Special Issue Article
Volume 5:3,2020
DOI: 10.37421/ijphs.2020.5.186

International Journal of Public Health and Safety
Open Access

A 3-Month Preliminary Epidemiological Assessment of Some Factors Affecting the Human-To-Human Transmission of Causal Agent SARS-CoV-2 Virus for Infection Rates of COVID-19

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Abstract

Aims: A preliminary epidemiological study, based on three months of diagnosed cases and deaths for COVID-19, for the beginning of the pandemic, January to 31 March 2020, was undertaken. Factors that were considered to affect the human-to-human transmission of the SARS-CoV-2 virus were: spike protein structure, the effect of country average monthly temperature. The study also investigated the median age of the country for the subjects who died and the corresponding case fatality rate (ratio) (%CFR).

Findings: The presence of the furin cleavage site, the 10 to 20 fold binding affinity of the spike protein, compared to SARS-CoV, were proposed as possible reasons for the much higher cases noted for COVID-19 compared to the SARS disease. The optimum temperature for viral infection with SARS-CoV-2, for COVID-19, appears to be ± 0.07ºC; viral transmission appears to be maximum at -2ºC up to +12ºC (95.3% of cases); transmission appears to decrease at >12ºC (2.7% of cases). The corresponding optimal temperature for SARS-CoV infection, for SARS disease, appears to be ± 6.25ºC. The average, global % CFR for COVID-19, based on 202 countries, is ± 3.2%. Subjects confirmed with COVID-19, in median age range 40.8 (± 4.7) years, are at higher risk of death. The USA has the highest number of infections (140640) as at 31 March 2020; Italy (CFR 11.4%) and Spain (CFR 8.6%) have the highest percentages of deaths (0.0192% and 0.0157%, respectively) from COVID-19 per population.

Conclusion: The preliminary study outcomes can be used for further investigation, to confirm the actual ages of subjects who died from COVID-19, to confirm the risk age groups for death from COVID-19, and to confirm these preliminary optimal temperature ranges that may potentially assist countries to predict risk of future infection based on monthly temperatures per country.

Keywords: Corona virus • SARS-CoV-2 • COVID-19 • Furin • Temperature • Median age • Case fatality rate

Introduction

A novel corona virus 2019-nCoV (SARS-CoV-2) associated with human-to-human transmission and severe human respiratory infection (COVID-19 – corona virus disease 2019) was recently reported from the city of Wuhan in Hubei province, China [1,2], with a 2-3% fatality rate. The virus is presumed to have been initially transmitted from an animal reservoir to human, possibly via an intermediate host. Most of the original cases had close contact with local fresh seafood and an animal market [3]. Human-to-human transmission was reported, leading to a sustained epidemic spread with 9776 confirmed human infections, including 213 deaths, globally, as at 30 January 2020. This prompted the WHO to declare it as a Global Health Emergency. After the viral genome was sequenced [4,5], Couthard et al. reported on their finding of a peculiar furin-like cleavage site in the spike glycoprotein, which was not observed in the lineage b of beta coronaviruses [6]. The estimated effective reproductive number (R) value of 2.90 (95%: 2.32-3.63) at the beginning of the outbreak raised the possibility of a pandemic [7]. On 11 March, with over 118,000 cases of the coronavirus illness in over 110 countries and territories around the world and the sustained risk of further global spread, the WHO declared COVID-19 as a pandemic: the declaration refers to the global spread of a new disease, rather than the severity of the illness it causes (WHO).

A total of 750890 confirmed cases, covering 202 countries around the globe, were reported as at 31 March 2020 [8]; of the confirmed cases, 36 405 had died, giving an estimated case fatality rate (ratio) of 4.9%. Of note was the fairly high CFR estimate for Italy, ± 11.4%, as at 31 March 2020, compared to China (± 4.0%), which was presumably attributed to the relatively older median age of the Italian population, compared to some of the other countries. Current preliminary data do indicate that the older age group of a population are at higher risk of dying from COVID-19. An unpublished study on the analysis of cases diagnosed as at 11 February in China showed that for the age group 30 to >80 years, the case fatality rate was: 1.3% for 50-59 year, 3.6% for 60-69 year, 8.0% for 70-79 year, and 14.8% for >80-year-old [9].

There has been some comment and speculation that lower temperatures may help to promote the transmission, and conversely, relatively higher temperatures may help to curb the spread of the virus between humans.

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Received: 12 May, 2020; **Accepted:** 22 June, 2020; **Published:** 30 June, 2020

Little is known about the environmental pattern in COVID-19 incidence and studies to date on COVID-19 transmission and meteorological factors, like temperature and humidity are few. There has also been conflicting reports regarding the effect of temperature on the SARS-CoV-2 viral transmission. At the time of preparation of this manuscript, Briz-Redon et al. reported a spatio-temporal study of daily temperature on the number of COVID-19 cases in Spain [10]. They found no evidence suggesting a reduction in COVID-19 cases at warmer mean, minimum and maximum temperatures.

A study by Qi et al. in China, noted that for every 1°C increase in the average temperature led to a decrease in the daily confirmed cases by 36% to 57% when relative humidity was in the range from 67% to 85.5% [11]. Every 1% increase in relative humidity led to a decrease in the daily confirmed cases by 11% to 22% when average temperature was in the range from 5.04°C to 8.2°C. However, the authors noted that these associations were not consistent throughout Mainland China.

Another COVID-19 temperature study by Wang et al. covered China and 26 other countries around the world, for the period 20 January to 04 February [12]. Their study found out that to a certain extent, temperature could significantly change the COVID-19 transmission. There may be an optimum temperature for viral transmission, which partly explains why it first broke out in Wuhan. They concluded that low temperature is beneficial for viral transmission; no temperature or range was proposed.

Thus the aim of this current study is to investigate:

- The effect of the spike glycoprotein structure on the transmission,
- The effect of temperature on transmission, and
- Higher risk of fatality for the aged that are diagnosed with COVID-19.

Materials and Methods

The number of diagnosed COVID-19 cases and deaths were obtained from the WHO website from the "situation reports" [13]. Temperature data were obtained from the stat.world website [14]; whilst this site has data up to the year 2013, it was noted that there were negligible differences in the average annual temperatures. COVID-19 testing data was obtained from Wikipedia [15]. Median age per country was obtained from Wikipedia web site [16].

Results and Discussion

Structure of the spike protein of 2019-nCoV (SARS-CoV-2)

The corona viruses are a diverse family of enveloped positive sensed RNA viruses distributed widely among animal species. The emergence of the human CoV, responsible for severe acute respiratory syndrome (SARS) highlights the public health risks associated with the evolution and zoonotic spread of new CoVs.

Based on its genome sequence, 2019-nCoV (SARS-CoV-2) belongs to lineage b of Beta coronavirus, which also includes t h e SARS-CoV and bat CoV ZXC21, the latter and CoV ZC45 being the closest to 2019-nCoV. 2019-nCoV shares ~ 76% amino acid sequence identity in the Spike (S)-protein sequence with SARS-CoV and 80% with CoV ZXC21 [4].

Currently, seven human CoVs (HCoVs) have been confirmed. Specifically, they are named as Human coronavirus NL63 (HCoV-NL63) and Human coronavirus 229E (HCoV-229E), which belong to the alpha-coronavirus genus; whereas Human coronavirus OC43 (HCoV-OC43), Human coronavirus (HCoV-HKU1), SARS-CoV, SARS-CoV-2 and Middle East respiratory syndrome coronavirus (MERS-CoV), belong to the beta-coronavirus genus. HCoV 229E, HCoV-NL63, HCoV-HKU1 and HCoV- OC43 strains of coronavirus cause mild respiratory diseases in humans. The SARS-CoV-2 is a zoonotic virus that belongs to the Coronaviridae family that can infect human and several animal species [17]. The SARS-CoV-2 belongs to the subgenus Sarbecovirus and mostly resembles a bat coronavirus, with which it shares 96.2% sequence homology [4].

The corona-virus S-protein is the structural protein responsible for the crown-like shape of the CoV viral particle, from which the original name corona virus was derived.

The virus belongs to the largest family of RNA viruses. Its genome ranges from 27 to 32 kilobases in size (~125 nanometers or 0.125 microns). It is a single stranded enveloped RNA virus which possess a positive-sense RNA genome also known as (+ssRNA) with a 5'-cap structure and 3'-poly-A tail. The viruses belonging to this category have a few common characteristics that are applicable to SARS-CoV-2 as well. The virus has four important structural proteins which are (E) the envelope protein, (M) the membrane protein, (S) the spike protein and (N), the nucleocapsid protein, which are required to regulate the function and viral structure [18]. The most important ones are N and S, where the former one helps the virus to develop the capsid and the entire viral structure appropriately and the latter one helps in the attachment of virus to the host cells [19,20]. The S protein has three major sections which are the large ectodomain, a single-pass transmembrane anchor and a short intracellular tail. These play a major role in anchoring the host cells. Among these sections the ectodomain has two subunits which are the S1 receptor-binding subunit and S2 the membrane fusion subunit.

