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Excess mortality in Northeast Iran caused by COVID-19: Neglect of offset community transformations of health

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ABSTRACT

Objective: To make evidence-based decisions based on broad mortality trends for Razavi Khorasan province, Iran.

Methods: In order to determine the baseline number of deaths, we used univariate time series analyses for monthly data from the monthly vital statistics reports (From April 2015 to March 2022). For excess mortalities, these baselines were subtracted from reported deaths with a 95% prediction interval. To compare time and causes, a P-score was calculated.

Results: From March 2020 to March 2022, there were 61 949 registered deaths, and the estimated deaths with a 95% confidence interval (*CI*) were 43 246.16 (35 718.28, 50 774.05). So, in 2020-2021 and 2021-2022, the death counts were 35.15% and 51.33% higher than projected. A total of 18 666 cardiovascular diseases were reported and a total of 15 704.46 (12 006.95, 19 401.96) was estimated. The P-score for this duration was 14.49% and 23.23% higher than expected. Infectious and parasitic diseases plus COVID-19 were 16 633 and estimated to be 1 044.87 (456.77, 1 632.96). A total of 4 420 diseases of the respiratory system were reported, and 4 564.94 deaths were predicted (2 277.43, 6 852.43). In the first year of the pandemic, the P-score dropped to -35.28% and in the second year, it jumped sharply to 22.38%.

Conclusions: Excess mortality, along with cause-specific mortality, can be helpful for monitoring trends and developing public health policies at the local, national, and international levels.

KEYWORDS: Mortality; COVID-19; Health Systems Plans; Prediction; Cardiovascular deaths

1. Introduction

As a result of its economic turmoil and international policy turbulence, Iran has suffered over the past decade. Furthermore, there are two major coherence crises underway, the first of which is an intensified sanction that is more emphasized in 2017[1], and the second of which is the COVID-19 pandemic that began in 2020, resulting in a significant amount of direct and indirect deaths[2]. Healthcare resources were diverted to prioritize treating COVID-19 patients early in the pandemic and throughout the epidemic because

Significance

Monitoring trends in broad mortality outcomes, such as changes in all- and specified-cause mortality, gives an insight into the magnitude of the mortality burden neglected that can be due to the performance of the healthcare system. The use of excess mortality together with cause-specific mortality can be useful for monitoring trends within and between countries and informing local, national, and international public health policy.

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of the high rate of COVID-19 deaths. The increase in non-COVID-19 deaths has been attributed to this neglect of other common diseases. In order to evaluate the effectiveness or failure of previous policies, to assess needs, set priorities, and to direct future evidence-based policies, it is necessary to evaluate the performance of the health-care system. The distribution of specific health indicators must, however, be comprehensively broken down at the national and subnational levels for this initiative[3–5]. To accomplish this, epidemiology and public health use an index called excess mortality. It is the number of deaths that occur during times of crisis over and above what would be expected under normal circumstances. Several studies have estimated excess mortality or used Farrington surveillance algorithm to compare total reported deaths to the number of deaths extrapolated from all available Centers for Disease Control and Prevention Wonder data[2,3,6,7]. Our study aims to provide this breakdown for Razavi Khorasan province, one of Iran's largest cultural and religious provinces located near Afghanistan and Turkmenistan in the North-Eastern portion of the country. This estimate is based on the changes in excess mortality during the past 6 years. The model is capable of capturing cyclical, seasonal, and trend variations in mortality. As a result of the emerging diseases in recent years, we can also find the neglected in offset of the major changes in community health.

2. Subjects and methods

2.1. Data sources

This analysis was conducted using monthly data taken from the monthly vital statistics reports (From April 2015 to March 2022): "Provisional death counts by gender and age, and underlying causes of death". According to "underlying causes of death (From April 2015 to March 2019)," we extrapolated how many deaths would have occurred if COVID-19 had not occurred. Those "enhanced deaths" identified in this analysis are “cardiovascular deaths (ICD-10: I00-I99), certain infectious and parasitic diseases (ICD-10: A00-B99) plus the COVID-19 lab result was positive (ICD-10: U07.1), and when the COVID-19 lab result is negative and the physician confirms the diagnosis is “COVID-19,” assign U07.2, and diseases of the respiratory system (ICD-10: J00-J99).

