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Original Research Article

H1N1 and COVID-19: surprising mortality pattern correlation

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ABSTRACT

Background: Explanation of observed differentials in mortality rates during the COVID-19 pandemic across regions and countries is a great dilemma. To improve current and future pandemic response and to shed a light on secrets of COVID-19 mortality variances, we design this study to compare mortalities / million (M) between Covid-19pandemic and H1N1 2009 pandemic mortalities.
Methods: One hundred thirty countries and territories that reported H1N1 cases up to September, 2009, were enrolled. COVID-19 accumulative deaths were considered up to January, 2021. Countries and territories < 2 million inhabitants population at 2009 were excluded. We used simple regression analyses to test the associations (SPSS-21).
Results: The pattern of variances in COVID-19 mortality rates across countries was surprisingly identical to the pattern of mortality rates across countries observed in H1N1 with meaningful linear regression tested in a two-tailed alternative statistical hypothesis. The slope value indicated that H1N1 deaths have a positive impact on COVID-19 mortality. with a very highly significant influence at p=0.0002. Relationship coefficient was accounted to (0.32789) with meaningful and a very high significant determination coefficient (R-Square = 10.75%). A very highly significant intercept (p=0.0000) reflects the severity of H1N1 and initial value even with no H1N1 deaths.
Conclusions: We are adding another risk factor that can be used as a predictor for current and future epidemics.

Keywords: H1N1, COVID-19, Mortality rate, SARS-Cov2

INTRODUCTION

According to the World Health Organization (WHO), influenza causes respiratory deaths in 290,000–650,000 deaths worldwide every year.[1] On average 41,400 people die of influenza-related illnesses each year in the United States, based on data collected between 1979 and 2001.[2] Seasonal influenza burden is not uniform across regions.[3,4] Furthermore, it has been noticed that morbidity and mortality variances existed across countries during different pandemics.

For example, the severity of the 1918 Spanish flu was high in severity in USA and Europe and was relatively mild in China.[5] The estimated variation between countries was in the range from 120 up to 44,500 per 100,000.[6]

A global pandemic mortality study found H1N1 2009 pandemic (p H1N1) mortality rates varied widely from one country to another.[7-9] Corroborating early reports of far greater pandemic severity in the Americas than in Europe, Australia and New Zealand.[9] Numerous studies have aimed to capture the global mortality impact of (pH1N1) caused by influenza A (H1N1 pdm09)and identify factors to explain mortality variations seen across populations.[7]

These studies were criticized because the number of factors studied was limited typically and focusing on a few at once and not looking at all together.

These factors include comorbidities, physiological factors, the difference in the population distribution, and climate.[7] Another suggested factor was attributed to the inter-country variability in data collection.[10] Furthermore, previous and co-circulation of different types of influenza virus, other bacterial and viral activity was also suggested to play an important role in the severity of influenza, for example, significant spatio-temporal patterns of the proportions of the existence of influenza B virus after and before p H1N1.[7,11]

During the COVID-19 pandemic, many risk factors associated with severe disease were studied such as age, gender, and subjects with diabetes mellitus, hypertension, cardiovascular disease, and malignancy , population density , physical distancing biological factors such as the prevalence of latent TB or malaria in community, and infection density.[12-17]

One possible risk factor is the previous circulation of the H1N1 pdm09 virus was not studied as far as we know, this viral circulation is reflected by the incidence of H1N1 morbidity or mortality. To shed a light on this possible risk factor, we design this study to examine the relationship between previous 2009 H1N1 mortality data (which reflects previous H1N1pdm09 activity and ongoing COVID-19 pandemic mortality data which reflects SARS-Cov2 activity.

METHODS

One hundred thirty countries and territories that reported 2009 H1N1 cases up to September, 2009, were enrolled in this study. This inclusion criteria included countries that have reported deaths due to H1N1 or not reported deaths due to H1N1 and their inhabitant counts to >2 million inhabitant population in 2009.

Exclusion criteria

This include: no reported cases before September, 2009, even if they had reported cases after that time, another exclusion criterion was population size below 2 million inhabitants. A full list of excluded countries and territories is included within the supplementary file.