It has been reported that the SARS-CoV and SARS-CoV-2 have similar kind of receptors, especially the receptor binding domain (RBD) and the receptor binding motif (RBM) in the viral genome [21-23]. It has also been proposed that SARS-CoV-2 mechanism of action in infection of humans is similar to the SARS. It has been reported that the RBM of the SARS-CoV-2 has a major amino acid residue (Gln493) that favors the attachment and fusion of the viral S protein with virus into the ACE2 protein of the human cell, especially the one present in the lungs which results in respiratory infections in humans [21,24].

The 1200 aa S-protein belongs to Class-I viral fusion proteins, and it contributes to the cell receptor binding, tissue tropism and pathogenesis [25,26]. The spike S-protein of corona viruses facilitates viral entry into target cells. Entry of the virus depends on binding of the surface unit S1, of the surface protein, to a cellular receptor, which facilitates viral attachment to the surface of the target (host) cells. In addition, entry requires S-protein priming by cellular proteases, which entails S- protein cleavage at the S1/S2 and S2' site, to allow the fusion of the viral and cellular membranes. The latter process is driven by the S2 subunit. The SARS S-protein engages angiotensin-converting enzyme 2 (ACE2) as the entry receptor [27], and employs the cellular serine protease TMPRSS2 for S-protein priming [28-30]. It has been found that 2019-nCoV S- protein uses ACE2 for host cell entry and that the serine protease TMPRSS2 primes the 2019-nCov S-protein for cellular entry [31,32]. However, it has been further shown, by biophysical and structural evidence that 2019-nCoV-S protein binds ACE2 with higher affinity, about 10-20-fold higher, compared to the SARS-CoV-S binding to ACE2 [33].

After the virus has entered the host cell, the next critical step for its survival is RNA replication. The process of replication in the SARS-CoV-2 similar to SARS-CoV virus is multifaceted and needs more understanding [22,34]. The two polyproteins of the virus contain the nsp proteins (Nsp1-11, nsp1-16) that play a vital role in keeping the virus alive by promoting basic synthesis, replication and translation.

One major, significant difference in the spike glycoprotein of 2019-nCoV is the presence of the furin cleavage site, not present in SARS-CoV, first reported by Couthard et al. [6]. They proposed that this furin-like cleavage site is supposed to be cleaved during virus egress for S-protein priming [26]. The authors were also the first to suggest that due to this structural difference, it may provide the virus a "gain of function" in terms of its human-human transmission, compared to the other lineage of b corona viruses, like SARS-CoV. The furin proteases are abundant in the respiratory tract. It is possible that SARS-CoV-2 S glycoprotein is cleaved upon exit from epithelial cells and consequently can efficiently infect other cells, the "gain of function" [35]. In contrast, the SARS-CoV S glycoprotein is uncleaved upon virus release from cells; it is likely cleaved during virus entry into a cell.

Subsequently, Walls et al. reported the presence of a polybasic cleavage site at the S1/S2 boundary of SARS-CoV-2 S, whereas the SARS-CoV S possesses a monobasic S1/S2 cleavage site processed upon entry of target cells [20]. They also speculated the almost ubiquitous expression of furin-like proteases that could participate in the expansion of SARS-CoV-2 cell and tissue tropism, as well as increasing its transmissibility and pathogenicity.

Hoffman et al. [32] speculated that furin-mediated pre-cleavage at the S1/S2 site in infected cells might promote the subsequent TMPRSS2-dependent entry into target cells, as reported for MERS-CoV [36,37]. At time of preparation of this manuscript, Zhang et al. [38] also reported this similar finding, that the S-protein of 2019-n-CoV contains a putative furin recognition motif (PRRARSV), similar to that of MERS-CoV, which has a PRSVRS motif that is likely cleaved by furin during virus egress. This insertion in the S1/S2 protease cleavage site that results in an "RRAR" furin recognition site in 2019-nCoV, rather than the single arginine in SARS- CoV, was again confirmed by Wrapp et al. who did cryo-EM, atomic structure analysis of the spike protein [33].

In addition, other changes noted in SARS-CoV-2 are an absent 8a, longer 8b and shorter 3b segments and different Nsp 2 and Nsp 3 proteins [39]. The Nsp2 consists of a mutation that is probably associated with the ability of the virus to be more contagious [40].

Human coronaviruses are predominantly concomitant with upper respiratory tract illnesses ranging from mild to moderate, including the common cold. The SARS-CoV and MERS-CoV are the two major causes of severe pneumonia in humans [41].

The COVID-19 is known to show symptoms slowly over an incubation period of around 2 weeks. During this time the virus replicates in the upper and lower respiratory tract, forming lesions [4]. The general symptoms observed in the infected individuals are fever, cough, dyspnea and lesion in the lungs [2]. In the advanced stage, the symptoms of this virus are pneumonia which can progress to severe pneumonia and acute respiratory distress syndrome (ARDS), which results in the need for life-support to sustain the patient's life [42].

SARS-CoV and SARS disease

With the outbreak of SARS in China, where initial cases were reported during November 2002, up to the last cases being reported during June 2003, the total number of confirmed cases, globally, covering 29 countries, was 8 096, with 774 deaths (Table 1), giving an average CFR of ± 9.6%. The corresponding SARS-CoV-2 confirmed cases and deaths are also summarized for comparison purposes; the SARS-CoV-2 case data for all the other countries (173 infected) are not included here.

Table 1. Comparison of total SARS cases vs. COVID-19 cases at 31 March 2020.

Country	SARS cases Total	% (SARS cases per country/Total SARS cases)	SARS % CFR[a]	Average temp / during SARS infection period (range)	COVID-19 cases[b] Total as at 30/03/ 2020	Average temp Jan-Mar 2020 (ºC)[c]	COVID-19 deaths Total as at 31/03/2020	COVID-19 % CFR	(COVID-19 cases/ SARS cases)	% (COVID-19 cases/ SARS cases)	COVID-19 tests % of popul= ation/as at (date)
China	5327	65,80	7	6,25 Nov-Jun[b]	82 545	-2,16	3 314	4,0	15	1 550	0,022 20 Feb 2020
China, Hong Kong Special Administrative Region	1755	21,68	17	22,59 Feb-May	-[d]	-17,82	-	-	-	-	0,877 31 Mar 2020
China, Taiwan	346	4,27	11	22,03 Feb-Jun	-	27,31	-	-	-	-	1,111 11 Apr 2020
Canada	251	3,10	17	-6,52 Nov-Jun	6 317	24,34	66	1,0	25	2 517	0,098 05 Apr 2020
Singapore	238	2,94	14	27,73 Feb-May	879	0,07	3	0,3	4	369	0,408 06 Apr 2020
Viet Nam	63	0,78	8	24,20 Feb-Apr	203	26,54	0	0,0	3	322	0,022 06 Apr 2020

United States	27	0,33	0	9,08 Nov-Jun	140 640	-2,16	2 398	1,7	5 209	520 889	0,877 **02 Apr** 2020
Philippines	14	0,17	14	27,12 Feb-May	1 546	-17,82	78	5,0	110	11 043	0,015 **05 Apr** 2020
Mongolia	9	0,11	0	-2,06 Nov-Jun	12	-12,24	0	0,0	1	133	
Germany	9	0,11	0	8,87 Nov-Jun	61 913	-0,17	583	0,9	6 879	687 922	1,096 **29 Mar** 2020
Thailand	9	0,11	22	28,07 May-Mar	1 524	26,45	9	0,6	169	16933	0,034 **03 Apr**
France	7	0,09	14	14,07 Nov-Jun	43 977	7,71	3 017	6,9	6 282	628 243	0,344 **02 Apr** 2020
Australia	6	0,07	0	22,31 Nov-Jun	4 359	28,23	18	0,4	727	72 650	1,190 **06 Apr** 2020
Sweden	5	0,06	0	1,54 Nov-Jun	4 028	-7,08	146	3,6	806	80 560	0,365 **31 Mar** 2020
Malaysia	5	0,06	40	26,98 Mar-Apr	2 626	26,89	37	1,4	525	52 520	0,147 **03 Apr** 2020
United Kingdom	4	0,05	0	9,37 Nov-Jun	22 145	3.85	1 408	6,4	5 536	553 625	0,240 **02 Apr** 2020
Italy	4	0,05	0	13,67 Nov-Jun	101 739	6,31	11 591	11,4	25 435	2 543 475	0,961 **02 Apr** 2020
Republic of Korea	3	0,04	0	9,73 Nov-Jun	9 786	2,34	162	1,7	3 262	326 200	0,865 **03 Apr** 2020
India	3	0,04	0	23,93 Nov-Jun	1 071	20,87	29	2,7	357	35 700	0,001 **18 Mar** 2020
Indonesia	2	0,02	0	26,64 Apr	1 414	26,57	122	8,6	707	70 700	0,003 **02 Apr** 2020
Russian Federation	1	0,01	0	-7,12 Nov-Jun	1 837	-14,98	9	0,5	1 837	183 700	0,517 **06 Apr** 2020