2.2. Calculating excess mortality

In this extrapolated result, we calculated how many deaths would have occurred under “normal” conditions if the pandemic had not occurred. To calculate the excess mortality rate, the mortality counts were monthly aggregated by specified cases and deaths in age subgroups, and we used a univariate time series analysis to determine the baseline number of deaths that would have occurred from March 2020 until the end of March 2022 under "normal" circumstances by regressing the number of deaths from April 2015 until the end of March 2019 with a 95% prediction interval. The time series model is capable of capturing cyclical, seasonal, and trend variations in mortality[8,9]. This baseline was subtracted from the reported total deaths and specific deaths in order to calculate excess cause mortality due to COVID-19. The excess mortality can be negative, whenever the observed number of deaths is below the baseline.

Equation 1:

Excess death=Reported deaths - Expected deaths

Counting excess deaths gives us a sense of scale, but it is less comparable across time, regions and population subgroups. These comparisons are made more easily by comparing the reported mortality rate with the projected mortality rate[7]. This metric is called the P-score and we calculate it as[10]:

Equation 2:

P-score=(Reported death-expected deaths)/(Expected deaths)×100

The P-score can be negative, whenever the observed number of deaths is below the baseline.

3. Results

3.1. Total excess mortality

Figure 1 illustrates mortality patterns reported versus projected monthly total mortality by sex group. March 2020 was the first month in which COVID-19 was reported in Razavi Khorasan Province. From March 2020 to March 2022, 61 949 deaths were recorded, estimated with a 95% Confidence Interval (*CI*) of 43 246.16 (35 718.28, 50 774.05) (Table 1). Thus, the total death counts in 2020-2021 and 2021-2022 was 35.15% and 51.33% higher than the projected total death count in two years (Table 2). For male, there were 35 151 deaths registered, and the estimated deaths with 95% *CI* were 24 404.93 (20 481.35, 28 328.53). For females, there were 26 644 deaths registered, and the deaths are projected to be 18 813.13 (14 873.20, 22 753.09) (Table 1). During the pandemic in 2020-2022 the patterns of death were similar for males and females. However, males were more susceptible to death during the first year