Data collection

We used publically available data. Patients were not involved. For pH1N1 data, we get these data as shown in the supplementary file:

ECDC reported the number of new and cumulative confirmed fatal pH1N1 cases in all countries. Regarding EU and EFTA countries ECDC reported the number of new and cumulative confirmed fatalities, as it was in 24 November 2009, 09:00 hours CEST. In the rest of the world, ECDC reported the number of new and cumulative confirmed fatal pH1N1 cases, as of 23 November 2009, 16:00 hours CEST. Other publically available sources for data as shown below were used to fill this one-day gap period for mortality and to obtained data for those countries and territories that reported H1N1 cases up to 24 September 2009.

PAHO/WHO | Regional Updates reported countries of the Americas information provided by Ministries of Health of the Member States and National Influenza Centers through reports sent to Pan American Health Organization (PAHO) or updates on their web pages. WHO African Region updates reported cases for pH1N1 in Africa.

Further data references are included in the supplementary file.

Accumulative COVID-19 mortality rates were obtained up to January 31, 2021. Through the following public sites:

"Mortality Analyses". Johns Hopkins University, Coronavirus Resource Center. COVID-19/Coronavirus Real-Time Updates With Credible Sources in US and Canada. WHO coronavirus disease (COVID-19) dashboard COVID-19 virus pandemic. COVID-19 dashboard by the center for systems science and engineering (CSSE) at Johns Hopkins University (JHU). Total Population 2009 data was taken through the World Bank.

Details are included within the supplementary file.

Statistical methods

An optimum a simple regression of highly fitted was simple regression analyses. which was chosen after checking several assumed linear and non-linear regression models, such as logarithmic, inverse, (polynomial regression of quadratic, and cubic), power, s-shape compound, growth, exponential, and logistic, which were proposed for estimation of predicted equation with their estimators, such as slope, determination C , correlation coefficient, intercept, coefficient, and regression ANOVA for testing the highly fitted model for studying the influence of "confirmed H1N1 deaths on" COVID-19 mortality. All statistical operations were performed using the ready-made statistical package statistical package for social sciences (SPSS), version. 21.

RESULTS

Table 1 and figure 1 show a meaningful linear regression (L=linear model) tested in two-tailed alternative statistical hypotheses. Slope value indicated that with increasing one unit of the "confirmed H1N1 deaths /m till September 24, 2009", there was a positive impact on the unit of "COVID-19 Mortality till 1st January 2021", and estimated by (0.822451), which was recorded with a very highly significant impact at p=0.0002 which is too small, as well as relationship coefficient that was accounted to (0.32789) with meaningful and very high significant determination coefficient (R-Square=10.75%).

Table 1: Impact of confirmed H1N1 deaths/million (M) till September 24, 2009 on COVID-19 mortality till 30th January among all sample.

Dependent variable Method... Linear Model "Covid-19 Mortality till 1st January 2021"					
Correlation Coefficient	0.32789 (VHS)	Meaningful linear regression tested in two tailed alternative statistical hypothesis			
R- Square	0.10751				
FStatistic of Reg. ANOVA	15.0575	Sign. F =	0.0002 (VHS) (*)		
Variables in the Equation					
Variable	B- Beta	SE.B	Stand. Beta	t-test	Sig. level (*)
Confirmed H1N1 deaths/M till 24/9/2009	0.822451	0.211950	0.32789	3.880	0.0002
(Constant)	346.212979	1577.549	-	8.348	0.0000
Predicted Equation : Linear -Shape Model					
$(\widehat{\text{Covid} - 19\ \text{Mortality}}) = 346.212979 + (0.822451) * (\text{Confirmed H1N1 Deaths})$					

(*) VHS: very high Sig. value at p<0.001; Testing Linear Regression: Model whose equation is Y = b0 * (b1x).

Table 2: Impact of confirmed H1N1 deaths/ million (M) till September 24, 2009, on COVID-19 mortality till 30th Janaury after exclusion countries with no H1N1 deaths.

