Covid-19 (Table 4). Diabetes mellitus was also found to be statistically significant positively associated with Covid-19 but with lower intensity than the other diseases (Table 4).

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 the USA. Canada,

Brazil, and Israel fell under a moderate risk group of countries with six other European countries. The third and the low risk group contained countries from Europe, Asia, North America, and South America. 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 also found to be in each group. The USA in high risk, Canada and Brazil at moderate risk, and Mexico and Chile were in low risk groups. Among Asian countries, Israel was at moderate risk, while Japan and the Republic of Korea were in the low risk groups. 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 to low risk. Asian countries were at low risk. It also showed that Covid-19 severity was not the same in the world.

Among the Covid-19 high risk group, the UK, Belgium, and Sweden seemed to be at the highest risk with an increase in mortality and severity of Covid-19. The fold change in Covid-19 positive cases and mortality rate both were very high in these countries in comparison to others in the same group. Belgium has already reached to the 88 percent share of total deaths caused by all diseases in one month (April 2020) on average. It may possible that Covid-19 keeps haunting in these countries with the same or in a more severe manner. In the moderate risk group, Brazil seemed to be at the highest risk with a high fold change (higher than high risk group countries) in Covid-19 positive cases and a mortality rate higher than the USA and Ireland. It may possible that Brazil could join the high risk group very soon. Among the low risk group countries, Mexico seemed very vulnerable with the highest fold change increase among all the countries with a high mortality rate. It may possible that Mexico could directly jump to the high risk group soon.

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, 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.

Ethical approval

This study did not require any ethical approval

Conflict of interest

The authors declare no conflict of interest

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