Romania	1	0,01	0	7,53 Nov-Jun	1 952	2,37	44	2,3	1 952	195 200	0,211 **06 Apr** 2020
Switzerland	1	0,01	0	8,60 Nov-Jun	15 412	-0,61	295	1,9	15 412	1 541 200	1,790 **04 Apr** 2020
Republic of Ireland	1	0,01	0	9,97 Nov-Jun	2 910	5,09	54	1,9	2 910	291 000	0,612 **30 Mar** 2020
New Zealand	1	0,01	0	11,68 Nov-Jun	600	15,24	1	0,2	600	60000	0,828 **06 Apr** 2020
Spain	1	0,01	0	14,71 Nov-Jun	85 195	8,62	7 340	8,6	85 195	8 519 500	0,759 **21 Mar** 2020
South Africa	1	0,01	100	17,64 Nov-Jun	1 326	22,81	3	0,2	1 326	132 600	0,075 **01 Apr** 2020
China, Macao Special Administrative Region	1	0,01	0	22,00 Nov-Jun	-	-	-	-	-	-	
Kuwait	1	0,01	0	25,18 Nov-Jun	266	14,44	0	0,0	266	26 600	0,632 **17 Mar** 2020
Average	279		9		22 932		1 182	2.8	6 367	636 737	0,528

[a]%CRF = total deaths/total confirmed cases x 100.

[b] Only countries that had SARS cases are shown here.

[c]Mean based on actual minimum and maximum, from November 2002 (first case reported) to June 2003 (last case) during these months (for years 2002 to 2003) for China; as case reporting information was not available for some countries, all other temperature data were defaulted to this period.

[d]Data not available.

At the time of the case reporting (infection) for SARS-CoV, the actual temperatures are recorded here, per country. For those countries where the case reporting period was not reported [43], the temperature was defaulted to that larger "window" as reported by China: November 2002 to June 2003. The temperatures ranged from a minimum of -26.41ºC (Russian Federation), up to a maximum of +36.35ºC (Thailand) for these 29 countries, indicating virus viability and transmission.

Human corona viruses, SARS-CoV, MERS, endemic human corona viruses (HCoV), can persist on inanimate surfaces for up to 9 days at room temperature [44].

Chan et al. showed that SARS can retain its viability for at least 5 days at typical air-conditioned temperature: 22-25ºC and relative humidity (40-50%) [43]. They also noted that virus viability was rapidly lost at higher temperature (38ºC) and higher relative humidity >95%. They concluded that SARS can retain its infectivity for up to 2 weeks at low temperature and low humidity environment and hence may facilitate its transmission, such as in Hong Kong (1755 SARS cases, with recorded temperatures of 13-28º C for Feb–May 2003). Conversely they proposed that the Asian countries, with a higher temperature and higher relative humidity environment, like Malaysia (5 cases, 23-33ºC), Indonesia (2 cases, 24-31ºC), Thailand (9 cases, 24-34ºC), did not have the major community outbreaks, like that observed in China (5327 cases) and Hong Kong (1755 cases).

At first glance, the data seem to indicate no consistent, expected relationship between relatively lower temperature and proportionally higher infection rates, or conversely, higher temperatures and lower infection rates. In general, viral transmission appears to occur between the lowest temperatures of -7.12ºC (Russia, 1 case) up to +28.07ºC (Thailand, 9 cases).

For the countries with the top 7 higher number of cases: the temperature ranged from a minimum of -22.72ºC (Canada), up to a maximum of 28.57ºC (Singapore): China: 5327 (65.8% of total, 6.25ºC), Hong Kong: 1755 (21.68% of total, 22.59ºC), Taiwan 346 (4.2% of total, 22.03ºC), Canada 251 (3.10% of total, -6.52ºC), Singapore 238 (2.94% of total, 27.73ºC), Vietnam 63 (0.78% of total, 24.20ºC), United States 27 (0.33% of total, 9.08ºC). The average temperature for this range is +2.93ºC. Except for Singapore (average temperature= 27.73ºC), the average temperature for all these countries was <25ºC. China was noted to have the highest number of infections, 5327 cases, with an average temperature of 6.25ºC.

For the rest of the countries, with the relatively lower number of cases, ranging from 14 cases (0.17% of total, Philippines), down to 1 case (0.01% of total), the temperature ranged from a minimum of -26.41ºC (Russian Federation) up to a maximum of 36.35ºC (Kuwait). The average temperature based on this range is +4.97ºC.

The relatively lower cases numbers seem to correspond to a relatively higher average temperature (>25 ºC) for: Singapore (238 cases, 2.94% of total, 27.73ºC), Philippines (14 cases, 0.17% of total, 27.12ºC), Malaysia (5 cases, 0.06% of total, 26.98ºC), Indonesia (2 cases, 0.02% of total, 26.64ºC), and for Kuwait (1 case, 0.01% of total, 25.18ºC)

For those countries with a relatively lower average temperature (<25ºC), there was an unexpectedly lower number of cases: Mongolia 9 (-2.06ºC), Germany 9 (8.87C), Sweden 5 (1.54ºC), United Kingdom 4 (9.37ºC), Korea 3 (9.73C), Russian Federation 1 (-7.12ºC), Romania 1 (7.53ºC), Switzerland 1 (8.60ºC), Ireland 1 (9.97ºC), the temperature ranged from: -26.4C (Russia) to 21.2ºC (Korea). The average temperature for this range is -2.61ºC. For these countries, with relatively lower temperatures, it is possible that there were much more cases of infection that were mis-diagnosed, or not detected, for example due to inaccurate testing, limited testing, etc.

A further plot of the relationship between average temperature (y-axis) vs the total number of SARS infection cases (x-axis) recorded during the months of the pandemic (November 2002 to June 2003), is illustrated in Figure 1.

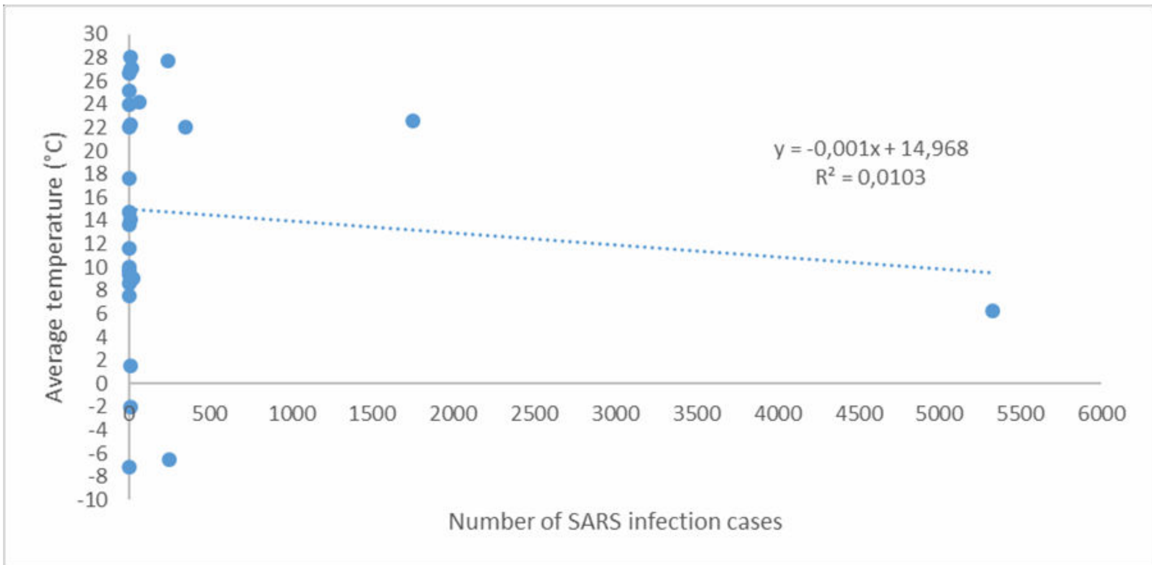

Figure 1. Relationship between the average temperature and the number of SARS-CoV infections (SARS cases).

There seems to be a weak, negative, linear correlation (r^2 = 0.0103) with a negative, low gradient (m = -0.001), which confirms the actual case numbers: a high of 5 327 down to 238 cases, then minimal difference from the low case numbers: 63 down to 1 case. The graph cuts the y-axis at c = 14.978 = 15.0ºC, corresponding to the minimum of zero infection cases. The negative gradient indicates an inversely proportional relationship between average temperature and the number of infections, as expected.