Dependent variable Method... Linear Model "Covid-19 mortality till 30/1/2021"					
List wise deletion of missing data					
Correlation Coefficient	0.28411 (HS)	Meaningful Linear regression Tested in two tailed alternative Statistical hypothesis			
R- Square	0.08072				
F Statistic of Reg. ANOVA	8.26568	Sign. F =	0.0053 (HS) (*)		
Variables in the Equation					
Variable	B	SE.B	Beta	t-test	Sig. level
Confirmed H1N1 deaths/M till 24/9/2019	0.655981	0.229560	0.284105	2.858	0.0053(*)
(Constant)	449.268079	51.936632	-	8.650	0.0000**
Predicted Equation : Linear -Shape Model					
$(\widehat{\text{Covid} - 19\ \text{Mortality}}) = 449.268079 + (0.655981) * (\text{Confirmed H1N1 Deaths})$					

(*) HS: Highly significant (**) VHS: very high Sig. value at p<0.001; Testing Linear Regression: Model whose equation is Y = b0 *(b1x).

Another source of variations that was not included in the studied model, i.e. "intercept" showed a very high significant level at p<0.0000 according to Microsoft office which is too small. This indicates that supplementary assignable factors interpret the other sources of variations or there was a starting COVID-19 deaths value within the sample, obtained by excluding the impact of the correlation of deaths for the two studied causes relationship i.e. (Initial COVID-19 deaths can be obtained before the influence of H1N1 deaths effect).

To reach a confirmation of the truth for the linear relationship between the numbers of deaths/M due to H1N1 and numbers of deaths due to COVID-19, the countries that had not recorded any deaths as a result of the H1N1 were excluded in the table 2 and figure 2.

Table 2 and figure 2 show a meaningful linear regression (Linear model) tested in the two-tailed alternative statistical hypothesis.

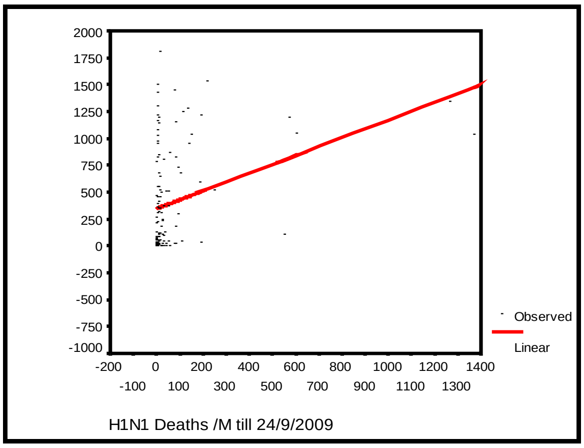

Figure 1: Long term trend of the scatter diagram concerning impact of confirmed H1N1 deaths /M till 24th September2009 " influenced on "COVID-19 mortality till 30th January among all sample.

Slope value indicated that with increasing one unit of the "confirmed H1N1 deaths/M till September 24, 2009", there was a positive impact on the "COVID-19 mortality till 1st January 2021", and estimated by (0.655981), which recorded a very high significant impact at p=0.0053, which is too small, as well as relationship coefficient which was accounted (0.28411) with meaningful and a very high significant determination coefficient (R-Square=8.072%). Other sources of variations that are not included in the studied model, i.e. "intercept" showed (according to statistical software) a very high significant value at p=0.0000, which is too small as it was seen in table1. These confirm the previous findings.

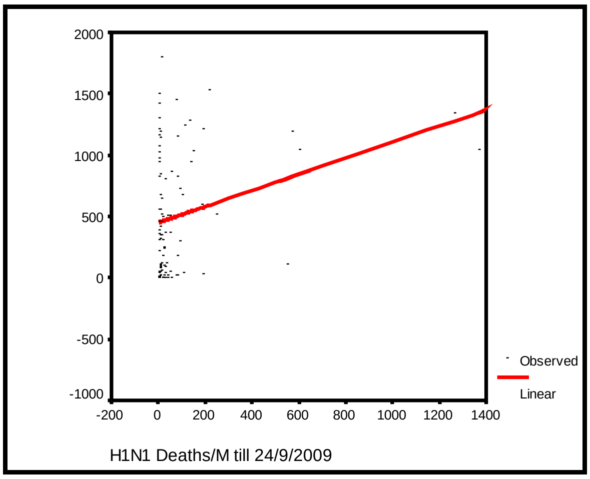

Figure 2: Long term trend of the scatter diagram concerning impact of "confirmed H1N1 deaths/M till 24th September 2009 influenced on "COVID-19 mortality till 30th January 2021 after exclusion countries with no H1N1 deaths.