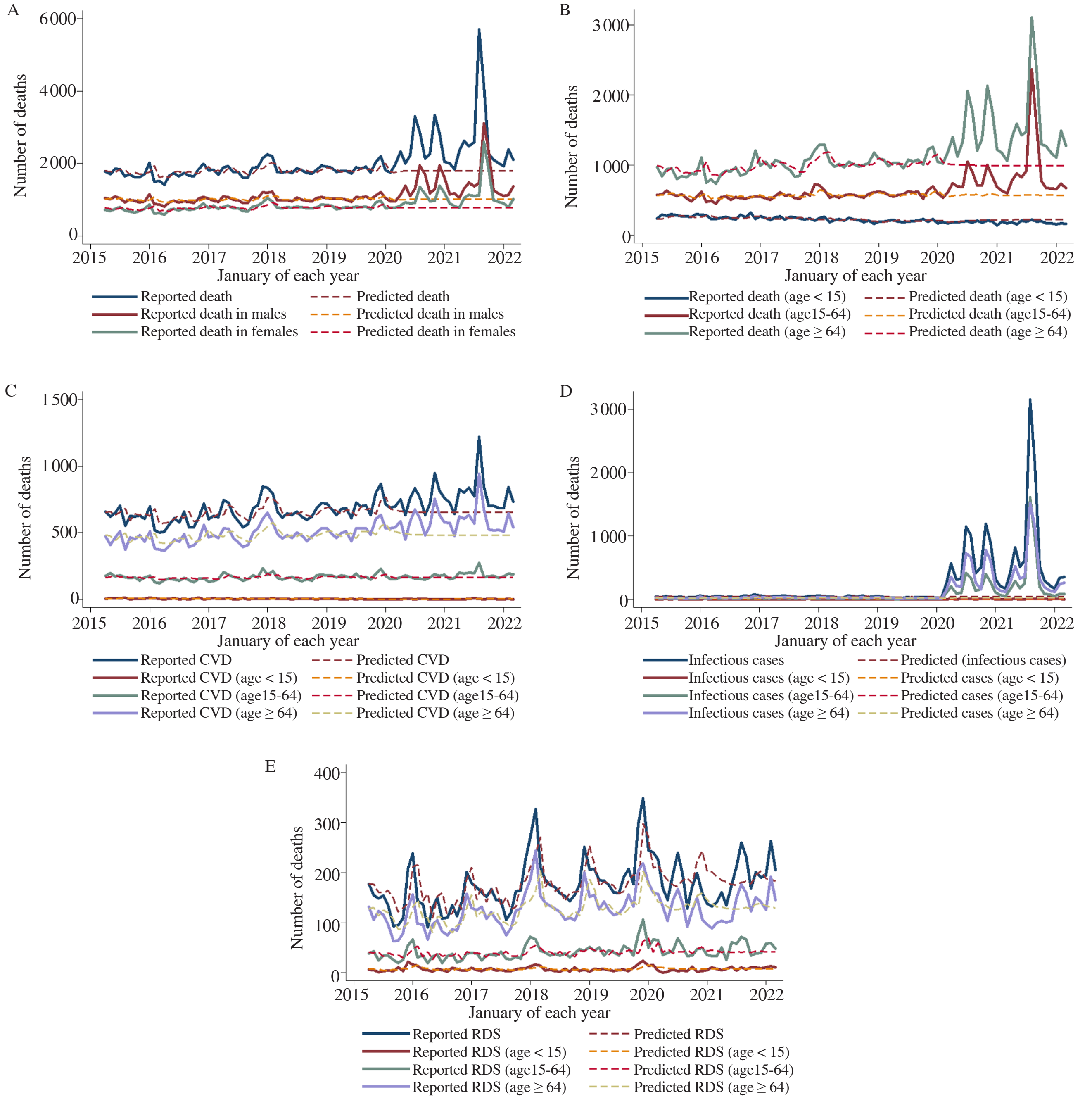

Figure 1. Trends in the total and cause-specific mortality and their transformation over time (2015-2022). (A) Reported *vs.* expected total mortality according to sex groups; (B) Reported *vs.* expected total mortality according to age groups; (C) Reported *vs.* expected cardiovascular (CVD) deaths and its age groups; (D) Reported *vs.* expected certain infectious and parasitic diseases plus COVID-19 and its age groups; (E) Reported *vs.* expected diseases of the respiratory system (RDS) and its age groups.

of the COVID-19 pandemic, and females were more susceptible during its second year. (P-scores for males were 39.17% in 2020-2021 and 48.88% in 2021-2022, while those for femals were 31.43% in 2021 and 51.81% in 2022, higher than projected total deaths) (Table 2). Figure 1A illustrates these monthly change patterns.

Figure 1B illustrates the monthly mortality patterns reported versus projected total mortality by age group: Under 15 years old, 15 years old to 64 years old, and 64 years old and over. From March 2020 to March 2022, 4434 deaths were registered for children aged under 15 years old, and 5199.16 (4056.29, 7253.85) deaths were estimated (Table 1). P-scores for this age group dropped to -10.67% in 2020-2021, and -18.50% in 2021-2022, overall mortality for this group was falling (Table 2). From March 2020 to March 2022, 20822 deaths were registered among adults (aged 15-64 years old), and 13741.71 (11299.04, 16184.38) deaths were estimated. The P-scores indicate this age group was more fragile in the second

Table 1. Mortality patterns reported versus projected from April 2015 to March 2022.