Here it is evident that viral transmission begins to increase at lower temperatures: <28ºC:28.07ºC (9 cases, Thailand), 27.73ºC (238 cases, Singapore), 22.03ºC (346 cases, China Taiwan), 22.59ºC (1755 cases, China Hong Kong), 17.64ºC (1 case, South Africa); <16ºC: 11.68ºC (1 case, New Zealand), 7.53ºC (1 case, Romania), to an optimum of 6.25ºC (5327 cases, China). For temperatures <6.25ºC, there is a decrease in the number of infections: 1.54ºC (1 case, Sweden), -6.52ºC (251 cases, Canada), -7.12ºC (1 case, Russian Federation). In general, the number of infections at very cold, <0ºC temperature seems to be far less than for those observed at ~ 6.25ºC. The SARS-CoV may be relatively unstable at these negative temperatures.

For higher temperatures, >16ºC, viral transmission appears to decrease: 17.64ºC (1 case, Spain), 22ºC (1 case, China Macao), 26.64ºC (2 cases, Indonesia), 28.07ºC (9 cases, Thailand).

SARS-CoV-2 and COVID-19

Effect of spike protein structure on transmission

Another great challenge to research is its ability to adapt and survive in different environmental conditions, making it nearly impossible to identify its exact mode of survival.

The SARS-CoV-2 shares homology with the SARS-CoV but the rate of transmission and infectivity of the SARS-CoV-2 has been remarkable. The peculiar furin-like cleavage site on the spike protein at the S1/S2 boundary of SARS-CoV-2 is a key structural feature not present in SARS-CoV.

Based on the similar structure of SARS-CoV-2 to the SARS-CoV, and clinical manifestations, we would expect fairly similar transmission rates of this new virus. Based on the SARS outbreak temperature data, we would also expect the SARS-CoV to be more efficient in spreading at relatively lower temperature.

The initial outbreak of SARS-CoV-2 was during the peak of winter season, where the environmental temperature ranged from -8.14 to +3.82ºC, during December/January 2019 to February, in China. Only the Case data for those countries that also had SARS disease as well (29 countries) are summarized in **Table 1** for comparison purposes. As at 31 March 2020, the WHO had reported a total of 596 222 COVID-19 confirmed cases, in a total of 202 countries.

In **Table 2**, for these 27 countries, it is clearly evident that in general, the number of corresponding cases for COVID-19 are, if not the same, (12 COVID-19 cases vs 9 SARS cases, for Mongolia), very much higher, ranging from a 3-fold increase (203 COVID-19 cases vs 63 SARS cases, for Vietnam), up to 85195-fold (85195 COVID-19 cases vs 1 SARS case, for Spain), compared to that for SARS (average fold increase = 6367-fold). In other words the percentage increase in cases ranges from +133% (Mongolia) up to +8519 500% (Spain), with an average increase of +636 737%.

Table 2. COVID-19 cases as at 31 March 2020 vs observed temperature.

Country[a]	Cases per country at 31/03/2020	% (cases per country/ Total cases)	Estimated average temp Jan-Mar 2020/range ºC	Total deaths	% CFR[b]	% Tests per population	Predicted average temp for Apr-Jun 2020/ range ºC	Estimated risk rating for COVID-19 infection for Apr-Jun 2020	Cases per country at 11/04/ 2020	% Increase in cases from 31 March to 11 April
United States	140 640	23,589	0,07 -2,14 to 2,29	2 398	1,7	0,408	13,59 6,97 to 20,20	Medium	461275	228,0
Italy	101 739	17,064	6,31 4,48 to 8,14	11 591	11,4	0,961	16,20 12,6 to 19,36	Medium	147577	45,1
Spain	85 195	14,289	8,62 6,99 to 10,25	7 340	8,6	0,759	15.78 12,19 to 19,36	Medium	157022	84,3
China	82 545	13,845	-2,16 -8,14 to 3,82	3 314	4,0	0,022	13,61 8,58 to 18,64	Medium	83369	1,0
Germany	61 913	10,384	-0,17 -0.73 to 0,39	583	0,9	1,096	12,07 8,21 to 15,93	Medium	117658	90,0
France	43 977	7,376	7,71 6,38 to 9,04	3 017	6,9	0,344	15,04 12,32 to 17,75	Medium	89683	103,9
United Kingdom	22 145	3,714	3,85 3,35 to 4,35	1 408	6,4	0,240	9,81 6,79 to 12,83	Medium	70276	217,3
Switzerland	15 412	2,585	-0,61 -2,54 to 1,33	295	1,9	1,790	10,96 7,22 to 14,69	Medium	24228	57,2
Republic of Korea	9 786	1,641	2,34 -1,95 to 6,62	162	1,7	0,865	16,46 10,47 to 22,44	Medium	10480	7,1
Canada	6 317	1,060	-17,82 -21,3 to -14,00	66	1,0	0,877	-1,48 -7,85 to 10,80	√ High	21226	236,0
Australia	4 359	0,731	28,23 26,59 to 29,86	18	0,4	1,190	19,66 16,02 to 23,30	Medium	6238	43,1
Sweden	4 028	0,676	-0,73 -7,81 to -6,36	146	3,6	0,365	7,40 1,06 to 13,74	√ High	9685	140,4
Republic of Ireland	2 910	0,488	5,09 4,46 to 5,72	54	1,9	0,612	10,73 7,80 to 13,66	Medium	8089	178,0
Malaysia	2 626	0,440	26,89 26,31 to 27,46	37	1,4	0,147	27,44 27,27 to 27,61	Low	4346	65,5
Romania	1 952	0,327	2,37 -1,68 to 3,05	44	2,3	0,211	15,37 11,28 to 19,45	Medium	5467	180,1

Russian Federation	1 837	0,308	-4,43 -25,53 to -16,67	9	0,5	0,517	5,17 -2,99 to 13,33	√ High	13584	639,5
Thailand	1524	0,256	26,45 24,37 to 28,53	9	0,6	0,034	29,11 28,32 to 29,89	Low	2518	65,2
Philippines	1546	0,259	26,54 25,58 to 27,50	78	5,0	0,015	28,42 28,17 to 28,67	Low	4195	171,3
Indonesia	1414	0,237	26,57 26,21 to 26,93	122	8,6	0,003	26,76 26,63 to 26,88	Low	3512	148,4
South Africa	1326	0,222	22,81 21,97 to 23,64	3	0,2	0,075	14,69 12,02 to 17,36	Medium	2003	51,1
India	1071	0,180	20,87 17,16 to 24,57	29	2,7	0,001	29,50 27,98 to 31,01	Low	7447	595,3
Singapore	879	0,147	27,31 26,56 to 28,05	3	0,3	1,111	28,22 27,77 to 28,66	Low	2108	139,8
New Zealand	600	0,101	15,24 14,85 to 16,62	1	0,2	0,828	9,37 6,46 to 12,28	Medium	1035	72,5
Kuwait	266	0,045	17,19 14,44 to 14,94	0	0,0	0,632	30,46 25,12 to 35,80	Low	993	273,3
Viet Nam	203	0,034	22,12 19,89 to 24,34	0	0,0	0,098	26,76 25,89 to 27,62	Low	257	26,6
Mongolia	12	0,002	-8,26 -20,50 to -3,98	0	0,0	-[c]	9,34 2,64 to 16,04	√ High	16	33,3

[a] Only countries that had SARS cases are shown here

[b]%CRF = (Total deaths/Total confirmed cases) x 100

[c]Data not available

The number of cases ranges from a minimum of 12, for Mongolia, up to a maximum of 101 739, for the USA. Based on the minimum and maximum temperatures for these countries, the 3-month average temperature was calculated. For all these countries, the actual temperatures, for January-March 2020, range from a minimum of ~ -25.53°C (Russian Federation) to a maximum of ~ 29.86°C (Australia), indicating the viability and transmission of the virus under these extreme temperature conditions in contrast to the SARS-CoV.

Based on the noticeably much higher number of case reports for COVID-19 in general, due to SARS-CoV-2, compared to the reported relatively lower number of SARS cases, it is proposed that either the distinct presence of the furin cleavage site ("gain of function" concept) [6], and the greater binding affinity of the SARS-CoV-2 S-protein [33], or both these factors, are largely responsible for the rapid human-to human transmission of the SARS-CoV-2 virus, compared the SARS-CoV.

Effect of temperature

Table 2, an adaptation of **Table 1**, shows the total COVID-19 cases, in descending order, as at 31 March, but only for those 29 countries that had cases for the SARS cases. The numbers for COVID-19 range from a maximum of 140 640, for the USA, down to a minimum of 12, for Mongolia.

The estimated country temperatures, for the 3-month period, and the 3-month average, for January 2020 to March 2020 are recorded. It is evident that the temperature ranges from a minimum of -25.53°C for the Russian Federation, to a maximum of 29.86°C for Australia, implying viral viability and transmission at these extremely low and high temperatures.

As the known data in this pandemic is initially the number of observed COVID-19 cases, this value was plotted as the known, independent variable, on x-axis, with the corresponding 3-month average temperature for the period January to March 2020, on the y-axis, shown in **Figure 2**.