DISCUSSION

One limitation of this study was the data included the confirmatory cases which represented the iceberg of the actual number of cases in pH1N1 and COVID-19.

At the end of pH1N1, 18,500 deaths were confirmed by WHO. However, the study by Dawood et al suggests that these numbers were underestimated and suggested the total number of deaths was actually between 151,700 and 575,400.[18]

After July 2, 2019 routine testing stopped, and presumed cases were treated without laboratory confirmation of the diagnosis in many countries, following the recommendations of the WHO.[19] Many countries stopped issuing estimates of the infected population.

Other limitations include the validity and comparability of the global datasets, different registration accuracy, and stage of pandemic. Regarding the H1N1 pandemic, this study did not consider the whole pandemic period because countries stopped issuing H1N1 confirmatory cases, following the recommendations of the WHO.[20]

It was recognized that even in developed countries the total numbers of pH1N1 deaths were uncertain.[20] The WHO stated in 2010 that total mortality (including unconfirmed or unreported deaths) from H1N1 flu was "unquestionably higher" than their own confirmed death statistics.[21] For these reasons, we examine H1N1 mortality data up to September 24, 2019, because up to this time we can get reliable data concerning pH1N1 that lasted about 19 months, from January 2009 to August 2010. On the other hand, this study is conducted during the mid-COVID-19 pandemic too.

Results in this study support evidence that common factors might be operated on giving the same mortality trends for both. This might reflect susceptible studied communities for both of the two viruses. Evidence suggests that host innate cross-immunity could have a role in susceptibility to SARS-Cov2 infection this might be back to 2009. [15,16] Control clinical trials and further epidemiological studies are recommended in this regard.

Studies showed that many similarities exist between the COVID-19 pandemic and both 2009 and 1918 influenza pandemics such as- the wave of COVID-19 matched the major wave of the 1918 influenza pandemic, both reaching similar magnitudes (in terms of estimated weekly new infections) and spending the same duration with over five cases per 1000 inhabitants over the previous two months, the years of life lost due to 1918 influenza pandemic were more appropriate comparison with years of life lost due to COVID-19 pandemic.[22] Among other similarities worth to be mentioned: serial interval is roughly 1 week for COVID-19 and probably the same for the A/H1N1 1918, comparable basic reproductive number (R0) which was 2.5, 2, and 1.7 for SARS-Cov2, 1918 H1N1 influenza and H1N1 pdm09 respectively, close comparable dispersion (k) parameter, K=0.94 for1918 influenza A/H1N1versus 0.8 for COVID-1923, with suggested similar patterns of viral shedding and possibly a similar latent period 4, and there was a strong seasonal similarity in timing of the pandemic waves between 1918 and 2019 pandemics which indicates the speed of spread around the world is surprisingly similar.[23-25]

In terms of severity, studies showed that SARS-CoV2 has higher R0, higher mortality, higher mortality among elderly, higher symptomatic people requiring hospital admission, higher risk of admission to the intensive care unit, and higher case fatality rates than H1N1pdm09.

This paper provides added another similarity in similarities scenario, furthermore, it significantly identifies how it is severe compared to pH1N1.[25-29]

A significant constant (y-intercept) denotes possible factors that exist other than examined factor which shows a very high significant association at p<0.0000 This could indicate the presence of supplementary assignable factors intercept with H1N1 mortality or there is baseline

COVID-19 death resulted by excluding the impact of the correlation of death numbers for two studied mortalities. Another point regarding the significant constant (y-intercept) is that it shows how severe the COVID-19 is, compared to H1N1 2009 disease.

Possibly the baseline mortalities represent the relation with morbidity due to H1N1 and hence potential H1N1 mortality, providing that H1N1 data was limited to September 24, 2009 therefore, data have not included all deaths during pH1N1. We recommend comparing the degree of severity of COVID-19 disease between three groups: H1N1 death deporting group, H1N1 case reporting but not death reporting group, and neither H1N1 case reporting nor death reporting group to confirm our statistical results and support our assumption generated through interpreting intercept significance. All such findings should be supported by control clinical trials.

CONCLUSION

A surprising finding in this study draws our attention to common risk factors that make mortality differences follow an identical pattern.

Recommendations

Possible risk factors common in both pandemics' studies should be studied in-depth as these factors may cause such similarity in mortality trends in current and in the next possible epidemics. These finding might help in planning for COVID-19 vaccination priorities among countries.