Cause of mortality	April 2015-February 2020		March 2020-March 2021		March 2021-March 2022	
	Reported cases	Predicted cases (95%*CI*)	Reported cases	Predicted cases (95%*CI*)	Reported cases	Predicted cases (95%*CI*)
Total deaths	108418	108207.90 (92219.52, 124196.20)	29206	21610.00 (17849.69, 25370.32)	32743	21636.16 (17868.59, 25403.73)
Male	61029	61079.49 (52325.80, 69833.18)	16966	12190.78 (10231.26, 14150.30)	18185	12214.15 (10250.09, 14178.23)
Female	47084	47049.76 (38669.1, 55430.41)	12367	9409.09 (7443.83, 11374.37)	14277	9404.04 (7429.37, 11378.72)
age<15 years old	14101	13981.57 (11377.02, 18166.64)	2246	2514.38 (1991.81, 3415.67)	2188	2684.79 (2064.48, 3838.18)
15≤ age <64 years old	34287	34219.24 (28887.68, 39550.8)	9288	6885.48 (5673.13, 8097.84)	11534	6856.22 (5625.91, 8086.54)
≥ 64 years old	60030	59830.75 (48076.65, 71584.85)	17672	12003.01 (9096.54, 14909.49)	19021	11965.32 (9021.82, 14908.83)
Cardiovascular deaths	39217	39195.59 (31528.69, 46862.50)	9000	7860.70 (6016.12, 9705.26)	9666	7843.77 (5990.83, 9696.70)
age<15 years old	295	323.24 (0.00, 69.61)	31	34.81 (0.00, 69.61)	45	40.68 (0.00, 81.36)
15≤ age< 64 years old	9941	9953.07 (7482.77, 12423.37)	2015	1987.12 (1451.02, 2523.21)	2313	1990.68 (1453.80, 2527.55)
≥64 years old	28981	28944.72 (22876.22, 35013.23)	6954	5832.39 (4383.52, 7281.26)	7308	5794.98 (4336.56, 7253.41)
Infectious & parasitic diseases plus COVID-19	2800	2590.04 (1261.19, 3918.89)	7080	525.71 (232.34, 819.08)	9553	519.16 (224.43, 813.88)
age<15 years old	205	202.24 (0.00, 404.48)	113	40.45 (0.00, 80.91)	97	40.45 (0.00, 80.91)
15≤ age < 64 years old	961	874.31 (321.89, 1426.72)	2341	174.38 (59.98, 288.78)	4039	174.88 (60.46, 289.31)
≥ 64 years old	1634	1511.14 (530.02, 2492.27)	4440	294.98 (85.51, 504.44)	5441	300.81 (90.61, 511.01)
Diseases of the respiratory system	10466	10426.77 (6189.66, 14663.88)	2019	2348.21 (1245.34, 3451.07)	2401	2216.73 (1032.09, 3401.36)
age <15 years old	461	466.03 (0.00, 932.07)	64	98.90 (0.00, 197.80)	115	93.96 (0.00, 187.93)
15≤ age <64 years old	2455	2443.78 (909.78, 3977.78)	508	527.66 (174.94, 880.38)	613	500.20 (141.67, 858.73)
≥ 64 years old	7550	7517.56 (4489.46, 10545.67)	1447	1652.76 (890.19, 2415.34)	1673	1572.39 (759.33, 2385.45)

year of the pandemic (34.89% in 2020-2021, and 68.22% in 2021-2022) (Table 2). During this pandemic, older people (≥64 years old) accounted for a higher percentage of deaths. In this age group, 36693 deaths were registered, and 23968.34 (18118.36, 29818.36) deaths are estimated (Table 1). In the first year, the P-score was the highest among the three age groups; however, in the second year, it was lower than the score of adults aged 15-64 years old (58.96% in 2020-2021, and 68.22% in 2021-2022) (Table 2).

3.2. Excess mortality associated with cardiovascular diseases (CVDs)

As shown in Figure 1C, monthly changes in CVD mortality over time are exhibited by age groups and are compared with projected mortality as well. The number of deaths from CVDs from March 2020 to March 2022 was 18666, and the number of deaths from this disease is estimated with 95% *CI* to be 15704.46 (12006.95, 19401.96) (Table 1). As a result, the CVDs death count for 2021 and 2022 was 14.49 % and 23.23% higher than projected (Table 2). Among children aged below 15 years old, 76 cases of CVDs deaths were registered, and 75.48 (0, 150.97) CVDs deaths are estimated (Table 1). The P-scores for this age group dropped to -10.94% in 2020-2021, and jumped sharply to 10.61% in 2021-2022 (Table 2). 4328 CVDs deaths were registered among adults (aged 15–64 years old) during this pandemic, and 3977.80 (2904.82, 5050.76) CVDs deaths are estimated (Table 1). According to P-scores, this age group was more fragile in the second year of the pandemic and P-scores jumped from 1% to 16.19% (Table 2). In 64 and upper years old age group, 14 262 CVD deaths were registered, and 11627.38 (8720.08, 14534.67) CVD deaths were estimated (Table 1). P-scores in the first and second years were 19.23 % and 26.10%, respectively (Table 2). So, elderly people were more affected by this cause of death than other age groups.

Table 2. Comparison of the P-score average of total and cause-specific mortality (2016-2022).