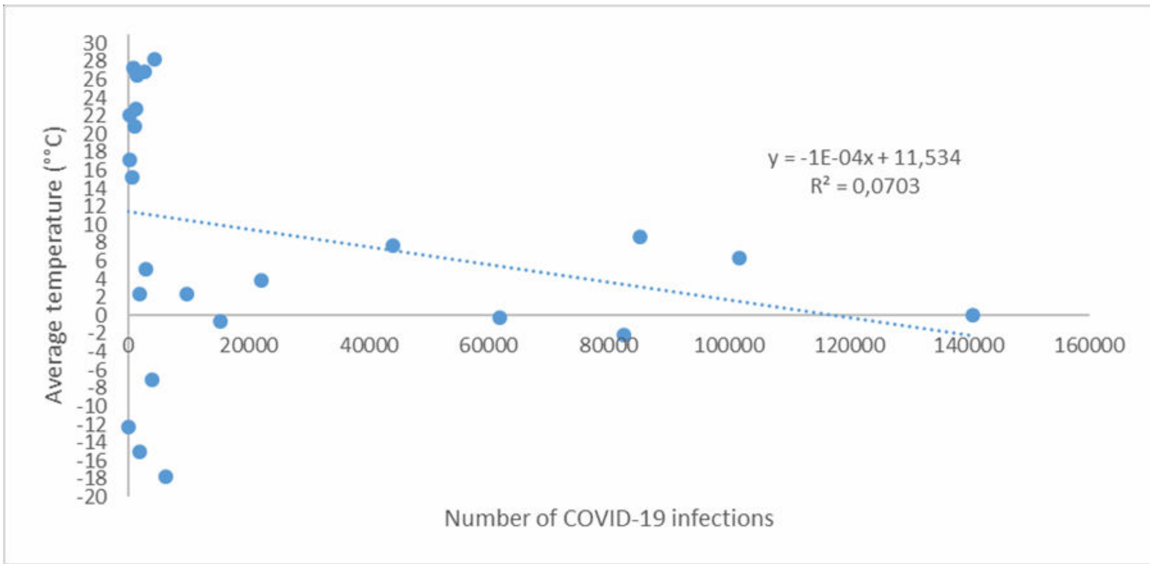

Figure 2. Relationship between average temperature and the number of SARS-CoV-2 infections (COVID-19 cases).

The graph is similar to that for SARS (Figure 1). The gradient is slightly higher than that for SARS (Figure 1). It intersects the vertical/y-axis at c= 11.534= 12ºC, corresponding to 0 (minimum) cases on the x-axis. As the average temperature drops to below 12ºC, approaching lower temperatures to ~ 0ºC, there seems to be an increase in the number of COVID-19 cases: 5.09ºC for Ireland (2910 cases), 3.85ºC for United Kingdom (22,145 cases), 7.71 for France (43,977 cases), -2.16ºC for China (82,545 cases), 8.62ºC for Spain (85195 cases), 6.31ºC for Italy (101739 cases), and 0.07ºC for United States (140640 cases). For colder average temperatures, below 0ºC, from < -2ºC down to -17.82ºC, there appears to be an overall decrease in the number of COVID-19 cases: -7.08ºC for Sweden (4028 cases), -12.24ºC for Mongolia (12 cases), -14.98ºC for the Russian Federation (1837 cases), -17.82ºC for Canada (6 317 cases). The virus, like SARS-CoV, may also be unstable at colder, negative temperatures. The viral transmission appears to be optimum at ~ +0.07ºC. The graph intersects the x- axis (0ºC) = ± 120 000 cases. If one extrapolates the graph down to -4ºC, the number of expected cases increase to ± 160 000. However, below -4ºC, there is a noticeable decrease in the number of infections: -7.08ºC (4028 cases, Sweden), -12.24ºC (12 cases, Mongolia), -14.98ºC (1837 cases, Russian Federation) and -17.82ºC (6317 cases, Canada).

For average temperatures ≥ 12ºC, there seems to be a relative decrease and/or fairly minimal change in the number of COVID-19 cases: 15.24ºC for New Zealand (600 cases), 22.81ºC for South Africa (1326 cases) 26.54ºC for Philippines (1546 cases), 28.23ºC for Australia (4359 cases).

The 3-month average predicted temperatures, for April to June 2020, for each country are also summarized in Table 2, to determine which countries are at a relatively higher risk for infection, for this period, based on the estimated optimum temperature ± 0.07ºC for viral transmission. The data indicates that Canada (1.48ºC), Russian Federation (5.17ºC), Sweden (7.40ºC), and Mongolia (9.34ºC) are at the highest risk for further infection.

For countries with predicted average temperatures of ≤12ºC: the following countries fall within this temperature range: United States (13.59ºC), Italy (16.00ºC), Spain (15.78ºC), China (13.61ºC), Germany (12.07ºC), France (15.04ºC),United Kingdom (9.81ºC), Switzerland (10.96ºC), Korea (16.46ºC), Republic of Ireland (10.73ºC), Romania (15.37ºC), South Africa (14.69ºC),New Zealand (9.37ºC), we can expect them to be at a relatively "medium" risk for infection.

For countries that have average temperatures >12ºC: like Malaysia (27.44ºC), Thailand (29.11ºC), Philippines (28.42ºC), Indonesia (26.76ºC), India (29.50ºC), Singapore (28.22ºC), Kuwait (30.46ºC), and Vietnam (26.76ºC), these countries can be expected to have reduced, or lower risk of viral infection or the case numbers may be stable, with no significant increase.

The observed case numbers were then assigned to the following temperature ranges:

>12ºC, 12 to 2ºC, +2 to -2ºC, and ≤ 2ºC, to determine relative composition with respect to the total infections (596 222 cases). The data indicated the following case numbers and percentages per temperature range: in decreasing order: 312 248 cases (52.4%) for +2 to -2ºC, 255 966 cases (42.9%) for 12 to 2ºC, 15814 cases (2.7%) for >12ºC and 12194 cases (2.0%) for <-2ºC. These findings appear to confirm the general trends noted with the graph in Figure 2.

At the time of preparation of this manuscript, two relevant papers just appeared. One was a recent study by Shi et al. [45], which covered 31 regions in China, from 20 January to 29 February. They confirmed a significant association between COVID-19 daily incidence and temperature. They concluded that temperature is an environmental driver of COVID-19 outbreak in China; the incidence of COVID-19 decreased with an increase in temperature. The daily confirmed cases rate had a bi-phasic relationship with temperature: with a peak at 10°C and the daily incidence of COVID-19 cases decreased at values below and above this value. Our study has, however, shown a significant number of case infections below 10°C.

The other was a study by Sajadi et al. [46], who analyzed temperature, humidity and latitude to predict potential spread and seasonality for COVID-19. They found a significant spread in cities and regions along a narrow east west latitude distribution roughly along the 30-50°N' corridor, that has consistently similar weather patterns of average temperature 5-11°C, combined with low specific (3-6 g/m^3) and absolute humidity (4-7 g/m^3).

Thus, to date, some of the recent peer-reviewed reported studies on temperature effects on COVID-19 transmission have indicated the following optimal temperature, or ranges, for viral transmission: 0-3°C, 10°C, 5.04-8.2°C and 5-11°C [45-47]. There are some comments regarding these temperatures and the incidence of infections. The initial outbreak of SARS-CoV-2 was during the peak of winter season, where the environmental temperature ranged from -8.14 to +3.82ºC, during December/January 2019 to February, in China. Our data has shown high infection numbers, covering the broad range: -17.82 to 26.23ºC for the 29 countries in this study, over the reporting period January to March 2020.

This study data seems to confirm these four recent reports but it indicates a broader optimal range of -2.7 up to 11.5°C [11,45-47]. It also supports the proposal by Sajadi et al. that viral occurrence appears to be seasonal [47].

The predictions for those countries at higher risk of infection were then checked by assessing the actual total cases of infection data as at 11 April 2020 for any increase as predicted by the "lower temperature-higher risk" trend [48]. The percentage increases are summarized in Table 2, and the relationship is graphically illustrated in Figure 3, with % Increase in case numbers on the x-axis, and average temperature on the y-axis.

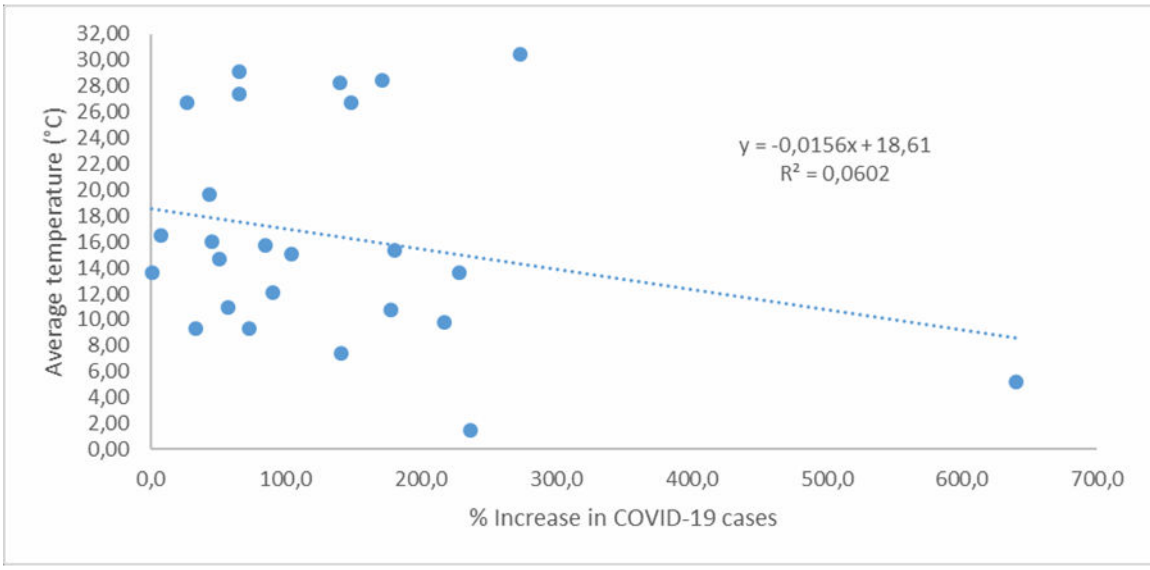

Figure 3. Relationship between the average temperature and the percentage increase in the number of SARS-CoV-2 infections (COVID-19 cases).

For India, there was surprisingly a much higher percentage increase (595.3%), although it was at a predicted "low" risk for increase of infection (average temperature: 29.50ºC). This anomaly may be due to increased testing for COVID-19, and hence a sudden spike in the number of infections that are only being diagnosed much later. The percentage for testing for India did increase from 0.001% (18 March 2020) to 0.0133 (Wikipedia), about 13.3 fold. This set of data points for India (x = 595.3%, y = 29.50ºC) was therefore regarded as an "outlier" and was excluded from the plot. As expected, the graph has a negative slope (m= -0.0156) indicating a general inverse relationship between average temperature and increase in cases of infection. As predicted, countries with a relatively "high" risk showed the following increases: Canada: 236.0%, Sweden: 140.4%, Russia: 639.5% and Mongolia: 33.3%, which was unexpectedly lower, compared to the increase for the predicted "medium" and "low" risk countries. For Philippines (171.3%), Indonesia (148.4%), Singapore (139.8%) and Kuwait (273.3%), the actual percentage increase was unexpectedly higher, as these countries with average temperatures >>12ºC, were predicted to be in the "low" risk of increase category. It was noted that COVID-19 testing had increased for: Philippines, Indonesia, Singapore and the USA during early April [15], but not as high as for the rate of increase as noted for India. Countries that were predicted with "medium" risk of increase did show the predicted increase: like the United States (228.0%), Spain (84.3%), Germany (90%), France (103.9%), United Kingdom (217.3%), Ireland (178.0%), Romania (180.1%) and New Zealand (72.5%). For China, with medium risk of increase, noticeably minimal (1%) increase was noted – this low figure confirms the reports that this is the only country, with severe: "lockdown measures, etc. implemented, that seems to have contained the spread of the pandemic fairly well under control, with about 70% recoveries as at 10 March 2020 [48].

Case fatality rate (ratio): Effect of patient age

The death rates usually quoted in the media, and those above, are case fatality rates (ratios) (CFRs): the number of deaths divided by the number of cases (multiply by 100 to convert to a percentage). Since the CFR only uses known cases and known deaths, it is heavily influenced by how well the COVID-19 testing and cause of death systems work in any country.

Based on the data as at 31 March 2020, the % CFR per country is ranked from highest to lowest, with the median population age per country, summarized in Table 3. The calculated % CFR figures are highly dependent on: the accuracy of the data supplied, especially the number of cases diagnosed, the extent of testing, which varies between the countries, the number tests in progress and data processing before finalization of results, etc. and should only be regarded as relative estimates per country.

Table 3. Global COVID-19 Case fatality rates vs median age per country.

Country	Total cases	Total deaths	% CFR	Median age/ years
Deaths/% CFR > 0				
Saint Lucia	9	5	55,6	34,8
Canada	6317	2398	38,0	42,2
Guyana	8	3	37,5	26,2
Belize	3	1	33,3	22,7
Gambia	3	1	33,3	21,0

Afghanistan	166	52	31,3	18,9
Djibouti	26	7	26,9	23,9
Grenada	9	2	22,2	31,5
Zimbabwe	5	1	20,0	20,0
Cabo Verde	5	1	20,0	25,4
Niger	20	3	15,0	15,4
Gabon	7	1	14,3	18,6
Tunisia	362	50	13,8	31,6
Iraq	630	83	13,2	20,0
Pakistan	1865	240	12,9	23,8
United States of America	140640	17987	12,8	38,1
Italy	101739	11591	11,4	45,5
San Marino	230	25	10,9	44,4
Saudi Arabia	1453	154	10,6	27,5
Bangladesh	49	5	10,2	26,7
Morocco	574	58	10,1	29,3
Syrian Arab Republic	10	1	10,0	24,3
Curaçao	11	1	9,1	36,1
Indonesia	1414	122	8,6	30,2
Spain	85195	7340	8,6	42,7
Qatar	693	59	8,5	33,2
Cayman Islands	12	1	8,3	40,0
Democratic Republic of the Congo	98	8	8,2	19,7
Iran (Islamic Republic of)	41495	3186	7,7	30,3
Netherlands	11750	864	7,4	42,6
Egypt	656	47	7,2	23,9
France	43977	3017	6,9	41,4
Oman	179	12	6,7	25,6
United Arab Emirates	611	41	6,7	30,3
The United Kingdom	22145	1408	6,4	40,5
Algeria	511	31	6,1	28,1
Mexico	993	60	6,0	28,3

Chile	2449	136	5,6	34,4
Saint Martin	18	1	5,6	32,5
Bolivia (Plurinational state of)	97	5	5,2	24,3
Philippines	1546	78	5,0	23,5
Albania	223	11	4,9	32,9
Burkina Faso	246	12	4,9	17,3
Peru	852	42	4,9	28,0
Paraguay	64	3	4,7	28,2
Belgium	11899	513	4,3	41,4
Cameroon	139	6	4,3	18,5
Kuwait	266	11	4,1	29,3
China	82545	3314	4,0	37,4
Guadeloupe	106	4	3,8	49,2
Trinidad and Tobago	82	3	3,7	36,0
Sweden	4028	146	3,6	41,2
Greece	1212	43	3,5	44,5
Jordan	268	9	3,4	22,5
Hungary	447	15	3,4	42,3
Puerto Rico	174	6	3,4	41,5
Ghana	152	5	3,3	21,1
Jersey	63	2	3,2	38,0
Costa Rica	314	10	3,2	31,3
Denmark	2577	77	3,0	42,2
Cyprus	230	7	3,0	36,8
Japan	1953	56	2,9	47,3
Togo	34	1	2,9	19,8
Honduras	139	4	2,9	23,0
Guatemala	36	1	2,8	22,1
Jamaica	36	1	2,8	26,0
Colombia	702	20	2,8	30,0
India	1071	29	2,7	28,1
Dominican Republic	901	24	2,7	28,1

Kenya	38	1	2,6	19,7
North Macedonia	285	7	2,5	37,9
Bosnia and Herzegovina	359	9	2,5	42,1
Ukraine	549	13	2,4	40,6
Venezuela (Bolivarian Republic of)	129	3	2,3	28,3
Romania	1952	44	2,3	41,1
Portugal	6408	140	2,2	42,2
Bulgaria	359	8	2,2	42,7
Andorra	370	8	2,2	44,3
Panama	989	20	2,0	29,2
Ireland	2910	54	1,9	36,8
Switzerland	15412	295	1,9	42,4
Mauritius	107	2	1,9	35,3
Lebanon	446	8	1,8	30,5
Martinique	111	2	1,8	43,7
Serbia	785	13	1,7	42,6
Republic of Korea	9786	162	1,7	41,8
Guam	58	1	1,7	29,0
Turkey	10827	168	1,6	30,9
Brazil	4256	66	1,6	32,6
Azerbaijan	273	4	1,5	31,3
Poland	2055	31	1,5	40,7
Malaysia	2626	37	1,4	28,5
Slovenia	763	11	1,4	44,5
Lithuania	484	7	1,4	43,7
Uzbekistan	149	2	1,3	28,6
Argentina	820	11	1,3	31,7
Montenegro	91	1	1,1	40,7
Austria	9618	108	1,1	44,0
Luxembourg	1988	22	1,1	39,3
Finland	1313	13	1,0	42,5
Germany	61913	583	0,9	47,1

Nigeria	111	1	0,9	18,4
Kosovo	106	1	0,9	29,1
Occupied Palestinian Territory	117	1	0,9	Not available
Czechia	3002	24	0,8	42,1
Croatia	790	6	0,8	43,0
Brunei Darussalam	127	1	0,8	30,2
Sri Lanka	120	1	0,8	32,8
Republic of Moldova	298	2	0,7	36,7
Norway	4226	26	0,6	39,2
Armenia	482	3	0,6	35,1
Thailand	1524	9	0,6	37,7
Uruguay	309	2	0,6	35,0
Russian Federation	1837	9	0,5	39,6
Australia	4359	18	0,4	38,7
Ecuador	1962	8	0,4	27,7
Israel	4831	17	0,4	29,9
Estonia	715	3	0,4	42,7
Singapore	879	3	0,3	34,6
Kazakhstan	312	1	0,3	30,6
New Zealand	600	1	0,2	37,9
Iceland	1086	2	0,2	36,5
South Africa	1326	3	0,2	27,1
Mean				**33,1**
No deaths/% CFR = 0				
Cambodia	107	0	0,0	25,3
Mongolia	12	0	0,0	28,3
Lao People's Democratic Republic	8	0	0,0	23,0
Latvia	376	0	0,0	43,6
Dominica	11	0	0,0	33,5
Suriname	8	0	0,0	29,8
Antigua and Barbuda	7	0	0,0	31,9
Nicaragua	4	0	0,0	25,7

Saint Kitts and Nevis	2	0	0,0	35,0
Saint Vincent and the Grenadines	1	0	0,0	33,6
Aruba	50	0	0,0	39,3
French Guiana	43	0	0,0	42,0
United States Virgin Islands	30	0	0,0	41,0
Bermuda	22	0	0,0	43,4
Saint Barthélemy	6	0	0,0	44,1
Saint Maarten	6	0	0,0	41,0
Montserrat	5	0	0,0	33,2
Turks and Caicos islands	5	0	0,0	33,3
Anguilla	2	0	0,0	34,8
British Virgin Islands	2	0	0,0	36,5
Cote d'Ivoire	169	0	0,0	20,9
Senegal	162	0	0,0	18,8
Rwanda	70	0	0,0	19,0
Madagascar	46	0	0,0	19,7
Gibraltar	69	0	0,0	34,7
Zambia	35	0	0,0	16,8
Uganda	33	0	0,0	15,8
Ethiopia	23	0	0,0	17,9
Congo	19	0	0,0	19,7
United Republic of Tanzania	19	0	0,0	17,7
Mali	18	0	0,0	15,8
Guinea	16	0	0,0	18,9
Equatorial Guinea	14	0	0,0	19,8
Namibia	11	0	0,0	21,2
Eswatini	9	0	0,0	21,7
Mozambique	8	0	0,0	17,2
Seychelles	8	0	0,0	35,4
Benin	6	0	0,0	18,2
Central African Republic	6	0	0,0	19,7
Eritrea	6	0	0,0	19,7

Chad	5	0	0,0	17,8
Mauritania	5	0	0,0	20,5
Liberia	3	0	0,0	17,8
Angola	2	0	0,0	15,9
Guinea-Bissau	2	0	0,0	17,8
Réunion	207	0	0,0	35,9
Mayotte	82	0	0,0	16,9
Barbados	33	0	0,0	38,6
El Salvador	30	0	0,0	27,1
Haiti	15	0	0,0	23,0
Bahamas	14	0	0,0	32,0
Fiji	5	0	0,0	28,9
Papua New Guinea	1	0	0,0	23,1
Slovakia	336	0	0,0	41,2
French Polynesia	36	0	0,0	31,9
New Caledonia	15	0	0,0	32,0
Northern Mariana Islands (Commonwealth of the)	2	0	0,0	33,6
Malta	156	0	0,0	42,6
Belarus	152	0	0,0	40,0
Liechtenstein	64	0	0,0	43,2
Monaco	49	0	0,0	53,1
Holy See	6	0	0,0	Not available
Faroe Islands	168	0	0,0	37,6
Guernsey	45	0	0,0	43,8
Isle of Man	42	0	0,0	44,2
Greenland	10	0	0,0	33,9
Kyrgyzstan	107	0	0,0	25,1
Georgia	103	0	0,0	38,1
Maldives	17	0	0,0	28,2
Myanmar	10	0	0,0	29,0
Nepal	5	0	0,0	24,1
Bhutan	4	0	0,0	27,6

Timor-Leste	1	0	0,0	19,6
Bahrain	515	0	0,0	32,3
Libya	8	0	0,0	28,9
Sudan	6	0	0,0	19,9
Somalia	3	0	0,0	18,0
Viet Nam	203	0	0,0	30,5
Cuba	170	0	0,0	41,5
Mean				**29,0**
Average % CFR, based on data for 202 countries			**3,2**	

It can also be rather misleading as seen here: for example, Saint Lucia has the highest % CFR: 55.6, but only 5 deaths per 9 cases vs countries with a much lower CFR, but an actually larger number of deaths: for example, Canada 3.0% (2398 deaths), USA 12.8% (17987 deaths), Italy 11.4% (11591 deaths), Spain 8.6% (8340 deaths), Iran 7.7% (3186 deaths), France 6.9% (3017 deaths), United Kingdom 6.4% (1408 deaths), China 4.0% (3314 deaths) and Germany 0.9% (583 deaths).

The average % CFR, based on the data for all 202 countries, as at 31/3/2020, is 3.2%. This figure increases to a CFR of 6.2%, if one excludes all those countries with zero deaths and this may grossly over-estimate the global CFR.

Table 4 is a summary of the % CFR only for all countries that had at least one death (%CFR>0), ranked by the number of deaths per country, which was the highest for the USA (17 987 deaths, CFR 12.8%), to the countries with the lowest number of deaths (1, for Belize, down to New Zealand), rather than by % CFR. The average CFR is now 6.2%, about twice that for all 202 countries (3.2%). The average median age is 33.0 (range: 15.4-45.4 years).

Table 4. Global COVID-19 CFR > zero vs median age per country as at 31 March 2020.

Country	Cases	Deaths	Median age (years)	%CFR	% (deaths/ total deaths)	Population	% (Deaths/ Population)
United States of America	140640	17987	38,1	12,8	32,434	331 002 651	0,0054
Italy	101739	11591	45,5	11,4	20,901	60 461 826	0,0192
Spain	85195	7340	42,7	8,6	13,235	46 754 778	0,0157
China	82545	3314	37,4	4,0	5,976	1 439 323 776	0,0002
Iran (Islamic Republic of)	41495	3186	30,3	7,7	5,745	83 992 949	0,0038
France	43977	3017	41,4	6,9	5,440	65 273 511	0,0046
Canada	6317	2398	42,2	38,0	4,324	37 742 154	0,0064
The United Kingdom	22145	1408	40,5	6,4	2,539	67 886 011	0,0021
Netherlands	11750	864	42,6	7,4	1,558	17 134 872	0,0050
Germany	61913	583	47,1	0,9	1,051	83 783 942	0,0007
Belgium	11899	513	41,4	4,3	0,925		
Switzerland	15412	295	42,4	1,9	0,532		
Pakistan	1865	240	23,8	12,9	0,433		
Turkey	10827	168	30,9	1,6	0,303		
Republic of Korea	9786	162	41,8	1,7	0,292		

Saudi Arabia	1453	154	27,5	10,6	0,278
Sweden	4028	146	41,2	3,6	0,263
Portugal	6408	140	42,2	2,2	0,252
Chile	2449	136	34,4	5,6	0,245
Indonesia	1414	122	30,2	8,6	0,220
Austria	9618	108	44,0	1,1	0,195
Iraq	630	83	20,0	13,2	0,150
Philippines	1546	78	23,5	5,0	0,141
Denmark	2577	77	42,2	3,0	0,139
Brazil	4256	66	32,6	1,6	0,119
Mexico	993	60	28,3	6,0	0,108
Qatar	693	59	33,2	8,5	0,106
Morocco	574	58	29,3	10,1	0,105
Japan	1953	56	47,3	2,9	0,101
Ireland	2910	54	36,8	1,9	0,097
Afghanistan	166	52	18,9	31,3	0,094
Tunisia	362	50	31,6	13,8	0,090
Egypt	656	47	23,9	7,2	0,085
Romania	1952	44	41,1	2,3	0,079
Greece	1212	43	44,5	3,5	0,078
Peru	852	42	28,0	4,9	0,076
United Arab Emirates	611	41	30,3	6,7	0,074
Malaysia	2626	37	28,5	1,4	0,067
Algeria	511	31	28,1	6,1	0,056
Poland	2055	31	40,7	1,5	0,056
India	1071	29	28,1	2,7	0,052
Norway	4226	26	39,2	0,6	0,047
San Marino	230	25	44,4	10,9	0,045
Dominican Republic	901	24	28,1	2,7	0,043
Czechia	3002	24	42,1	0,8	0,043
Luxembourg	1988	22	39,3	1,1	0,040
Panama	989	20	29,2	2,0	0,036

Colombia	702	20	30,0	2,8	0,036
Australia	4359	18	38,7	0,4	0,032
Israel	4831	17	29,9	0,4	0,031
Hungary	447	15	42,3	3,4	0,027
Ukraine	549	13	40,6	2,4	0,023
Serbia	785	13	42,6	1,7	0,023
Finland	1313	13	42,5	1,0	0,023
Oman	179	12	25,6	6,7	0,022
Burkina Faso	246	12	17,3	4,9	0,022
Albania	223	11	32,9	4,9	0,020
Kuwait	266	11	29,3	4,1	0,020
Slovenia	763	11	44,5	1,4	0,020
Argentina	820	11	31,7	1,3	0,020
Costa Rica	314	10	31,3	3,2	0,018
Jordan	268	9	22,5	3,4	0,016
Russian Federation	1837	9	39,6	0,5	0,016
Bosnia and Herzegovina	359	9	42,1	2,5	0,016
Thailand	1524	9	37,7	0,6	0,016
Democratic Republic of the Congo	98	8	19,7	8,2	0,014
Bulgaria	359	8	42,7	2,2	0,014
Andorra	370	8	44,3	2,2	0,014
Lebanon	446	8	30,5	1,8	0,014
Ecuador	1962	8	27,7	0,4	0,014
Cyprus	230	7	36,8	3,0	0,013
North Macedonia	285	7	37,9	2,5	0,013
Lithuania	484	7	43,7	1,4	0,013
Djibouti	26	7	23,9	26,9	0,013
Croatia	790	6	43,0	0,8	0,011
Cameroon	139	6	18,5	4,3	0,011
Puerto Rico	174	6	41,5	3,4	0,011
Ghana	152	5	21,1	3,3	0,009
Saint Lucia	9	5	34,8	55,6	0,009

Bangladesh	49	5	26,7	10,2	0,009
Bolivia (Plurinational state of)	97	5	24,3	5,2	0,009
Guadeloupe	106	4	49,2	3,8	0,007
Honduras	139	4	23,0	2,9	0,007
Azerbaijan	273	4	31,3	1,5	0,007
Niger	20	3	15,4	15,0	0,005
Guyana	8	3	26,2	37,5	0,005
Paraguay	64	3	28,2	4,7	0,005
Trinidad and Tobago	82	3	36,0	3,7	0,005
Venezuela (Bolivarian Republic of)	129	3	28,3	2,3	0,005
Armenia	482	3	35,1	0,6	0,005
Estonia	715	3	42,7	0,4	0,005
Singapore	879	3	34,6	0,3	0,005
South Africa	1326	3	27,1	0,2	0,005
Grenada	9	2	31,5	22,2	0,004
Jersey	63	2	38,0	3,2	0,004
Iceland	1086	2	36,5	0,2	0,004
Mauritius	107	2	35,3	1,9	0,004
Uruguay	309	2	35,0	0,6	0,004
Martinique	111	2	43,7	1,8	0,004
Uzbekistan	149	2	28,6	1,3	0,004
Republic of Moldova	298	2	36,7	0,7	0,004
Belize	3	1	22,7	33,3	0,002
Gambia	3	1	21,0	33,3	0,002
Zimbabwe	5	1	20,0	20,0	0,002
Cabo Verde	5	1	25,4	20,0	0,002
Gabon	7	1	18,6	14,3	0,002
Syrian Arab Republic	10	1	24,3	10,0	0,002
Curaçao	11	1	36,1	9,1	0,002
Cayman Islands	12	1	40,0	8,3	0,002
Saint Martin	18	1	32,5	5,6	0,002
Togo	34	1	19,8	2,9	0,002

Guatemala	36	1	22,1	2,8	0,002
Jamaica	36	1	26,0	2,8	0,002
Kenya	38	1	19,7	2,6	0,002
Guam	58	1	29,0	1,7	0,002
Montenegro	91	1	40,7	1,1	0,002
Nigeria	111	1	18,4	0,9	0,002
Kosovo	106	1	29,1	0,9	0,002
Occupied Palestinian Territory	117	1	20,8	0,9	0,002
Brunei Darussalam	127	1	30,2	0,8	0,002
Sri Lanka	120	1	32,8	0,8	0,002
Kazakhstan	312	1	30,6	0,3	0,002
New Zealand	600	1	37,9	0,2	0,002

For the countries with the top 10 highest number of deaths, the highest is noted for the USA, followed by Italy, Spain, China, Iran, France, Canada, United Kingdom, Netherlands, and Germany. The median age for these top 10 countries range from to 30.3 to 47.1 years (mean ± SD= 40.8 ± 4.7) years.

Table 5 is a summary of the 13 COVID-19 deaths, as at 06 April 2020, for South Africa. It is evident that risk of death increases from age 40 upwards and it maximum for the age group of ≥ 80 year (7 deaths, 53.8%). A similar trend was noted by the nationwide Chinese study, as at 11 February 2020 for increasing risk with age: but from age 19 upwards, and was maximum, for age ≥ 80 years: 208 deaths (%CFR 14.8%). For this study in China, the overall CFR was 2.3%, which is lower than the calculated global average obtained by this study (3.2%).

Table 5. Patient details of COVID-19 deaths in South Africa as at 06 April 2020.

Number	From Province	Age (years)	Gender	Available clinical information
South Africa				
1	Western Cape	48	Female	
2	Free State	85	Male	
3	Gauteng	79	Male	Respiratory distress
4	KwaZulu-Natal	46	Female	Chronic asthma and hypertension
5	KwaZulu-Natal	74	Male	Flu-like symptoms, respiratory complications
6	KwaZulu-Natal	63	Female	Respiratory distress
7	KwaZulu-Natal	81	Female	Pneumonia
8	KwaZulu-Natal	80	Female	
9	KwaZulu-Natal	80	Male	
10	KwaZulu-Natal	80	Male	
11	Western Cape	82	Female	

12	KwaZulu-Natal	86	Male	Bronchopneumonia and respiratory distress; underlying condition of chronic obstructive airway disease (COAD).	
13	Western Cape	57	Male		
Summary					
South Africa as at 06 April 2020			**China study as at 11 February 2020**		
Age group (years)	**Number of deaths**	**% of total deaths**	**Age group**	**Number of deaths**	**% of total deaths**
0-9	0	0,0	0-9	0	
10-19	0	0,0	10-19	1	0.2
20-29	0	0,0	20-29	7	0.2
30-39	0	0,0	30-39	18	0.2
40-49	2	15,4	40-49	38	0.4
50-59	1	7,7	50-59	130	1.3
60-69	1	7,7	60-69	309	3.6
70-79	2	15,4	70-79	312	8.0
≥ 80	7	53,8	≥ 80	208	14.8

Conclusion

The present preliminary study has indicated the following:

- The presence of the furin cleavage site, the 10 to 20- fold binding affinity of the spike protein of the SARS-CoV-2 virus, compared to SARS-CoV, are possible reasons for the much higher cases noted for COVID-19 compared to the SARS disease.
- The optimum temperature for viral infection with SARS-CoV-2, for COVID-19, appears to be ± 0.07°C; viral transmission appears to be maximum at +2 to -2°C (52.4% of cases) and at 12 to 2°C (42.9% of cases); transmission appears to decrease at >12°C (2.7% of cases).
- The average % CFR for COVID-19, based on 202 countries, is 3.2%, as at 31 March 2020.
- Subjects confirmed with COVID-19, in median age range 40.8 (± 4.7) years, are at higher risk of death; for South Africa and China, the “maximum” risk age range appears to be ≥ 80 years.

The % CFR is also impacted by other factors, like co-morbidity, due to pre-existing respiratory diseases, lifestyle diseases, like cardiovascular disease, diabetes, AIDS/HIV, Tuberculosis, history of smoking, etc., which are very prevalent in Sub- Saharan Africa.

The preliminary study outcomes can be used for further investigation, to confirm the actual ages of subjects who died from COVID-19, to confirm the risk age groups for death from COVID-19, and to predict risk of future infection based on monthly temperatures per country. As more data becomes available, future studies must continue in the area of temperature and other environmental vectors on rates of viral transmission and virus stability that can aid countries at risk toward implementing appropriate public health mitigation measures.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

The author acknowledges the WHO, stat.world, Wikipedia for use of the data, and Ms Caroline Taylor, Journal Coordinator (IJPHS), for arranging discounted article processing fees.

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How to cite this article: Thavrin Manickum. "A 3-Month Preliminary Epidemiological Assessment of Some Factors Affecting the Human-To-Human Transmission of Causal Agent SARS-CoV-2 Virus for Infection Rates of COVID-19". Int J Pub Health Safe 5 (2020) doi: 10.37421/ijphs.2020.5.186