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APPENDIX 1

				H1N1cases/M	COVID-19 cases /M
	Countries	Confirmed Deaths till 24/9 /2010	Pop 2009	Per /M 2009 till /2019	per/M till30/1/2021
1	**EU AND EFTA countries**				
2	**Austria**	3	8210281	0.365	457
3	**Belgium**	12	10414336	1.1523	1,806
4	**Bulgaria**	5	7204687	0.694	1,307
5	**Czech Republic**	3	10211904	0.294	1,499
6	**Denmark**	3	5500510	0.545	359
7	**Finland**	12	5250275	2.286	121
8	**France~**	84	64057792	1.311	1,157
9	**Germany**	7	82329758	0.085	679
10	**Greece**	8	10737428	0.745	555
11	**Hungary**	134	9905596	13.528	1,283
12	**Ireland**	16	4203200	3.806	647
13	**Italy**	76	58126212	1.307	1,454
14	**Lithuania**	1	3555179	0.281	1,023
15	**Netherlands**	28	16715999	1.675	804
16	**Norway**	23	4660539	4.935	105
17	**Poland**	4	38482919	0.104	972
18	**Portugal**	3	10707924	0.280	1,168
19	**Romania**	1	22215421	0.045	950
20	**Slovakia**	1	5463046	0.183	823
21	**Spain**	115	40525002	2.838	1,247
22	**Sweden**	11	9059651	1.214	1,144
23	**Switzerland**	1	7604467	0.132	1,076
24	**United Kingdom**	216	61113205	3.534	1,533
25	**Georgia**	0	4615807	0	790
	Other European countries and Central Asia				
26	Azerbaijan	2	8238672	0.243	307
27	Belarus	20	9648533	2.073	180
28	Bosnia and Herzegovina	1	4613414	0.217	1,425
29	Croatia	5	4489409	1.114	1,215
30	Moldova	8	4320748	1.852	850
31	Russia	19	143,326,904	0.133	498
32	Serbia	16	7379339	2.168	457
33	Ukraine	15	4570095	3.282	516
34	Albania	0	3639453	0	472
35	Kyrgyzstan	0	5431747	0	214
36	Kazakhstan	0	15399437	0	131
37	Tajikistan	**0**	7349145	0	9
38	**Mediterranean and Middle-East**				
39	Egypt	11	83082869	3.346	89
40	Iran	100	66429284	1.505	683
41	Iraq	10	28945657	0.345	320
42	Israel	51	7233701	7.050	511
43	Jordan	11	6342948	1.734	417
44	Lebanon	3	4017095	0.747	394
45	Morocco	1	34859364	0.029	222
46	Occupied Palestinian Territory	9	3,935,249	2.287	353
47	Oman	27	3418085	7.899	373
48	Saudi Arabia	81	28686633	2.824	181
49	Syria	50	20178485	2.478	51

Continued.

				H1N1cases/M	COVID-19 cases /M
50	Tunisia	2	10486339	0.190	555
51	Turkey	93	76805524	1.211	303
52	United Arab Emirates	6	4798491	1.250	83
53	Yemen	22	23822783	0.923	22
	Africa				
54	Ghana	1	23832495	0.041	12
55	Madagascar	1	20653556	0.048	10
56	Mozambique	2	21669278	0.092	11
57	South Africa	91	49052489	1.855	730
58	Sudan	1	41087825	0.024	40
59	Tanzania	1	41048532	0.024	0.3
60	Ivory Coast	0	20617068	0	6
61	Burundi	0	8988091	0	0.2
62	Cameroon	0	18.879.301	0	17
63	Guinea	0	10057975	0	6
64	Somalia	0	9832017	0	9
65	Chad	0	10329208	0	7
66	Malawi	0	14,128,161	0	6
67	Angola	0	12799293	0	14
68	Botswana	0	1990876	0	56
69	Mali	0	12666987	0	16
70	Republic of the Congo	0	68692542	0	21
71	Ethiopia	0	85237338	0	18
72	Zimbabwe	0	11392629	0	80
73	Zambia	0	11862740	0	39
74	Rwanda	0	10473282	0	14
75	Kenya	0	39002772	0	32
76	Senegal	0	13711597	0	36
77	Uganda	0	32369558	0	7
78	Democratic Republic of the Congo	0	4012809	0	21
79	Nigeria	0	149229090	0	7
80	Libya	0	6310434	0	266
81	Mauritania	0	3129486	0	89
82	Algeria	0	34178188	0	65
83	Nepal	0	28563377	0	69
	North America				
84	Canada	250	33487208	7.466	521
85	Mexico	573	111211789	5.152	1,196
86	United States	1265	307212123	4.118	1,344
	Central America and Caribbean				
86	Costa Rica	40	4253877	9.403	508
87	Cuba	7	11451652	0.611	19
88	Dominican Republic	22	9650054	2.280	241
89	El Salvador	26	7185218	3.618	247
90	Guatemala	18	13276517	1.356	308
91	Honduras	16	7792854	2.053	355
92	Jamaica	6	2825928	2.123	116