Cause of mortality	Average P-score		
	April 2015 -February 2020	March 2020 -March 2021	March 2021 -March 2022
Total deaths	**0.19**	**35.15**	**51.33**
Male	-0.08	39.17	48.88
Female	0.07	31.43	51.81
<15 years old	0.85	-10.67	-18.50
15 ≤ age < 64 years old	0.19	34.89	68.22
≥ 64 years old	0.33	47.22	58.96
Cardiovascular deaths	**0.05**	**14.49**	**23.23**
<15 years old	-8.73	-10.94	10.61
15 ≤ age < 64 years old	-0.07	1.00	16.19
≥ 64 years old	0.12	19.23	26.10
Infectious & parasitic diseases plus Covid–19	**8.10**	**1246.74**	**1740.09**
<15 years old	1.36	179.31	139.77
15 ≤ age < 64 years old	9.91	1242.44	2209.49
≥64 years old	8.12	1405.17	1708.75
Diseases of the respiratory system	**0.37**	**–14.09**	**8.31**
<15 years old	-1.08	-35.28	22.38
15 ≤ age < 64 years old	0.21	-2.34	22.82
≥ 64 years old	0.43	-12.44	6.39

3.3. Excess mortality associated with infectious and parasitic diseases plus COVID–19

Table 1 shows that 16633 people died from infectious and parasitic diseases plus COVID-19 from March 2020 to March 2022, and the number of deaths from the disease is estimated at 1044.87 (456.77, 1632.96). As a result, this death count for 2020-2021 and 2021-2022 was 1246.74% and 1740.09% higher than projected (Table 2). The pattern and rapid change of this cause of monthly mortality over time are shown in Figure 1D. According to this graph, there are also changes in this pattern according to age group. Among children aged below 15 years old, 210 deaths were registered, and 80.90 (0.00, 161.82) deaths are estimated (Table 1). According to P-scores, this age group was more fragile in the first year of the pandemic, and the death count for 2020-2021and 2021-2022 was 179.31% and 139.77% higher than projected (Table 2). Among ages 15-64 groups, 6380 deaths were registered, and 349.26 (120.44, 578.09) deaths are estimated (Table 1). In the first and second years of the pandemic, the P-scores were 1242.44% and 2209.49%, respectively, so this group was affected by this cause (Table 2), and in 64 and upper years old, 9881 deaths were registered, and 595.79 (176.12, 1015.45) deaths were estimated. P-scores in the first and second years were 1405.17% and 1708.75%, respectively, so the elderly was affected by this cause of death (Table 1 and 2).

3.4. Excess mortality associated with diseases of the respiratory system (RDS)

Figure 1E shows changes in monthly RDS mortality over time by age group and compared to projected mortality. According to Table 1, 4420 people died from RDS between March 2020 and March 2022, and the estimated number of deaths with 95% *CI* is 4564.94 (2277.43, 6852.43). The P-score dropped to -14.09% in 2020-2021, and jumped sharply to 8.31% in 2021-2022 (Table 2). Among children aged below 15 years old, 179 RDS deaths were registered, and 192.86 (0, 385.73) deaths are estimated (Table 1). The P-score of this age group dropped to -35.28% in 2020-2021, and jumped sharply to 22.38% in 2021-2022 (Table 2). Among adults (aged 15-64 years old), 1121 RDS deaths were registered, and 1027.86 (316.61, 1739.11) deaths are estimated (Table 1). Based on the P-scores, the second year of the pandemic seemed to be more fragile for this age group (-2.34% in the first year, and 22.82% in the second year). For over 64 years of age group, 3120 deaths were registered, and 3225.15 (1649.52, 4800.79) deaths were estimated with 95% *CI*. The P-scores of this group were vulnerable in the second year of the pandemic as well (-12.44% in the first year, and 6.39% in the second year).

4. Discussion

Prior to two years ago, P-scores of mortalities broken down by age groups were a normal occurrence. These regular trends, however, showed varying degrees of wavering during the COVID-19 pandemic. In just two years, the COVID-19 pandemic has profoundly impacted all segments of society. A mitigation strategy has placed enormous strain on most countries' health care systems[11]. In addition to being highly effective and safe, the vaccines delivered were also highly innovative, since they were among the world's first to be marketed using these new technologies. While the global population needed these vaccines at the same time, manufacturers and policymakers were suffering from shortages in supply chains. Vaccination strategies had to be prioritized by countries, and the majority of them followed World Hhealth Organization recommendations[12]. The elderly and vulnerable groups should be prioritized, since most COVID-19 related mortality occurs among those over 50 years old, and mainly among those over 75 years old[13]. Additionally, health care workers were often prioritized. In Iran, mass vaccination campaigns began more slowly and with more delay. Vaccination campaigns began with a significant proportion of elderly immunized, allowing for early observations and foreseeing of future effects. This study shows some evidence of these effects. During two years Iran experienced five waves of COVID-19. P-scores for all cases of infectious and parasitic diseases, along with COVID-19, CVDs, and other causes of death within all and segmented populations could represent the disease profile of this epidemiological situation. There is a shift from a disease that severely affects the elderly to a disease where the majority of patients are young[13,14]. The mortality rate for women is typically lower than that for men under normal circumstances[15]. According to this study, the excess mortality rate increased more for males than for females. However, in the second year of the pandemic females overtook males (51.81% in female *vs*. 48.88% in males). It can be concluded that the sex-differences observed during the COVID-19 pandemic are not unique to that pandemic, but are more generally associated with excess mortality. It is important to investigate sex differences in excess mortality, especially because they may provide knowledge and tools for supporting sex equality in the management of public health and the prevention of excess mortality[15]. The study found that CVDs was the leading cause of death for segments of the population. There were several factors related to the functioning and organization of healthcare systems that prevented patients with acute coronary syndrome (ACS) from receiving timely recognition and treatment during the pandemic. Myocardial infarction (MI) patients were often delayed in transport and treatment because of frequent emergency calls that overwhelmed and disturbed emergency services whose personnel were busy transporting COVID-19 patients[16,17]. Furthermore, the stay-at-home order has strongly influenced the decision to call for medical help in an emergency[18]. There is a possibility that a number of "missing" ACSs may end up as Out of Hospital Cardiac Arrests due to the prolonged time between call and ambulance arrival[19]. Elective coronarography, valvuloplasty, percutaneous aortic valve implantation, atrial septal defect closure, and other non-urgent cardiologic procedures have decreased between 50% and 90% worldwide as a result of diverted resources caused by altered urgent pathology[20]. ACS symptoms should be further publicized and healthcare-seeking behaviors should be encouraged. By doing so, unrecognized cases, delays in action, and consequent unnecessary Hospital Cardiac Arrests events should be reduced in all population subgroups, especially in the elderly. In general, people aged 65 years or older and upper-risk people below 65 years old represent high-risk groups who should receive vaccinations first. Various estimates of the COVID-19 infection fatality rate by risk group, ranging from 1% for those over 65 years old, 2% for those over 75 years old, and 25% for institutionalized frail elderly[21,22]. Children's CVD P-scores increased sharply in the second year of the pandemic, according to this study. According to other evidences, pediatric patients with SARS-CoV-2 infections are increasingly experiencing cardiovascular complications. Among pediatric deaths related to COVID-19, 18% were caused by pre-existing CVD and 12% by periprocedural myocardial infarction. As compared to the rest of pediatric COVID-19 cases, periprocedural myocardial infarction has a ten-fold mortality rate. Children with impaired cardiovascular systems during SARS-CoV-2 infection have a worse prognosis[22,23]. The availability of accurate data is a major limitation when monitoring a global pandemic. It is only possible to calculate excess mortality based on accurate, high-frequency mortality data from previous years. The cause of death may be incorrectly recorded due to critical conditions for a variety of reasons.

In both chronic and acute conditions, the COVID-19 pandemic has contributed to greater medical neglect and inequalities globally. Public health will only become fully appreciated over time. Monitoring trends in broad mortality outcomes, such as changes in all- and specified-cause mortality, gives an insight into the magnitude of the mortality burden neglected that can be due to the performance of the healthcare system. It has resulted in unintended consequences for non-COVID-19 health services. As a metric of COVID-19's overall mortality impact, excess mortality includes all causes of death. It is important to disentangle the constituent parts-of direct COVID-19 deaths and indirect, non-COVID-19 excess deaths. In addition, national bodies need to report all-cause mortality as soon as possible. The use of excess mortality together with cause-specific mortality can be useful for monitoring trends within and between countries and informing international, national, and local public health policy.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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Authors’ contributions

NE contributed to the study concept, design, analysis, interpretation of data and wrote the manuscript, and, critical revision of the article.

SJH contributed to the study concepts, design, and critical revision of the article. MJB contributed to the study concepts, and manuscript editing, MTSH contributed to the study design, manuscript editing and final approval of the version to be published. ZIM contributed to the study concepts, and manuscript review. HRH contributed to the study concepts, and manuscript review. MHDD contributed to the study concepts, and manuscript review. All authors have read and approved the final manuscript.

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