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Impact of physical factors on Covid-19: A four months statistical study for designing Covid-19 chambers and isolation centers

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Abstract

SARS-CoV-2 is a deadly virus that has locked down the whole universe and still prevailing at a very rapid rate. As of 11th 2020, the reported confirmed cases of SARS-CoV-2 count reached 4,006,257 around the world, and it reported 278,892 deaths globally. There is no specific vaccination or other cure available until now. SARS-CoV-2 is highly sensitive to abiotic factors. The viral structure is strongly affected by temperature, Relative Humidity and UV Index. In our review, we studied the impact of abiotic factors on SARS-CoV-2 by using regression and correlation statistical analysis. These analyses helped out in finding that the countries with comparatively high temperature, Relative Humidity and UV Index are at lower risk of the pandemic and vice versa. The death ratio is also lower in countries with higher values of abiotic factors. Therefore, it is suggested to design specific "COVID-19" chambers with adjustable figures of three discussed abiotic factors and, on the same bases, isolation centers could be adjusted accordingly. The temperature of 38°C, the relative humidity of >95% and UV radiation of 254nm assisted with the airflow is optimized for lowering the activity of SARS-CoV-2 keeping in view the bearable amounts for human bodies. However, these values could be altered according to the condition of the patients.

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Introduction

Coronaviruses belong to *Coronaviridae* family and *Nidovirales* order(Yang *et al.*, 2020). They are classified into four genera; Alpha (α), Beta (β), Gamma (γ) and Delta (δ) coronaviruses. (Shereen, Khan, Kazmi, Bashir, & Siddique, 2020). Among humans, out of seven strains of coronaviruses HCoV-229E, HCoV-NL63, HCoV-OC43 and HCoVHKU1, can cause mostly mild respiratory illness but Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV). The Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and newly emerged Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) causes severe respiratory diseases. (Gorbalenya *et al.*, 2020; Gralinski & Menachery, 2020; Khan *et al.*, 2020). Recently, in late December 2019, patients started admitting in the hospitals showing initial symptoms of pneumonia of an unknown etiology. This led world to the introduction to a new coronavirus which is officially named as SARS-CoV-2 and associated illness as COVID-19 by WHO. Due to its enormous rate of transmission, it prevailed in the whole universe within no time. Therefore, these days' world experiences the COVID-19 pandemic. As of May 11th 2020, the reported confirmed case counts of SARS-CoV-2 reached 4,006,257 around the world, and it caused 278,892 reported deaths globally. The worst victim of SARS-CoV-2 is USA with maximum cases of 1,271,645 and most deaths as 76,916 while the confirmed cases in Spain are 224,390, in Russian Federation 221,344, in United Kingdom 219,187 and in Italy are 219,070 till 11th May. There is still no vaccine and drug available for the affective treatment of COVID-19(Tang *et al.*, 2020). The world is also facing the deficiencies of ventilators. Therefore, this study under discussion, intends to investigate the relationship between the abiotic factors and epidemic transmission rate and then designing the specific chambers to treat COVID-19 patients and isolation centers for suspected carriers of SARS-CoV-2 so that the death rate could be brought to minimum level. It could also become feasible for the curing staff to treat maximum patients. By using these chambers and measures in quarantine centers, activity of SARS-CoV-2 could be dragged at near the finishing line.

The physical structure of SARS-CoV-2

Coronaviruses including SARS-CoV-2 by having a fringe of large, bulbous surface projections are roughly spherical and moderately pleomorphic. SARS-CoV-2 and other CoVs have a very small size of about 60–140 nm in diameter. Coronaviruses are named so because they represent crown-like spikes on their outer surface. These viruses are single-stranded (Bhatraju *et al.*), positive-sense (+ S) non-segmented and enveloped RNA viruses with the largest genome size among all the known genomes of RNA viruses(P. Zhou *et al.*, 2020). The surface spikes or peplomers of these viruses, variously described as club-like, pear-shaped, or petal-shaped, which project 17–20 nm from the virion surface(Cascella, Rajnik, Cuomo, Dulebohn, & Di Napoli, 2020)(Fig. 1).

Molecular structure

The genome of SARS-CoV-2 and other coronaviruses encodes four major structural proteins, i.e.; Spike (S), Envelope (E), Membrane (M) and Nucleocapsid (N) with five to eight accessory proteins and 16 nonstructural proteins named as nsp1–16. (Wu *et al.*, 2020). Among all these proteins, S protein plays an essential role in viral attachment, fusion, entry and transmission. The transfection of coronaviruses is more infectious than other positive-strand RNA viruses due to the presence of N protein (Grossoehme *et al.*, 2009). The S glycoproteins are composed of two further subunits named S1 and S2. Homodimers of N-terminal S1 subunit compose the spikes on the viral surface, which guides them to the host receptors and the C-terminal S2 subunit is responsible for the cell-virus membrane fusion (Cascella *et al.*, 2020; Du *et al.*, 2017). S1 is further divided into an N-terminal domain (NTD) and a receptor-binding domain (RBD). When a human being is infected, CoV first binds to the host cell through the interaction between S1subunit and RBD and then cell membrane receptor triggers conformational changes in S2 subunit that results in the viral entry within the target cell. (Y. Zhou, Yang, Huang, Jiang, & Du, 2019). SARS-CoV-2 has the feature of being optimized to bind the human receptor ACE2 (Letko & Munster, 2020; Menachery *et al.*, 2015; Walls *et al.*, 2020). Moreover, phylogenetically SARS-CoV-2 shares approximately 82% genomic sequence identity with SARS-CoV. (J. F.-W. Chan *et al.*, 2020; P. Zhou *et al.*, 2020).

Statistical analysis

The statistical model renovated with tables, figures, correlation and regression analyses comprised of the data of temperature, Relative Humidity and UV Index for January, February, March and April from 15 countries of different regions around the world.

This data is analyzed for designing the specific "COVID-19 chambers" for the treatment of COVID-19 patients and, on the same bases, the isolation centers for the suspected patients of COVID-19. Weather data was collected from the daily values of the observations about weather from different websites. Temperature is displayed in Celsius scale while the Relative Humidity (RH) was calculated from temperature and dew point using the following formula for each time point:

$$RH = \frac{7.5D}{e237.3+D} - \frac{7.5T}{237.3+T} \times 100 \qquad T<0$$

$$RH = \frac{7.5D}{10237.3+D} - \frac{7.5T}{237.3+T} \times 100 \qquad T\geq 0$$

where RH is the Relative Humidity, D is the dew point in degrees Celsius, T is the temperature in degrees Celsius, and e is the base of the natural log. The wavelength of UV light is measured in nanometers. Statistics of confirmed cases were obtained from the official website of World Health Organization.(Organization, 2020a, 2020b).

The graphical and tabular data analysis reveals that the novel SARS-CoV-2 spreads more rapidly in colder regions as compared to the hotter regions. The analysis shows that at 5% probability level and $P<0.05$ as statistically significant, the correlation of abiotic factors is highly significant with the emergence of SARS-CoV-2. However, the contribution of other factors also has a significant impact. Similarly, the death rate is >20% in the countries of hotter regions while that of colder regions exceeds 20%. Variance with these results is due to the factors other than abiotic factors. Moving on, this concept is used in designing COVID-19 chambers to provide optimum abiotic factors to combat SARS-CoV-2. (Table. 1) (Table. 2) (Table. 3).

Table 1. Correlation matrix.

	Cases Reported	Death Percentage	Month	Temperature °C	Relative Humidity %	UV Index
Cases reported	1.000					
Death Percentage	0.098	1.000				
	0.487					
Month	0.319*	0.395**	1.000			
	0.020	0.003				
Temperature °C	-0.142	-0.033	0.401**	1.000		
	0.309	0.812	0.002			
Relative Humidity %	0.115	0.129	-0.150	-0.406	1.000	
	0.414	0.358	0.254	0.001		
UV Index	0.031	0.053	0.457**	0.799**	-0.362**	1.000
	0.824	0.709	0.000	0.000	0.004	

Upper values indicate Pearson's correlation coefficient; Lower values indicate level of significance at 5% probability.

* = Significant ($P<0.05$); ** = Highly significant ($P<0.01$).

It has been optimized through statistics and analysis that the coronaviruses completely disintegrate at the temperature above 60°C. Similarly, the percentage of the Relative Humidity >95 also destroys the virus, and, on the same bases, the UV light above 254nm helps in damaging the structure of the said virus. (K. H. Chan *et al.*; Darnell, Subbarao, Feinstone, & Taylor, 2004).

Table 2. Death percentage and variation of abiotic factors in different countries.

Country	Temperature °C	Relative Humidity %	UV index	Death percentage
Australia	25.5	54.25	9	27.53516
China	6.75	77.75	6.5	20.64341
France	10.25	70.75	2.25	75.7177
Germany	5.25	70.75	2.5	15.80654
India	22.5	49.75	7	12.99809
Iran	15.75	50.5	5	19.08133
Israel	18	43.25	5.5	4.029907
Italy	9.25	70.75	2.75	54.38694
Pakistan	25	62.25	8.25	6.586712
Saudi Arabia	21.25	43	9	1.467153
Spain	14.75	71.5	5.75	34.20347
Thailand	29.5	69.75	10.5	7.277628
UAE	23	63	9	3.285008
United Kingdom	9	87.25	2	47.38448
United States	5.75	67	4.25	20.88807

Design for the COVID-19 Chambers

In 1927, Philip Drinker and Louis Agassiz Shaw invented the first tank respirator or iron lung at Harvard University. The device was intended to artificially breathe the patients with impaired breathing ability like in the later stages of Poliomyelitis, Asthma, etc. (Currie, 2012).

Table 3. Regression analysis of the Cases reported Month-wise with Temperature, Relative Humidity and UV Index.

Source	SS	Df	MS		
Model Residual	1.6712e+11 6.0800e+10	4 48	4.1780e+10 1.2667e+10	Number of obs F (4, 48) Prob > F	= 53 = 3.30 = 0.0182
Total	7.7511e+11	52	1.4906e+10	R-squared Adj R-squared Root MSE	= 0.2156 = 0.1502 = 1.1e+05

Table 3. Continued.

Cases Reported	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]
Month	46277.35	16196.51	2.86	0.006	13712.09 78842.61
Temperature C	-5850.25	2734.604	-2.14	0.038	-11348.54 -351.9592
Relative Humidity	813.1351	1192.923	0.68	0.499	-1585.398 3211.668
UV Index	9295.252	7573.889	1.23	0.226	-5933.072 24523.58
_cons	-95570.85	100614.5	-0.95	0.347	-297869.9 106728.2

. xtset Country
panel variable: Country (balanced)
. xtreg Cases reported Month Temperature, Relative Humidity and UV Index, re
Random-effects GLS regression Number of obs = 53
Group variable: Country Number of groups = 15
R-sq: Obs per group:
within = 0.1904 min = 2
between = 0.2854 avg = 3.5
overall = 0.2156 max = 4
Wald chi2 (4) = 13.19
corr(u_i, X) = 0 (assumed) Prob > chi2 = 0.0104.

Table 3. Continued.

Cases reported	Coef.	Std. Err.	z	P>|z|	[95% Conf. Interval]
Month	46277.35	16196.51	2.86	0.004	14532.78 78021.92
Temperature	-5850.25	2734.604	-2.14	0.032	-11209.98 -490.5237
Relative Humidity	813.1351	1192.923	0.68	0.495	-1524.951 3151.222
UV Index	9295.252	7573.889	1.23	0.220	-5549.297 24139.8
_cons	-95570.85	100614.5	-0.95	0.342	-292771.7 101630
sigma_u			0s		
sigma_e			112067.81		
Rho			0 (fraction of variance due to u_i)		

John Emerson succeeded in designing an iron lung that was more well-structured and better as a respirator with the cost reduced to almost half of the former one. When the iron lung invented, it intended not to be a permanent device for the patients and to be used until the patient could survive without it, but it became a permanent compulsion for a lot of patients, wondering the medical field that if keeping anybody alive was the best option (Raymondos *et al.*, 2012).

Table 4. Regression analysis of the Death percentage Month-wise with Temperature, Relative Humidity and UV Index.

Source	SS	Df	MS		
Model Residual	1347.51859	4	336.879649	Number of obs	= 53
	4735.02615	48	98.646378	F (4, 48)	= 3.42
Total	6082.54474	52	116.972014	Prob > F	= 0.0155
				R-squared	= 0.2215
				Adj R-squared	= 0.1567
				Root MSE	= 9.9321

Table 4. Continued

Death Percentage	Coef.	Std. Err.	T	P>|t|	[95% Conf. Interval]	
Month	4.84878	1.429329	3.39	0.001	1.974921	7.72264
Temperature C	-.2161037	0.2413268	-0.90	0.375	-.7013237	.2691163
Relative Humidity	0.1280755	0.1052746	1.22	0.230	-.0835932	.3397442
UV Index	0.1953271	0.66839	0.29	0.771	-1.148561	1.539215
_cons	-13.87672	8.879155	-1.56	0.125	-31.72945	3.976021

. xtreg Death percentage Month Temperature Relative Humidity UV Index, re
Random-effects GLS regression Number of obs = 53
Group variable: Country Number of groups = 15
R-sq: Obs per group:
within = 0.1948 min = 2
between = 0.3003 avg = 3.5
overall = 0.2215 max = 4
Wald chi2 (4) = 13.66
corr(u_i, X) = 0 (assumed) Prob > chi2 = 0.0085

Table 4. Continued

Death Percentage	Coef.	Std. Err.	z	P>|z|	[95% Conf. Interval]	
Month	4.84878	1.429329	3.39	0.001	2.047346	7.650214
Temperature	-.2161037	.2413268	-0.90	0.371	-.6890955	.2568881
Relative Humidity	.1280755	.1052746	1.22	0.224	-.0782589	.3344099
UV Index	.1953271	.66839	0.29	0.770	-1.114693	1.505347
_cons	-13.87672	8.879155	-1.56	0.118	-31.27954	3.526107
sigma_u				0		
sigma_e				9.6777659		
Rho				0 (fraction of variance due to u_i)		

The idea is clicked that if the tank respirators are modified for curing the patients of COVID-19 as “COVID-19 chambers”, it would be beneficial to cure those patients on the medical bases. It is not necessary to arrange a heavy metal for this purpose, a cylindrical or a cubical chamber could be made up of plastic instead of iron. Many purposes could be achieved by managing a closed chamber instead of a ventilator. As the use of oxygen tank is necessary for the COVID-19 patients, so instead of using one cylinder for one patient, in which pressure could only be adjustable for one patient, 3-4 supplies could be given from one cylinder and all the supplies could be adjusted according to the requirements of the patient with the help of pressure gauge provided with the chamber. This setting will improve the practicability of continuous external negative-pressure ventilation in an intubated patient in which flow is delivered from the conventional mechanical ventilator through the endotracheal tube. Apertures in the bottom, below the frame, could be used to lead out all the connections to the patient, and trimmed-to-fit sponge rubbers could be used to seal these apertures. (Raymondos *et al.*, 2012).

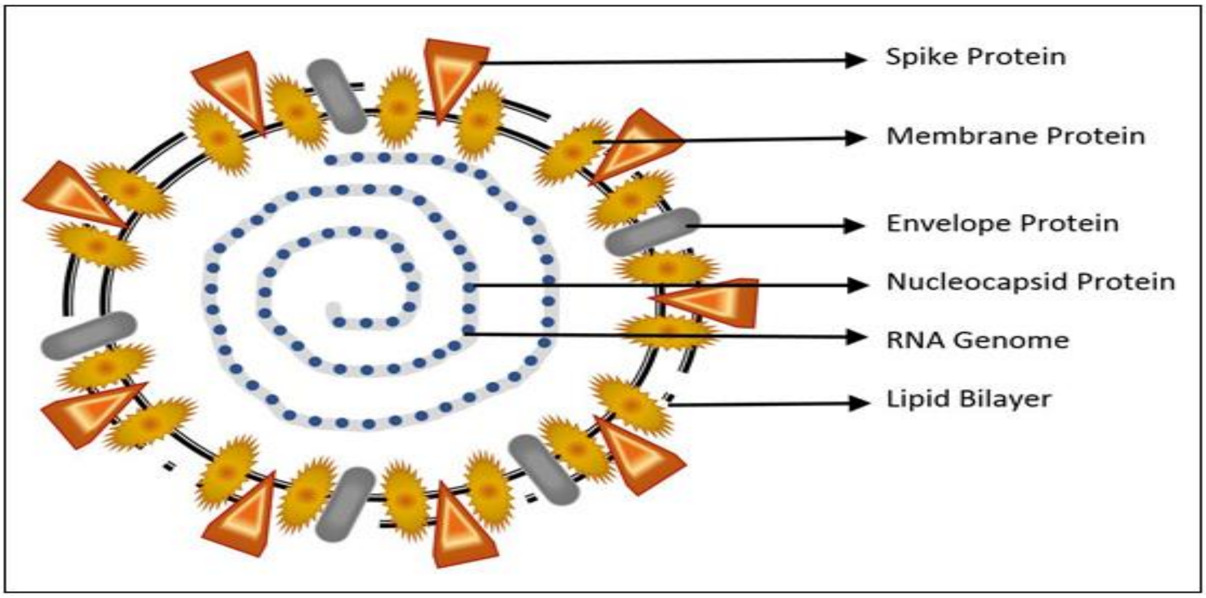

Fig. 1. Structure of respiratory syndrome causing human coronaviruses.

Moreover, Relative Humidity to control SARS-CoV-2 could also be adjusted accurately in the chamber and the whole ward could not be affected with this humidity. By doing so, the risk of the direct or indirect transmission of the virus will be reduced to a minimum as the patients will be in a closed chamber and the atmosphere of the ward for the doctors and the nursing staff will be more comfortable to work with the patients.

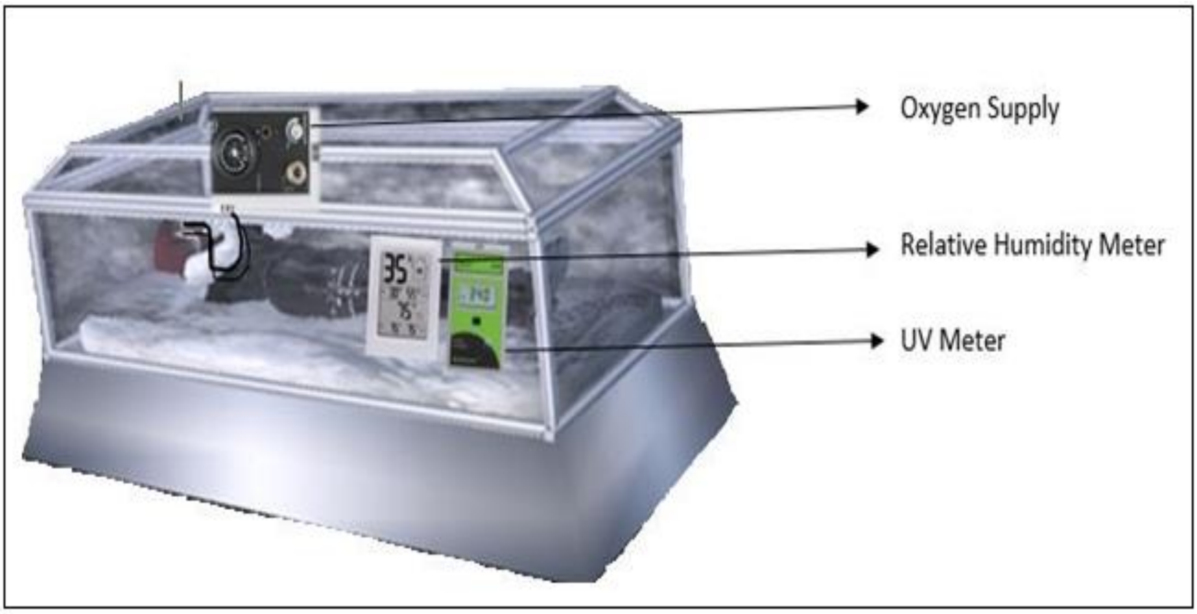

Fig. 2. Schematic diagram of COVID-19 Chamber.

Temperature suitable for the disintegration of SARS-CoV-2 is best achievable within the chamber. Setting the overall temperature of the ward more than 35°C will not be suitable for the staff treating with the patients while adjusting the temperature within the chamber is easily accessible and suitable for both; the patients and the staff. Fifthly to avoid the heat, airflow could easily be provided within the chamber instead of the whole ward. Sixthly, more chambers could be adjusted in a ward rather than the traditional beds and hence the shortage of wards and hospitals could be managed more easily.

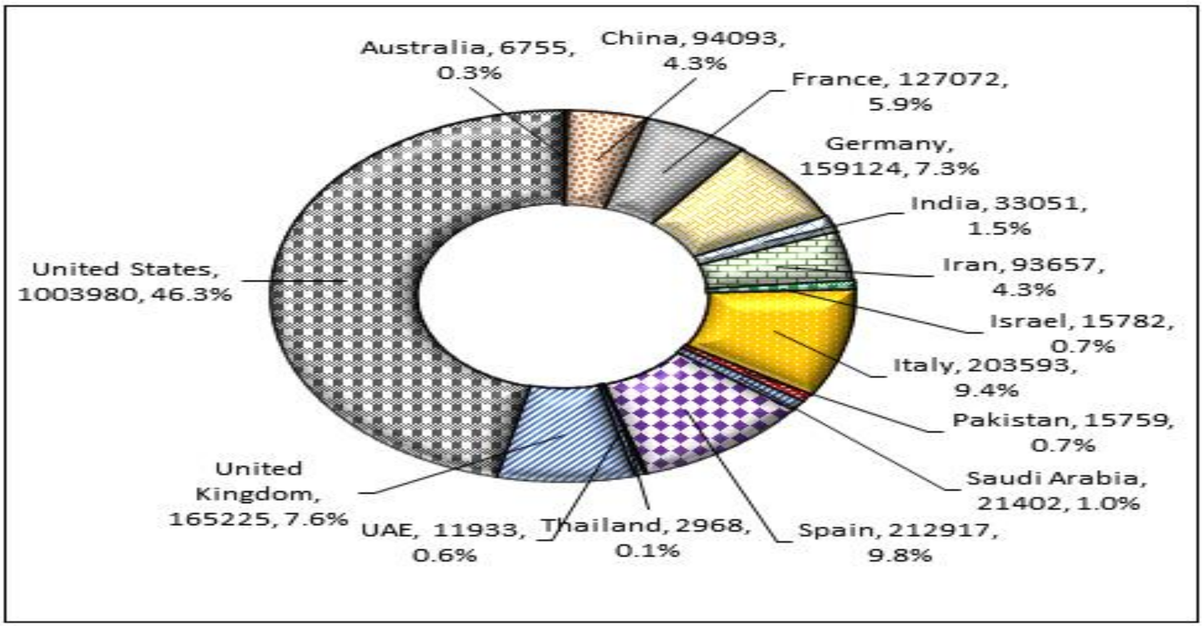

Fig. 3. Country wise total cases reported (January to April).

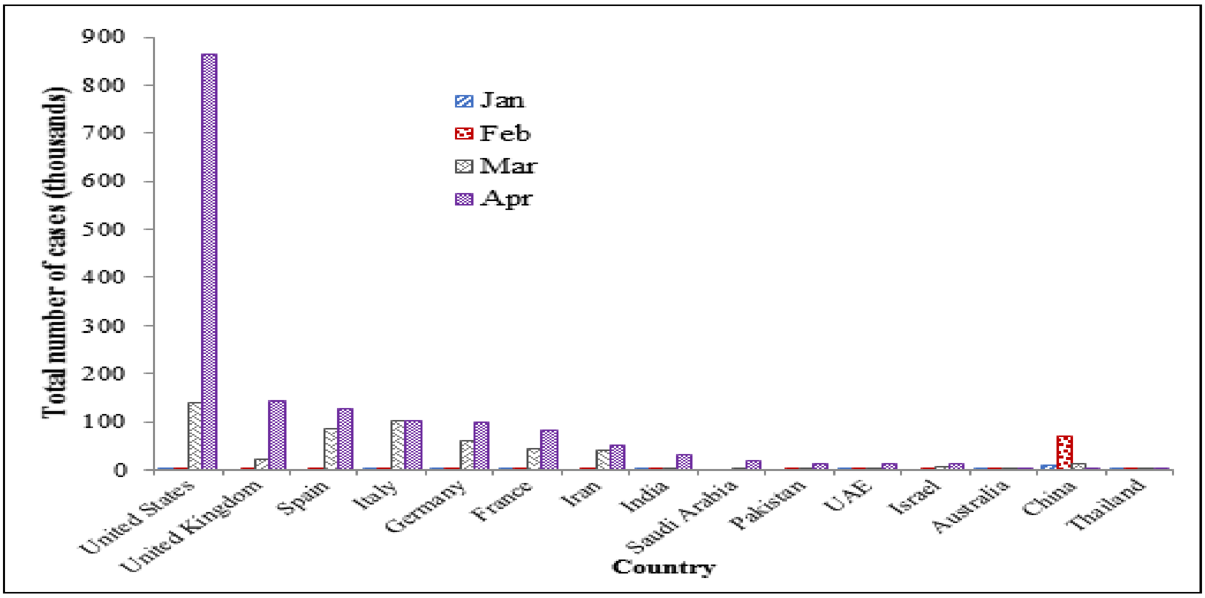

Fig. 4. Graphical representation of total number of cases per month among different countries.

The novel SARS-CoV-2 virus disintegrates among high temperatures. It disintegrates if heated for 15 minutes at 58°C or without heating above 65°C. Its lipid bilayer envelope disintegrates at high temperature, but, at the temperature of 38°C(K. H. Chan *et al.*), most of its activity is restricted due to the challenge of maintaining its structure which is going to be disintegrated due to the lipid bilayer. Providing temperature above 50°C to the patients for a long time is not possible, so a temperature of 35-40°C according to the physical conditions of the patient (age, gender, severity, etc.) and most preferably 38°C could be given to the patients in the specifically designed chambers which we call "COVID-19" chambers to cure rapidly. The activity of SARS-CoV-2 could be restricted above 95% Relative Humidity (K. H. Chan *et al.*) and UV of 254 nm, so providing the Relative Humidity of >95% in COVID-19 chambers as per the physical condition of the patient (age, gender, severity, etc.) could help out in the cure of the disease. Keeping in mind the necessities of a ventilator (Wang *et al.*, 2020), following is the model which could be modified accordingly for treating COVID-19 patients as per the above-mentioned requirements (Fig. 2).

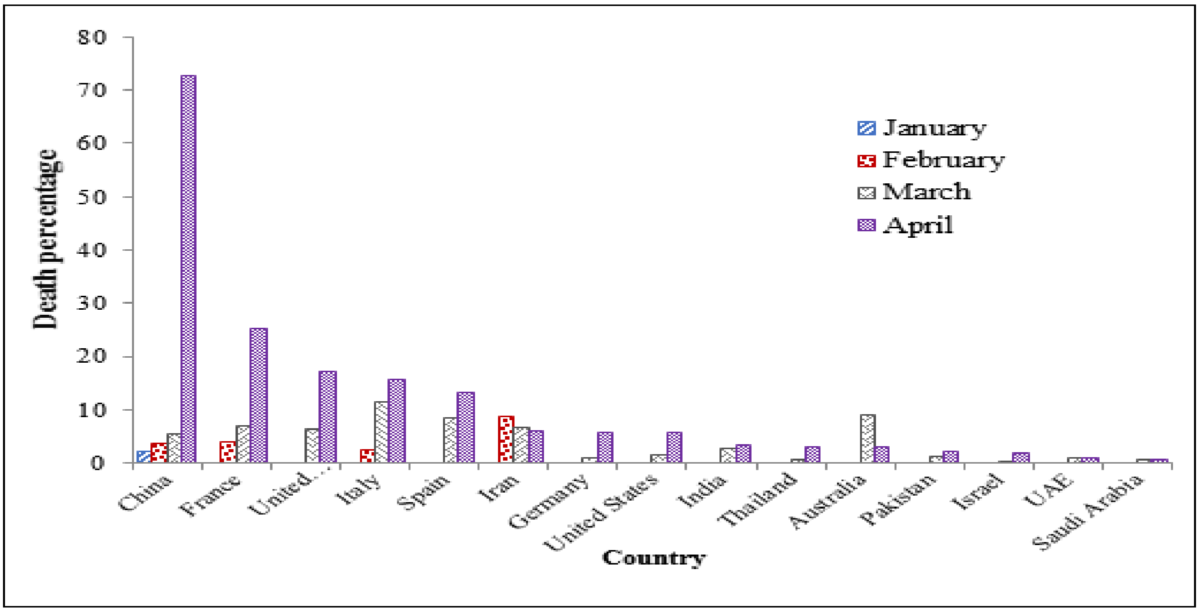

Fig. 5. Graphical representation of death percentage among different countries.

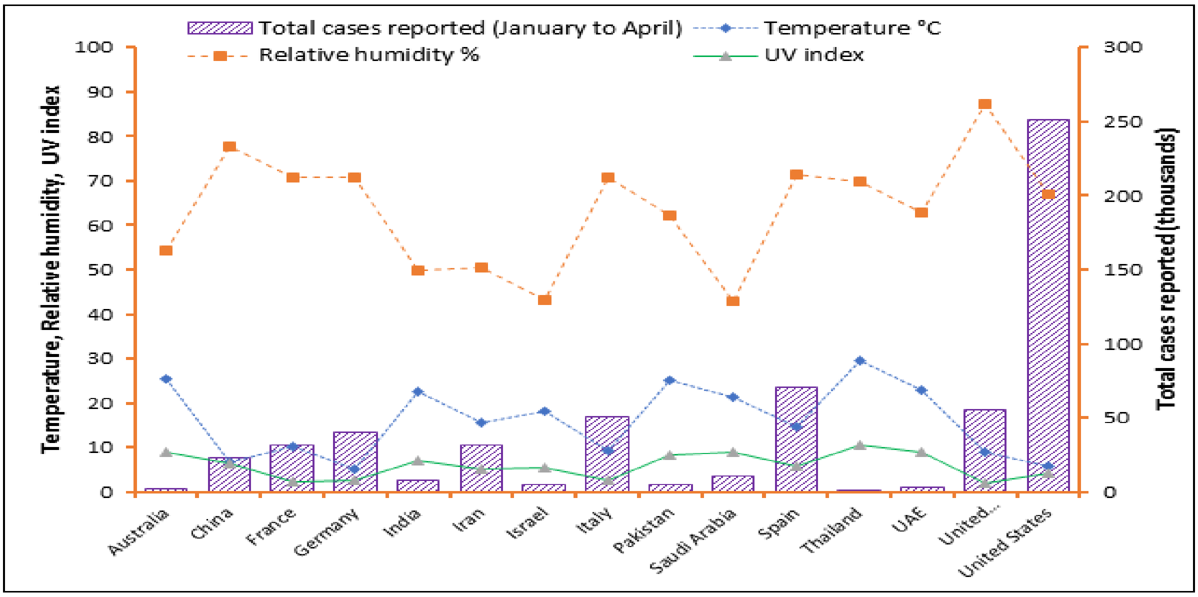

Fig. 6. Graphical representation of abiotic factors with total cases reported among different countries.

Design for the isolation centers

Isolation centers throughout the world have just been declared to some constructions without amendments. If some simple measures are maintained, then not only the expected patients will remain unaffected with the SARS-CoV-2 but also the positive patients of SARS-CoV-2 will be cured rapidly and further activity of the virus could be reduced. Firstly, the isolation centers must be declared to the hotel rooms or the rooms with the facility of the air conditioners with the option of heating mode.

Those air conditioners will be used to maintain the temperature between 35-40°C along with the airflow which will reduce the activity of SARS-CoV-2 to the minimum level. Secondly, the air conditioners could also be set to maintain the Relative Humidity of the room above 95% which will also help out in reducing the activity of the virus. Thirdly, the isolation rooms should also have at least one window directly towards the direction of the sun, as when the window will open, direct sunlight will enlighten the room as well as the patient. This sunlight will not only provide heat or high temperature but also a certain amount of UV which will help figure out SARS-CoV-2.

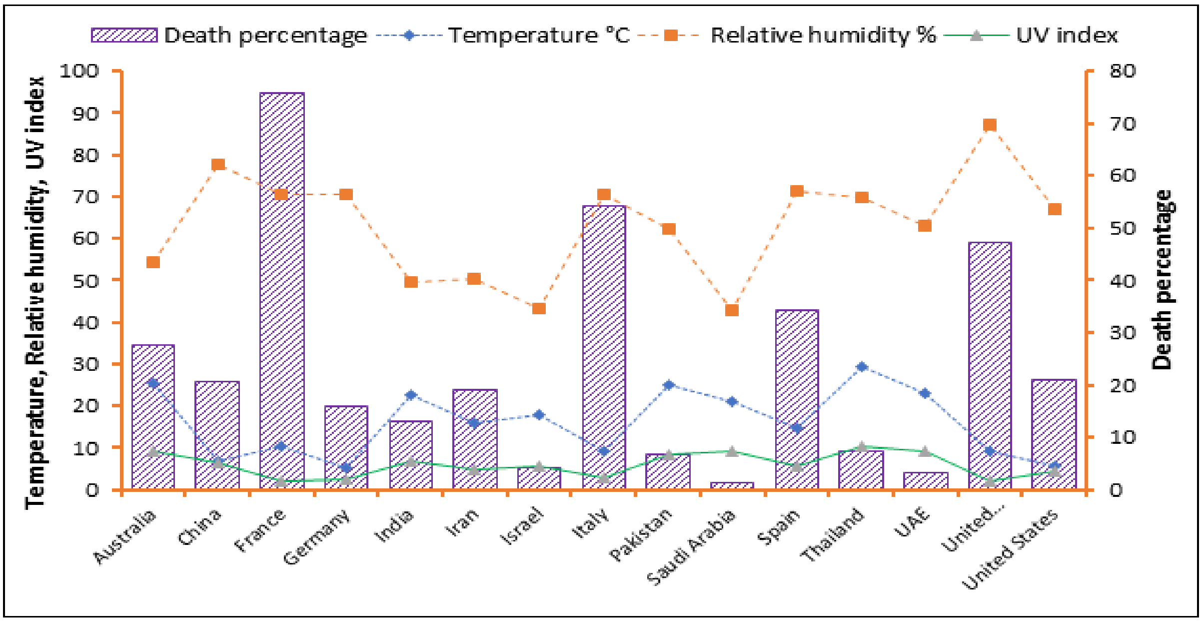

Fig. 7. Graphical representation of abiotic factors with death percentages of different countries.

The practice of keeping one patient in one room will also help out in reducing the spread of the virus. As the health conditions of all the persons are not alike, so, the patients with comparably good health conditions could be adjusted with high temperature while the patients with comparably bad health conditions could be adjusted accordingly because the patients with good physical health or less severe attack will be cured more rapidly than the others, otherwise, they could be affected more by the interaction with other patients having a severe attack.

Conclusion

From all over the discussion above, it is concluded that COVID-19 chambers with optimum adjustable abiotic factors should be prepared to disintegrate SARS-CoV-2 efficiently and quickly. Moreover, these chambers could not only be used for COVID-19 patients but also the patients of any contagious or viral disease.

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Declaration of Interest

None.

Conflicts of Interest

None.

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References

Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, Evans L. 2020. Covid-19 in critically ill patients in the Seattle region—case series. New England Journal of Medicine **382(21),** 2012-2022.

Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. 2020. Features, evaluation and treatment coronavirus (COVID-19) StatPearls [Internet]: StatPearls Publishing.

Chan JFW, Kok KH, Zhu Z, Chu H, To KK.-W., Yuan S, Yuen KY. 2020. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. Emerging microbes & infections, **9(1),** 221-236.

Chan KH, Peiris JSM, Lam SY, Poon LLM, Yuen KY, