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VERY HIGH MORTALITY OF CARDIOMETABOLIC DISEASE IN COVID-19 AND NON-COVID-19 POPULATION DURING THE PANDEMIC FIRST WAVE IN PERU

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ABSTRACT

OBJECTIVE: To describe the mortality of cardio-metabolic diseases by non-COVID-19 during the pandemic first wave 2020.

METHODOLOGY: We analyzed open data from Peruvian death certificates from March 01 to December 31, 2020, and 2019. Confirmed and suspected cases of COVID-19 by ICD-10 and the text of the diagnosis were included. We calculate the excess mortality 2020/2019 according to demographic characteristics, cardiometabolic disease, a primary cause of death. We performed a Poisson regression analysis for the prevalence rates of non-communicable

diseases non-COVID-19 / COVID-19 adjusted to sex, age, place of deaths, Insurance, altitude, poverty quintile, precedence regio, degree of instruction.

RESULTS: Deaths registered in first wave compared to 2019 resulted excess of 92,395 (+96%). The mortality rate was 25.1/10,000 inhabitants, 60% were male, 72.6% were older than 60 years and 38% died in Lima/Callao. 57% of deaths were due non-COVID disease. In this population, stroke was 51% more frequent (PR 1.51; CI95% 1.49-1.52; $p<0.001$); coronary disease was 29% (PR 1.29 CI95% 1.28-1.30; $p<0.001$), an diabetes was 5% (PR 1.06; CI95% 1.05-1.08; $p<0.001$). In COVID subjects, only obesity was more frequent in 37% (PR 1.37; CI95%1.35-1.39; $p<0.001$). There was an increase in cardiovascular death of 113% compared to 2019. Likewise, it was 13.9 times more frequent in non-COVID-19 compared to COVID-19 (PR 13.29; CI95% 12.32 – 14.34; $p<0.001$) adjusted a epidemiological characteristics.

CONCLUSION: During the first wave of COVID-19 in Peru, six out of ten were unrelated to COVID-19. The associated cardiometabolic diseases in COVID-19 deaths were obesity, while non-COVID-19 deaths were stroke, coronary disease, and diabetes mellitus.

Keywords: COVID-19; mortality; diabetes mellitus; hypertension; coronary disease; stroke; obesity; cardiovascular diseases.

INTRODUCTION

The COVID-19 pandemic due to high morbidity and excess mortality has collapsed the world's different health systems, affecting high, middle, and low-income countries [1]. Many deaths have happened in the uninfected population by delays in health care and the inefficiency of health systems, mainly in countries with limited resources. Direct and indirect deaths have been primarily to cardiometabolic diseases as diabetes, hypertension, and coronary heart disease [2,3].

In developed countries with efficient vital registration systems and confirmation tests, the excess of death oscillated between 20-50%, and only 40-70% was due COVID19 [4,5]. In developing countries, such as Latin America, information systems have great structural difficulties [6]. Peru is one of the countries with the highest mortality. In the beginning of first wave, Perú doesn't made an extensive molecular test for shortage of diagnostic tests. This

delayed the reporting of confirmatory COVID-19 cases, producing inexact information of mortality [7,8]. The excess deaths by COVID-19 and non-COVID-19 are relevant in public health decisions.

Previous to the pandemic, there was an increase in mortality from non-communicable diseases from 63.9% to 83.6% between 2003-2016 in Peru[9]. In a similar period, the death attributed to diabetes mellitus (DM) was 2.7%, and the population mortality in 2015 was 9.5% [10]. In the actual context, it was predictable higher morbidity and mortality in cardiometabolic diseases.

The database of the National Death Information System (SINADEF in Spanish) collects information from death certificates filled out by physicians. This system is the most accurate database of deaths at the nation-wide [11]. This investigation describes the excess of mortality in the Peruvian population during the first wave of the COVID-19 pandemic, emphasizing cardiometabolic diseases such as diabetes, hypertension, obesity, and cardiovascular disease.

MATERIALS AND METHODS

Design and study population

We performed a cross-sectional analysis of the deaths registered in the National System of Deaths of Peru (SINADEF) from March 01 to December 31, 2020. We compared it with the same period from 2019. SINADEF is an open data register of Peruvian deaths since 2017. Only physicians can register online way through its official website <https://www.datosabiertos.gob.pe/dataset/informaci%C3%B3n-de-fallecidos-del-sistema-inform%C3%A1tico-nacional-de-defunciones-sinadef-ministerio> [12]

Peru is in the central and western parts of South America. They have 33 million inhabitants, and a third of the population is in Lima, its capital. The health system is limited in infrastructure, equipment, and trained personnel, with partial coverage, without developed primary care.

COVID 19 was detected for the first time in Lima on March 06, 2020, and the first death happened on March 19. The peak of fatalities occurred during May to August, culminating the first wave at the end of November, being the lowest point since the beginning of the pandemic, but even higher compared to 2019

The study included citizens who died in Peru and had Peruvian residence addresses. We exclude subjects without cause of death in the online register.

COVID death

The deaths with COVID-19 were registered according to the International Classification of Disease (ICD10). The confirmed code was U07.1. Suspect code was U07.2; B34X and B97X. Those without ICD10 code but with the following descriptions: "COVID," "Coronavirus," or "SARS" in the death certificate were included.[13]

Demographic characteristics

We collected the following information: sex (Female/male), age group (<18; 18-59; ≥60 years old), instruction degree (illiterate; elementary; high; college, not specified), health insurance (government insurance, formal workers, army force, private, not identified); place of death (health center, home, public/transit road, not specified) altitude (<500, 500-2999, >3000 above sea meters level), natural region (Lima/Callao, coast, highlands, jungle), and monetary poverty quintile (1st to 5th quintile, the first quintile was the poorest).

The poverty quintile, altitude, and natural region data of the 1854 Peruvian districts were obtained from Peru's National Institute of Statistics and Informatics. [14–16].

Cardiometabolic diseases and basic death cause.

Diabetes mellitus, hypertension, obesity, coronary disease, and stroke were defined according to the ICD 10 code record in the death certificate. In patients who did not present coding, we searched a combination of terms according to Supplementary Table 1.

Supplementary table 1. ICD10 codes of cardiometabolic diseases.

	ICD10	Text word
Diabetes Mellitus	E10.0 a E14.9	"mellit","melit", "diabetic", "hiperglic".
Hipertension arterial	I11 a I15	"Hipertensión art", "HTA", "HT arterial", "hipertensiv"
Obesity	E66	"Obesidad", "sobrepeso", "exceso de peso".
Cardiovascular disease	I20 a I25	"IMA", "Infarto mioc", "infarto de m", "infarto car", "infarto agu", "angina", "coronario", "SICA" "SCA"
Brain-vascular disease	I60 a I69	"cerebrovascular", "cerebro vascular", "ACV", "ECV", "DCV", "Ictus", "stroke", "infarto cer", "A.C.V."
Kidney disease	N17- N19	"enfermedad renal", "ERC", "IRC", "IRCT - HD", "renal ag", "renal cr".[31]

The Peruvian death certificates contain three causes of death: direct, intermediate, and basic. The basic cause of death initiates the chain of pathological events that leads directly to death and is used to measure mortality attributed to some diseases.[17,18]. The basic cause of death was regrouped according to a modification of the 10/110 strategy of the Pan American Health Organization [19], according to Supplementary Table 2.

Supplementary table 2. ICD10 codes

	ICD 10
Respiratory infection.	J09 a J22
Other infectious diseases	A00 -A99, B00-B99, J00-J15, G00-G03
Cardiovascular disease	I20 – I25 , I60 a I69
Non- communicable disease	C, D, E, F, G, H, I00 a I19, I26 a I59; I70 a I99, K, L, M, N, O, P, Q y J30 a J99
External injury	S, T, V, W, X, Y
Non-specified	“Paro cardio-respiratorio”, “Descomposición sin posibilidad de saber causa” "Paro cardiaco"

Data analysis

The SINADEF database was downloaded on January 10, 2021, when COVID-19 first wave finished. In the Microsoft Excel spreadsheet (Microsoft, Redmond, Washington, USA), we evaluated the presence of extreme values, recoded the texts to pre-specified codes, and generated new variables. Stata v 15.1 program (Stata Corp, College Station, Texas, USA) was used to perform statistical analysis with a significance level of 0.05%.

We obtained the percentage of non-reported COVID-19 death of the official Peruvian database of the Ministry of Health (MINSA) [20] compared with the SINADEF database [12]. Excess mortality was calculated between March 01 to December 31th, 2020, and 2019 according to demographic data, cardiometabolic diseases, and basic cause of death.

Using the Pearson chi test, we compared clinical characteristics according to COVID-19 in the same period and evaluated differences between groups. We considered a significance level of 5%.

We calculated the prevalence of general mortality and prevalence rate of each cardiometabolic disease. The prevalence rate was obtained through the Generalized Linear model with the Poisson family, log link and robust variance. We adjusted to sex, age group,

instruction degree, health insurance, place of death, altitude, and natural region. We focused each general mortality PR in COVID subject and non-COVID subjects with a confidence interval of 95%

Likewise, we calculated the prevalence of cardiovascular death. We calculated adjusted prevalence rates to non- covid disease, sex, age group, instruction degree, health insurance, place of death, altitude, and natural region in the same way.

RESULTS

Excess of deaths

Between March 01, 2020, and December 31th 2020, Peru experienced deaths, 96% more than expected. In general, basic cause of death during the pandemic was mainly respiratory infectious with an excess of 194%. While cardiovascular death was 113% compared with 2019. All cardio-metabolic diseases had an excess of death, mainly DM, coronary heart disease, HTN, and obesity, with 176%, 192%, 205%, and 1365%, respectively, compared to 2019. (Table1)

Table 1. Excess mortality according to the socio-demographic characteristic of deaths in 2019 -2020

	Deaths 2019		Deaths 2020		Mortality Excess	
	n	(%)	n	%	Δ	%
General	96083	(100)	188478	(100)	92395	(96)
Sex						
Female	44346	(46.2)	74189	(39.4)	29843	(67)
Male	51730	(53.8)	114285	(60.6)	62555	(121)
Age group						
<18 y	6963	(7.3)	5810	(3.1)	-1153	(-17)
18 – 59 y	22878	(23.8)	45804	(24.3)	22926	(100)
> 60 y	66182	(68.9)	136812	(72.6)	70630	(107)
Instruction degree						
Illiterate	16577	(17.3)	25006	(13.3)	8429	(51)
Elementary School	28369	(29.5)	44339	(23.5)	15970	(56)
High School	20397	(21.2)	42889	(22.8)	22492	(110)

College/Technical	10710	(11.1)	20404	(10.8)	9694	(91)
Not specified	20030	(20.8)	55840	(29.6)	35810	(179)
Health insurance						
MINSA	48846	(50.8)	88604	(47.0)	39758	(81)
Formal workers (Essalud)	28488	(29.6)	68822	(36.5)	40334	(142)
Army Force	2225	(2.3)	5603	(3.0)	3378	(152)
Private	4745	(4.9)	8875	(4.7)	4130	(87)
Not specified	11779	(12.3)	16574	(8.8)	4795	(41)
Place of death						
Health center	54523	(56.7)	109873	(58.3)	55350	(102)
Home	34635	(36.0)	71865	(38.1)	37230	(107)
Public/transit road	6681	(7.0)	6439	(3.4)	-242	(-4)
Not specified	244	(0.3)	301	(0.2)	57	(23)
Altitude						
<500 masl	55180	(57.7)	132542	(70.5)	77362	(140)
500 – 2999 masl	21025	(22.0)	31158	(16.6)	10133	(48)
>= 3000 masl	19376	(20.3)	24369	(13.0)	4993	(26)
Natural region						
Lima-Callao	30121	(31.5)	72633	(38.6)	42512	(141)
Coast	19880	(20.8)	51397	(27.3)	31517	(159)
Highlands	34856	(36.5)	47491	(25.3)	12635	(36)
Jungle	10724	(11.2)	16548	(8.8)	5824	(54)
Poverty quintile ^b						
Quintile 5	57854	(60.5)	129578	(68.9)	71724	(124)
Quintile 4	17089	(17.9)	33499	(17.8)	16410	(96)
Quintile 3	8719	(9.1)	12317	(6.5)	3598	(41)
Quintile 2	6962	(7.3)	7681	(4.1)	719	(10)
Quintile 1	4957	(5.2)	4994	(2.7)	37	(1)
Non-communicable diseases						
Coronary disease	7347	(7.6)	21450	(11.4)	14103	(192)

Stroke	7214	(7.5)	9558	(5.1)	2344	(32)
Diabetes	5964	(6.2)	16437	(8.7)	10473	(176)
Hypertension	8006	(8.3)	24399	(12.9)	16393	(205)
Kidney failure	7698	(8.0)	11013	(5.8)	3315	(43)
Obesity	251	(0.3)	3676	(2.0)	3425	(1365)

The basic cause of death

Respiratory infections ^c	29611	(30.8)	87069	(46.2)	57458	(194)
Others infections ^d	12375	(12.9)	19720	(10.5)	7345	(59)
Cardiovascular disease ^e	11135	(11.6)	23719	(12.6)	12584	(113)
Other non-communicable disease ^f	35566	(37.0)	47309	(25.1)	11743	(33)
External injuries ^g	5851	(6.1)	8322	(4.4)	2471	(42)
Not specified	1545	(1.6)	2339	(1.2)	794	(51)

Source: National System of Deaths (SINADEF) March 01- December 31, 2019, and 2020. MINSA:Health Ministry. Masl: meters above sea level.

^b Poverty according to the National Institute of Statistics and Informatics from Peru (INEI-2020).

General mortality in COVID19 first wave

The epidemiological characteristics of pandemic first wave compared to 2019 showed a higher prevalence of males, older, college/technical instruction, attended in EsSalud hospitals (formal workers' Insurance), with the place of death in health centers, living in altitude less than 500 meters above sea level such as Lima-Callao, and poverty quintile five (less needy). (Table 1)

The accumulated mortality rate from COVID-19 first wave, according to SINADEF data in December 2020, was 25.1 deaths per 10 000 inhabitants. However, official MINSA data underreported COVID deaths compared to the SINADEF database in 54%. (Figure 1). The exact gap by the Peruvian region is in Supplementary Table 3 and 4.

Supplementary table 3. Mortality excess COVID-19 first wave in Peru.

2019-2020 compared mortality			2020 mortality			
Deaths 2019	Deaths 2020	Mortality excess	COVID-19	Confirmed COVID-19 ^b	Suspected COVID-19 ^c	Non COVID-19 ^d

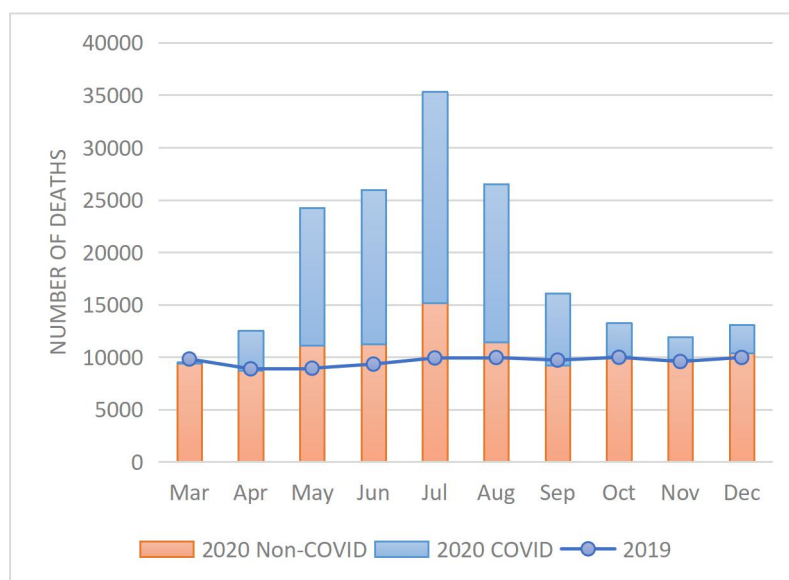
	n	n	Δ	%	n (%)	n (%)	n (%)	n (%)
TOTAL	96083	188478	+92395	+96%	81919 (43)	48903 (26)	33016 (17)	106559 (57)
Mar	9818	9512	-306	-3%	85 (1)	2 (0)	83 (1)	9247 (99)
Apr	8880	12532	+3652	+41%	3776 (30)	1176 (9)	2600 (21)	8756 (70)
May	8938	24243	+15305	+171%	13128 (54)	5211 (21)	7917 (33)	11115 (46)
Jun	9332	25967	+16635	+178%	14735 (57)	8224 (32)	6511 (25)	11232 (43)
Jul	9918	35322	+25404	+256%	20176 (57)	12956 (37)	7220 (20)	15146 (43)
Aug	9959	26520	+16561	+166%	15070 (57)	10669 (40)	4401 (17)	11450 (43)
Sep	9713	16094	+6381	+66%	6865 (43)	4994 (31)	1871 (12)	9229 (57)
Oct	9980	13291	+3311	+33%	3220 (24)	2274 (17)	946 (7)	10071 (76)
Nov	9579	11915	+2336	+24%	2163 (18)	1527 (13)	636 (5)	9752 (82)
Dec	9966	13082	+3116	+31%	2701 (21)	1870 (14)	831 (7)	10381 (79)

Source: National System of Deaths (SINADEF) March 01 to December 31, 2019 and 2020.

^a COVID-19: Confirmed or suspected COVID19. ^b Confirmed COVID19: ICD-10 U07.1 ^c Suspected COVID19: ICD-10 (U07.2 , B34.X or J97.X) or by written diagnosis ("COVID", "Coronavirus", "SARS CoV-2").

^d Non COVID-19: Confirmed or suspected absent COVID-19.

Supplementary fig 1. Monthly mortality comparative 2019 -2020 COVID-19 first wave



Source: National System of Deaths (SINADEF) March 01 to December 31, 2019 and 2020

COVID-19: Confirmed or suspected COVID19. Confirmed COVID19: ICD-10 U07.1 Suspected COVID19: ICD-10 (U07.2 , B34.X or J97.X) or by written diagnosis ("COVID", "Coronavirus", "SARS CoV-2"). Non COVID-19: Confirmed or suspected absent COVID-19

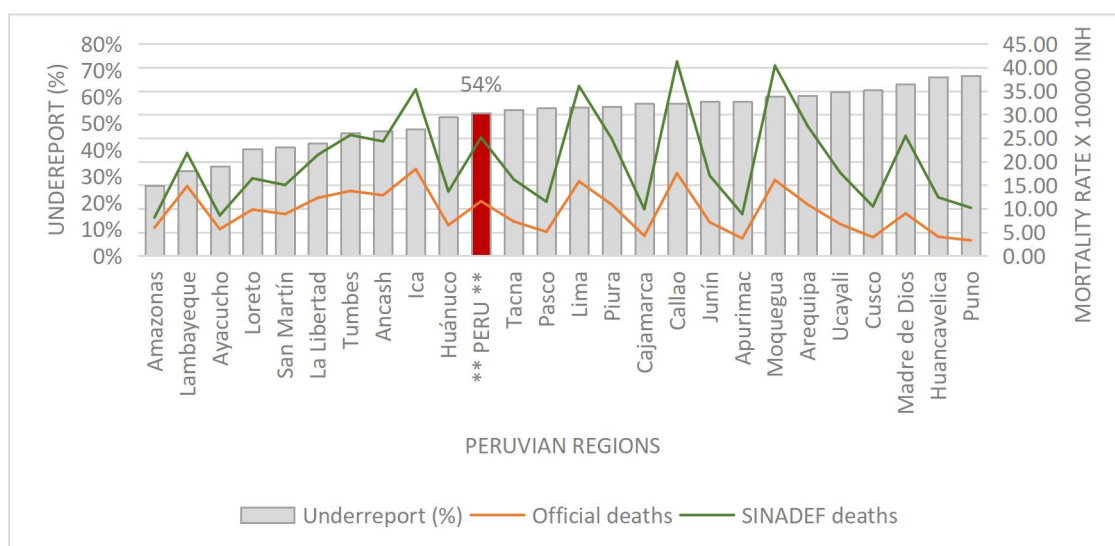
CHD: Coronary heart disease. DM: Diabetes mellitus HTN: Hypertension KF: Kidney failure. Obesity: OBE.

Supplementary table 4. Underreport according to Peruvian region from March 01 to December 31, 2020.

Región	Population	Official deaths	SINADEF deaths	Official deaths rate x 10000 inh	SINADEF deaths rate x 10000 inh	% Under report
** PERU **	32,625,948	37724	81,924	11.56	25.11	54%
Amazonas	426806	254	346	5.95	8.11	27%
Ancash	1180638	1517	2867	12.85	24.28	47%
Apurimac	430736	159	381	3.69	8.85	58%
Arequipa	1497438	1630	4129	10.89	27.57	61%
Ayacucho	668213	378	571	5.66	8.55	34%
Cajamarca	1453711	611	1435	4.20	9.87	57%
Callao	1129854	1979	4660	17.52	41.24	58%
Cusco	1357075	533	1422	3.93	10.48	63%
Huancavelica	365317	147	453	4.02	12.40	68%
Huánuco	760267	494	1037	6.50	13.64	52%
Ica	975182	1794	3444	18.40	35.32	48%
Junín	1361467	969	2320	7.12	17.04	58%
La Libertad	2016771	2480	4319	12.30	21.42	43%
Lambayeque	1310785	1938	2856	14.79	21.79	32%
Lima	10628470	16791	38307	15.80	36.04	56%
Loreto	1027559	1008	1689	9.81	16.44	40%
Madre de Dios	173811	156	442	8.98	25.43	65%
Moquegua	192740	310	778	16.08	40.37	60%
Pasco	271904	138	312	5.08	11.47	56%
Piura	2047954	2227	5098	10.87	24.89	56%
Puno	1237997	403	1260	3.26	10.18	68%
San Martín	899648	797	1351	8.86	15.02	41%
Tacna	370974	270	602	7.28	16.23	55%
Tumbes	251521	346	645	13.76	25.64	46%
Ucayali	589110	395	1038	6.71	17.62	62%

Source: Official deaths from Ministry of health . SINADEF (National system of deceased in Spanish).

Figure 1. Underreport and mortality rates of official and SINADEF deaths from Peruvian regions during COVID-19 first wave



Source: National System of Deaths (SINADEF) and COVID-19 mortality MINSA, March 01- December 31, 2020.

According basic cause of death, the nation-wide cardiovascular mortality trend from 2017 to 2019 was between 11.5 to 12.0%. In absolute values of 2020, cardiovascular deaths increased in almost 100%. (Supplementary table 5).

Supplementary table 5. Causes of mortality in Peruvian population 2017- 2020

	2017	2018	2019	2020
General	98977	112809	114946	207435
Cardiovascular ^a	11839 (12.0)	13833 (12.3)	13262 (11.5)	25937 (12.5)
Other non-communicable^b	38245 (38.6)	45912 (40.7)	42396 (36.9)	54958 (26.5)
Respiratory infection^c	28193 (28.5)	31784 (28.2)	35557 (30.9)	92622 (44.7)
Other infections ^d	14050 (14.2)	13088 (11.6)	15100 (13.1)	21719 (12.5)
External injuries^e	6434 (6.5)	7593 (6.7)	7043 (6.1)	9782 (4.7)
Not encoded^f	216 (0.2)	599 (0.5)	1588 (1.4)	2417 (1.2)

Source: National System of Deaths (SINADEF) 2017 -2020

^c Respiratory infections: ICD-10 codes: J18 - j22, J80, and J96. ^d Others infections: ICD-10 codes: A00 -A99, B00-B99, J00-J15 and G00-G03,

^e Cardiovascular disease: ICD-10 codes: I20 to I25 and I60 to I69. ^f Other non-communicable diseases. ICD10 chapters: C, D, E, F, G, H, I00-I19, I26-I59; I70-I99, K, L, M, N, O, P, Q, J30 - J99, except J80 and J96. ^g External injuries: ICD-10 chapters: S, T, V, W, X, Y. Not encoded: Includes cardiorespiratory arrest, decomposition without the possibility of knowing the cause, among others

Mortality according to COVID19

During the pandemic first wave, 57% of deaths were due to non-COVID disease. These deaths were mainly women, older, with less instruction, care in the public health system (MINSA), deaths occurred at home, and more significant poverty (quintile 3, 2, and 1). (Table 2).

Table 2. Clinical and epidemiological characteristics of deaths in 2020 according to COVID disease during the first wave

	Non-COVID19		COVID19		p-value
	n	%	N	%	
General	106556	100%	81918	100	
Sex					
Female	49098	46.1%	25091	30.6	
Male	57458	53.9%	56827	69.4	<0.001
Age group					
<18 y	5395	5.1%	415	0.5	<0.001
18 – 59 y	22635	21.2%	23169	28.3	
> 60 y	78494	73.7%	58318	71.2	
Instruction degree					
Illiterate	19953	18.7%	5053	6.2	<0.001
Elementary School	33599	31.5%	10740	13.1	
High School	25768	24.2%	17121	20.9	
College/Technical	13265	12.4%	7139	8.7	
Not specified	13974	13.1%	41866	51.1	
Health insurance					
Public (MINSA)	52854	49.6%	35750	43.6	<0.001
Formal workers (Essalud)	35390	33.2%	33432	40.8	
Army Force	2342	2.2%	3261	4.0	
Private	5616	5.3%	3259	4.0	
Not specified	10357	9.7%	6217	7.6	
Place of death					

Health center	37022	34.7%	72851	88.9	<0.001
Home	64250	60.3%	7615	9.3	
Public/transit road	5107	4.8%	1332	1.6	
Not specified	180	0.2%	121	0.1	
Altitude					
<500 masl	68145	64.1%	64397	78.8	<0.001
500 – 2999 masl	20295	19.1%	10863	13.3	
>= 3000 masl	17878	16.8%	6491	7.9	
Natural region					
Lima-Callao	38808	36.5%	33825	41.4	<0.001
Coast	24712	23.2%	26685	32.6	
Highlands	32904	30.9%	14587	17.8	
Jungle	9894	9.3%	6654	8.1	
Poverty quintile ^b					
Quintile 5	68976	64.9%	60602	74.1	<0.001
Quintile 4	18973	17.8%	14526	17.8	
Quintile 3	8519	8.0%	3798	4.6	
Quintile 2	5968	5.6%	1713	2.1	
Quintile 1	3882	3.7%	1112	1.4	
Non-communicable diseases					
Coronary disease					
No	85682	80.4	81346	99.3	<0.001
Sí	20877	19.6	573	0.7	
Stroke					
No	98112	92.1	80808	98.6	<0.001
Sí	8447	7.9	1111	1.4	
Diabetes					
No	96776	90.8	75265	91.9	<0.001
Sí	9783	9.2	6654	8.1	
Hypertension					

No	89261	83.8	74818	91.3	<0.001
Sí	17298	16.2	7101	8.7	
Kidney failure					
No	98472	92,4	78993	96.4	<0.001
Sí	8087	7.6	2926	3.6	
Obesity					
No	106047	99.5	78755	96.1	<0.001
Sí	512	0.5%	3164	3.9	

Source: National System of Deaths (SINADEF) March 01- December 31, 2019, a, and 2020. MINSA:Health Ministry.
Masl: meters above sea level.

COVID-19: Confirmed or suspected COVID19. Confirmed COVID19: ICD-10 U07.1 Suspected COVID19: ICD-10 (U07.2 , B34.X or J97.X) or by written diagnosis ("COVID", "Coronavirus", "SARS CoV-2"). Non COVID-19: Confirmed or suspected COVID-19 absent. ^b Poverty according to the National Institute of Statistics and Informatics from Peru (INEI-2020).

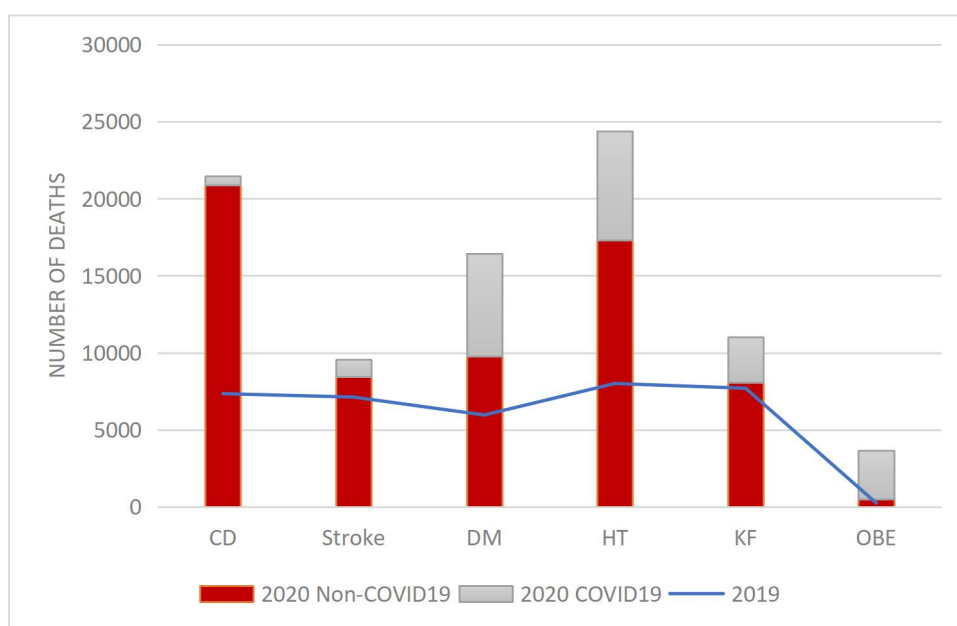
A 97.3% of subjects with coronary disease died due non-COVID19 causes, 88.4% with stroke, a 73.4% with kidney failure, 70.9% in hypertension, 59.5% in diabetes mellitus, and 13.9% in obesity. (Table 3 and Figure 2)

Table 3. General mortality according to cardiometabolic diseases during the first wave

Non communicable diseases	Cases / Total	General mortality Prevalence (IC95%)	Crude análisis PR (CI95%)	p-value	Adjusted análisis PR (CI95%)	p-value
Positive COVID19 deaths						
Coronary disease						
No	81346 / 167028	48.7 (48.4-48.9)	1.00		1.00	
Sí	5737 / 21450	2.7 (2.62-2.73)	0.05 (0.05-0.06)	<0.001	0.13 (0.12-0.14)	<0.001
Stroke						
No	80808 /178920	45.2 (44.9-45.4)	1.00		1.00	
Sí	1111 /9558	11.6 (11.0–12.3)	0.25 (0.24-0.27)	<0.001	0.30 (0.29-0.32)	<0.001
Diabetes						
No	75265 /172041	43.8 (43.5-43.9)	1.00		1.00	
Sí	6654 / 16437	40.5 (39.7-41.2)	0.93 (0.91-0.94)	<0.001	0.95 (0.94-0.96)	<0.001
Hypertension						

No	74818 / 164079	45.6 (39.7- 41.2)	1.00		1.00	
Sí	7101 / 24399	29.1 (28.5- 29.7)	0.64 (0.63- 0.65)	<0.001	0.99 (0.97- 1.001)	0.087
Kidney failure						
No	78993 / 177465	44.5 (44.3- 44.7)	1.00		1.00	
Sí	2926 / 11013	26.6 (25.7- 27.4)	0.60 (0.58- 0.62)	<0.001	0.58 (0.57- 0.60)	<0.001
Obesity						
No	78755 / 184802	42.6 (42.4- 42.8)	1.00		1.00	
Sí	3164 / 3676	86.1 (84.9- 87.2)	2.01 (1.99- 2.05)	<0.001	1.37 (1.35- 1.39)	<0.001
Negative COVID19 deaths						
Coronary disease						
No	85682 / 167028	51.3 (51.1- 51.5)	1.00		1.00	
Sí	20877 / 21450	97.3 (97.1- 97.5)	1.90 (1.89- 1.91)	<0.001	1.29 (1.28- 1.30)	<0.001
Stroke						
No	98112 /178920	54.8 (54.6- 55.1)	1.00		1.00	
Sí	8447 / 9558	88.4 (87.7- 89.0)	1.61 (1.60- 1.63)	<0.001	1.51 (1.49- 1.52)	<0.001
Diabetes						
No	96776 /172041	56.3 (56.0- 56.5)	1.00		1.00	
Sí	9783 / 16437	59.5 (58.8- 60.3)	1.05 (1.04- 1.07)	<0.001	1.06 (1.05- 1.08)	<0.001
Hypertension						
No	89261 / 164079	54.4 (54.2- 54.6)	1.00		1.00	
Sí	17298 / 24399	70.9 (70.3- 71.4)	1.30 (1.29- 1.32)	<0.001	1.00 (0.99- 1.01)	0.984
Kidney failure						
No	98472 / 177465	55.5 (55.2- 55.7)	1.00		1.00	
Sí	8087 / 11013	73.4 (72.6- 74.3)	1.32 (1.31- 1.34)	<0.001	1.39 (1.37- 1.41)	<0.001
Obesity						
No	106047 / 184802	57.4 (57.2- 57.6)	1.00		1.00	
Sí	512 / 3676	13.9 (12.8- 15.1)	0.24 (0.22- 0.26)	<0.001	0.37 (0.34- 0.39)	<0.001

Fig 2. Non-communicable disease mortality comparative 2019-2020 COVID-19 first wave



Source: National System of Deaths (SINADEF) March 01 to December 31, 2019, and 2020

COVID-19: Confirmed or suspected COVID19. Confirmed COVID19: ICD-10 U07.1 Suspected COVID19: ICD-10 (U07.2 , B34.X or J97.X) or by written diagnosis ("COVID", "Coronavirus", "SARS CoV-2"). Non COVID-19: Confirmed or suspected absent COVID-19

CD: Coronary disease. DM: Diabetes mellitus HT: Hypertension KF: Kidney failure. Obesity: OBE.

Adjusted to epidemiological characteristics, general mortality due non-COVID causes was 51% more frequent in stroke (PR 1.51; CI95% 1.49-1.52; p<0.001); 29% in coronary disease (PR 1.29 CI95% 1.28-1.30;p<0.001), and 5% in diabetes (PR 1.06; CI95% 1.05-1.08;p<0.001). General mortality due COVID cause was 37% more frequent in obesity (PR 1.37; CI95%1.35-1.-39; p<0.001). (Table 3). Full multivariate regression is shown in Supplementary table 6.

Supplementary table 6. Full Multivariate regression of associated factors of non-COVID mortality,

	Non-COVID		COVID		Crude analysis	p-value	Adjusted analysis	p-value
	n	%	N	%				
General	106556	100%	81918	100				
Sex								
Female	49098	46.1%	25091	30.6	1.00		1.00	
Male	57458	53.9%	56827	69.4	0.75 (0.75-0.77)	<0.001	0.85 (0.85-0.86)	<0.001
Age group								

<18 y	5395	5.1%	415	0.5	1.00		1.00	
18 – 59 y	22635	21.2%	23169	28.3	0.53 (0.51-0.55)	<0.001	0.61 (0.60-0.62)	<0.001
> 60 y	78494	73.7%	58318	71.2	0.62 (0.60-0.64)	<0.001	0.59 (0.58-0.60)	<0.001
Instruction degree								
Illiterate	19953	18.7%	5053	6.2	1.00		1.00	
Elementary School	33599	31.5%	10740	13.1	0.95 (0.93-0.97)	<0.001	0.98 (0.97-0.99)	<0.001
High School	25768	24.2%	17121	20.9	0.75 (0.74-0.77)	<0.001	0.91 (0.90-0.92)	<0.001
College/Technical	13265	12.4%	7139	8.7	0.81 (0.80-0.83)	<0.001	0.99 (0.98-1.001)	0.094
Not specified	13974	13.1%	41866	51.1	0.31 (0.30-0.32)	<0.001	0.54 (0.53-0.55)	<0.001
Health insurance								
Public (MINSA)	52854	49.6%	35750	43.6	1.00		1.00	
Formal workers (Essalud)	35390	33.2%	33432	40.8	0.86 (0.85-0.87)	<0.001	1.01 (0.99-1.02)	0.088
Army Force	2342	2.2%	3261	4.0	0.70 (0.67-0.73)	<0.001	0.92 (0.90-0.95)	<0.001
Private	5616	5.3%	3259	4.0	1.06 (1.03-1.09)	<0.001	1.15 (1.13-1.16)	<0.001
Not specified	10357	9.7%	6217	7.6	1.05 (1.03-1.07)	<0.001	1.06 (1.05-1.07)	<0.001
Place of death								
Health center	37022	34.7%	72851	88.9	1.00		1.00	
Home	64250	60.3%	7615	9.3	2.65 (2.63-2.67)	<0.001	1.97 (1.96-1.99)	<0.001
Public/transit road	5107	4.8%	1332	1.6	2.35 (2.31-2.39)	<0.001	1.86 (1.83-1.89)	<0.001
Not specified	180	0.2%	121	0.1	1.77 (1.61-1.95)	<0.001	1.56 (1.43-1.71)	<0.001
Altitude								
<500 masl	68145	64.1%	64397	78.8	1.00		1.00	
500 – 2999 masl	20295	19.1%	10863	13.3	1.27 (1.25-1.29)	<0.001	1.08 (1.06-1.10)	<0.001
>= 3000 masl	17878	16.8%	6491	7.9	1.42 (1.40-1.45)	<0.001	1.11 (1.08-1.13)	<0.001
Natural region								
Lima-Callao	38808	36.5%	33825	41.4	1.00		1.00	
Coast	24712	23.2%	26685	32.6	0.90 (0.89-0.91)	<0.001	0.89 (0.88-0.90)	<0.001
Highlands	32904	30.9%	14587	17.8	1.29 (1.28-1.31)	<0.001	0.98 (0.96-1.004)	0.123
Jungle	9894	9.3%	6654	8.1	1.12 (1.10-1.14)	<0.001	0.99 (0.98-1.01)	0.684
Poverty quintil ^b								

Quintil 5	68976	64.9%	60602	74.1	1.00		1.00	
Quintil 4	18973	17.8%	14526	17.8	1.06 (1.05-1.07)	<0.001	0.97 (0.96-0.98)	<0.001
Quintil 3	8519	8.0%	3798	4.6	1.30 (1.28-1.31)	<0.001	1.04 (1.03-1.05)	<0.001
Quintil 2	5968	5.6%	1713	2.1	1.46 (1.44-1.48)	<0.001	1.04 (1.02-1.05)	<0.001
Quintil 1	3882	3.7%	1112	1.4	1.46 (1.44-1.48)	<0.001	1.05 (1.03-1.06)	<0.001
Non communicable diseases								
Coronary disease								
No	85682	80.4	81346	99.3	1.00		1.00	
Sí	20 877	19.6	573	0.7	1.90 (1.89-1.91)	<0.001	1.29 (1.28-1.30)	<0.001
Stroke								
No	98112	92.1	80808	98.6	1.00		1.00	
Sí	8 447	7.9	1 111	1.4	1.61 (1.60-1.63)	<0.001	1.51 (1.49-1.52)	<0.001
Diabetes								
No	96776	90.8	75265	91.9	1.00		1.00	
Sí	9 783	9.2	6 654	8.1	1.05 (1.04-1.07)	<0.001	1.06 (1.05-1.08)	<0.001
Hypertension								
No	89261	83.8	74818	91.3	1.00		1.00	
Sí	17 298	16.2	7 101	8.7	1.30 (1.29-1.32)	<0.001	1.00 (0.99-1.01)	0.984
Kidney failure								
No	98472	92,4	78993	96.4	1.00		1.00	
Sí	8 087	7.6	2 926	3.6	1.32 (1.31-1.34)	<0.001	1.39 (1.37-1.41)	<0.001
Obesity								
No	106047	99.5	78755	96.1	1.00		1.00	
Sí	512	0.5%	3 164	3.9	0.24 (0.22-0.26)	<0.001	0.37 (0.34-0.39)	<0.001

Cardiovascular mortality in non-COVID19.

The prevalence of mortality due cardiovascular cause in the first wave was 21.5% in non-COVID deaths and 0.95% in COVID deaths. In the same way, cardiovascular mortality in subjects with hypertension was 35.1%, in diabetes was 16.8%, and in obesity was 5.1%. Adjusted to epidemiological characteristics, cardiovascular mortality was 13.2 times more frequent in non-COVID-19; 2.3 times in subjects with hypertension (PR 2.31; CI95% 2.24-

2.37;p<0.001), 31% more in subjects with obesity (PR 1.31 ; CI95% 1.14-1.52;p<0.001) and 3% more in subjects with diabetes mellitus (PR 1.03; CI95% 0.99-1.07; p<0.090). (Table 4).

Table 4. Cardiovascular mortality in Peruvian population during the first wave

	Cases /Total	Cardiovascular mortality Prevalence % (IC95%)	Crude analysis PR (I95%)	P-value	Adjusted analysis PR (I95%)	P-value
COVID19						
Yes	782 / 81919	0.95 (0.89 – 1.02)	1.00		1.00	
Not	22937 / 106559	21.5 (21.3 – 21.8)	22.5 (20.9-24.2)	<0.001	13.29 (12.32-14.34)	<0.001
Sex						
Female	10603 / 74189	14.3 (14.0-14.5)	1.00		1.00	
Male	13116 /114285	11.5 (11.3-11.7)	0.80 (0.78 – 0.82)	<0.001	1.05 (1.03-1.08)	<0.001
Age group						
<18 y	258 / 5810	4.4 (3.9-5.0)	1.00		1.00	
18 – 59 y	3652 / 45804	7.9 (7.7-8.2)	1.79 (1.58-2.03)	<0.001	2.31 (2.03-2.63)	<0.001
> 60 y	19807 / 136812	14.5 (14.3-14.7)	3.26 (2.88-3.68)	<0.001	2.72 (2.40-3.09)	<0.001
Instruction degree						
Illiterate	3471 / 25006	13.9 (13.4-14.3)	1.00		1.00	
Elementary School	8929 / 44339	20.1 (19.8-20.5)	1.45 (1.39-1.51)	<0.001	1.08 (1.04-1.12)	<0.001
High School	6244 / 42889	14.6 (14.2-14.9)	1.04 (1.01-1.09)	0.024	1.04 (1.002-1.09)	0.040
College/Technical	2906 / 20404	14.2 (13.8-14.7)	1.03 (0.97-1.08)	0.306	0.95 (0.90-1.01)	0.111
Not specified	2169 / 55840	3.9 (3.72-4.05)	0.27 (0.26-0.30)	<0.001	0.86 (0.82-0.92)	<0.001
Health insurance						
MINSA	10648 / 88648	12.0 (11.8-12.2)	1.00		1.00	
Formal workers (Essalud)	8565 /68822	12.5 (8.1-9.6)	1.03 (1.01-1.07)	0.016	0.99 (0.96-1.02)	0.591
Army Force	494 / 5603	8.8 (14.1-15.6)	0.73 (0.67-0.80)	<0.001	0.97 (0.89-1.07)	0.642
Private	1316 / 8875	14.8 (15.7-16.8)	1.23 (1.16-1.30)	<0.001	1.11 (1.04-1.17)	0.001
Not specified	2696 / 16574	16.3 (15.7-16.8)	1.35 (1.29-1.41)	<0.001	1.14 (1.09-1.19)	<0.001

Place of death						
Health center	4578 / 109873	4.2 (4.1-4.3)	1.00		1.00	
Home	18482 / 71865	25.7 (25.4-26.0)	6.17 (5.97- 6.37)	<0.001	2.10 (2.02- 2.18)	<0.001
Public/transit road	640 / 6439	9.9 (9.2-10.7)	2.38 (2.19- 2.59)	<0.001	1.22 (1.12- 1.33)	<0.001
Not specified	19 /301	6.3 (3.8-9.7)	1.51 (0.96- 2.37)	0.071	1.09 (0.69- 1.72)	0.686
Altitude						
<500 masl	18014 / 132542	13.6 (13.4-13.8)	1.00		1.00	
500 – 2999 masl	3458 /31158	11.1 (10.8-11.5)	0.81 (0.78- 0.84)	<0.001	1.02 (0.94- 1.12)	0.527
>= 3000 masl	2217 / 24369	9.1 (8.73-9.45)	0.67 (0.64- 0.70)	<0.001	0.74 (0.67- 0.82)	<0.001
Natural región						
Lima-Callao	10278 / 72633	14.2 (13.8-14.4)	1.00		1.00	
Coast	7271 /51397	14.2 (13.8-14.5)	0.99 (0.97- 1.03)	0.986	1.04 (1.01- 1.07)	0.007
Highlands	4852 / 47491	10.2 (9.9-10.5)	0.72 (0.69- 0.74)	<0.001	0.75 (0.68- 0.82)	<0.001
Jungle	1288 / 16548	7.8 (7.4-8.2)	0.55 (0.52- 0.58)	<0.001	0.60 (0.56- 0.65)	<0.001
Poverty quintile ^b						
Quintile 5	16038 / 129578	12.4 (12.2-12.6)	1.00		1.00	
Quintil 4	4778 / 33499	14.3 (13.9-14.6)	1.15 (1.11- 1.19)	<0.001	1.14 (1.10- 1.18)	<0.001
Quintil 3	1558 / 12317	12.7 (12.1-13.2)	1.02 (0.97- 1.07)	0.413	0.97 (0.92-1- 03)	0.307
Quintil 2	794 / 7681	10.3 (9.66-11.03)	0.83 (0.78- 0.90)	<0.001	0.90 (0.83- 0.97)	0.009
Quintil 1	521 / 4994	10.4 (9.59-11.31)	0.84 (0.77- 0.92)	<0.001	0.95 (0.86- 1.04)	0.294
Cardiometabolic diseases						
*						
Diabetes						
No	20959 / 172041	12.2 (12.0-12.3)	1.00		1.00	
Sí	2760 / 16437	16.8 (16.2-17.4)	1.37 (1.32- 1.43)	<0.001	1.03 (0.99- 1.07)	0.090
Hypertension						
No	15151 / 164079	9.2 (9.09-9.37)	1.00		1.00	
Sí	8568 /24399	35.1 (34.5-35.7)	3.80 (3.70 – 3.90)	<0.001	2.31 (2.24-2- 37)	<0.001
Obesity						
No	23533 / 184802	12.7 (12.5-12.8)	1.00		1.00	

Sí	186 /3676	5.1 (4.4-5.8)	0.40 (0.34 – 0.45)	<0.001	1.31 (1.14- 1.52)	<0.001
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DISCUSSION

The data obtained show a very high mortality excess in Peru during the COVID-19 pandemic first wave near 100% compared to the 2019 rate. Three out of five were unrelated to COVID-19. The associated cardiometabolic diseases in COVID-19 deaths were obesity, while non-COVID-19 deaths were stroke, coronary disease, and diabetes mellitus.

Excess deaths during the COVID-19 pandemic have been reported in most countries; however, the health policies for each country have led to mortality not directly related to the infection. [21] A comparative study of global excess mortality until March 2021 ranks Peru in the first place of excess death with more than 355 deaths per 100,000 inhabitants, while Mexico, Ecuador, Bolivia as well Eastern European countries and South Africa, maintain excess mortality between 200 and 300 deaths per 100,000 inhabitants [1].

In the first quarter of 2020, Wuhan showed an increase of 56% compared to 2019. This increase was due to COVID-19 in 8 times. But also cardiovascular disease and DM increased in 29% and 83% respectively [22]. In the United Kingdom until June 2020, 94% of acute cardiovascular deaths were in people without COVID-19, showing an absolute excess compared to the previous year of 8%, mostly occurring at home with an increase of 35%. The most common conditions were stroke 36%, acute coronary disease 25%, and heart failure 23%. [23]. In Denmark, there was no excess mortality in 2020 compared to 2019; however, the home mortality rate increased by 4%, being ore frequent in those with heart failure, peripheral arterial disease, and DM [24]. In Latin America, reports on excess death are scarce, and the frequency of its components is uncertain [6].

A multifactorial approach can explain this excess death due to non-COVID deaths. For example, deterioration in the support network of the primary health care level, the timely work of the health team in the care of the health emergency was hampered by the paralysis of the outpatient clinic and the conversion of general hospitals to exclusive ones for COVID-19 and lack of recognition of warning signs to go to emergency services [25,26]. A survey by the World Health Organization (WHO) carried out in 105 countries between May and June 2020 described that 90% of the surveyed countries partially or wholly interrupted at least 1 of the 25 essential health services, being the most frequent immunization services, non-communicable diseases, and family planning services [27].

In Non-COVID patients, the results show a slight association between diabetes and hypertension with mortality. But this relationship is non-precious because the basic cause of death is coronary disease and stroke. In addition, we observed a progressive trend since 15 years in cardiometabolic mortality, and we expected high mortality percentages in light of these extreme confinement measures.[10]

Some authors classify death from COVID 19 as a cardiovascular and non-infectious cause. This rating is due to thrombosis, and anticoagulant treatment is promoted in patients with severe disease.[28] Less than 1% of deaths with COVID were presented as the basic cause of cardiovascular death. The high risk of contagion and the public policy of cremation and early burial limited the autopsy of these patients. [29]

Public health importance

The extreme restrictive measures applied in the same way without differentiating geographical risk, indirectly increased Non-COVID death. Coronary heart disease or stroke was the typical way of death for a large part of this population with diabetes, hypertension, or obesity. It is not clear, the true impact of non-covid mortality on the population. We must be describe mortality characteristics and factors as a first step and then to start improvement plans,. [30,31]

Likewise, two epidemiological mortality phenotypes identified during the first wave. The first who died with COVID-19 were males, with death in health establishments and Quintile 5 of poverty. A second one corresponded to non-COVID-19 person, mainly women, older, with less education, 60% of deaths occurred at home and greatest poverty (quintile 3, 2 and 1).

The underreport of 54% was officially recognized in April 2021. Suspected cases were included, thus reducing the information gap. The data reaffirmed that we maintain the place with the highest mortality. However, many countries also have information gaps. Comparisons should be made considering similar calculation methodologies and the type of death report, and the diagnostic method used for COVID. [32].

Limitations and strengths

The limitations in this investigation were the quality of completion of death certificates by physicians, including lack of documentation of the basic cause of death and the lack of coding [33]. Also, serological tests during the first months of the pandemic delayed a molecular diagnosis and the confirmed COVID-19 code. The reference to determine excess mortality was 2019; other authors use the expected mortality taken from the last 5 years.

Among the strengths, we were able to determine the basic cause of death in all the data, since about 50% of it does not have an ICD10 coding. We also add poverty level, altitude and natural region of each deceased, important confounding variables in the mortality analysis.

Conclusion

During the first wave of COVID-19 in Peru, three out of five were unrelated to COVID-19. The associated cardiometabolic diseases in COVID-19 deaths were obesity, while non-COVID-19 deaths were stroke, coronary disease, and diabetes mellitus. Historical, social shortcomings, such as the universal health insurance gap, the inequity of basic services, labor informality, and an expanding epidemiological transition, have triggered this excessive mortality [34].

Contributors

SNS was the author of the idea and design of the investigation. SNS and MYA were the authors of the statistics and interpretation of results. SNS and MYA participated in the research and article preparation and approved the final article.

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