Continued.

				H1N1cases/M	COVID-19 cases /M
93	Nicaragua	11	5891199	1.867	25
94	Panama	11	3360474	3.273	1,193
95	Haiti	0	9035536	0	21
	South America				
96	Argentina	600	40913584	14.665	1,048
97	Bolivia	57	9775246	5.831	869
98	Brazil	1368	198739269	6.883	1,043
99	Chile	140	16601707	8.433	950
100	Colombia	151	45644023	3.308	1,034
101	Ecuador	82	14573101	5.627	830
102	Paraguay	52	6995655	7.433	373
103	Peru	190	29546963	6.430	1,218
104	Uruguay	33	3494382	9.444	125
105	Venezuela	107	26814843	3.990	41
	North-East and South Asia				
106	Afghanistan	14	33609937	0.417	61
107	Bangladesh	6	156050883	0.038	49
108	China (mainland)	53	1338612968	0.040	3
109	Hong Kong	40	7055071	5.670	23
110	India	553	1166079217	0.474	111
11	Japan	28	127078679	0.220	43
112	Mongolia	17	3041142	5.590	0.6
113	Pakistan	1	176242949	0.006	52
114	South Korea	82	49052489	1.672	27
115	Sri Lanka	5	21324791	0.234	14
116	Taiwan	29	22974347	1.262	0.3
117	N. Korea	0	22665345	0	0
	South-East Asia				
118	Cambodia	4	14494293	0.276	0
119	Indonesia	10	240271522	0.041	107
120	Laos	1	6834942	0.146	0
121	Malaysia	77	25715819	2.994	22
123	Philippines	30	97976603	0.306	96.6
124	Singapore	18	4657542	3.865	5
125	Thailand	185	65905410	2.807	597
126	Vietnam	41	86967524	0.471	0.4
127	Myanmar	0	50,250,365	0	57
	Australia and Pacific				
128	Australia	189	21262641	8.889	35
129	New Zealand	20	4213418	4.747	5
130	Papua New Guinea	0	6057263	0	1.0

APPENDIX 2: COVID-19 MORTALITY REFERENCES

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APPENDIX 3: REFERENCES OF H1N1 DEATHS DATA (ADDITIONAL COUNTRY SPECIFIC REFERENCES)

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APPENDIX 4: TOTAL POPULATION 2009 REFERENCES

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APPENDIX 5: REFERENCES OF H1N1 DEATHS DATA

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APPENDIX 6: EXCLUSION LIST

Excluded list< 3 Million population: Iceland, Luxembourg, Malta, Kosovo, Bahrain, Qatar , Mauritius,Sao Tome and Principe, Latvia, Slovenia, Namibia, Kuwait, Macedonia, Armenia, Cape Verde, Cyprus, Seychelles, Bahamas, Barbados, Cayman Islands, Saint Kitts and Nevis, Saint Lucia, Suriname, Trinidad-Tobago, Macao, Maldives, Brunei Darussalam, Cook Islands, Marshall Islands, Samoa, Solomon Islands, Tonga, and Fiji , Andorra, Akrotiri and Dhekelia (UK), Bhutan, Micronesia, Antigua and Barbuda, Isle of Man (UK) , Gibraltar (UK), Belize, Turks and Caicos Islands (UK), Monaco. Gabon ,Lesotho, Swaziland, Anguilla, Aruba, Bermuda, British Virgin Islands.
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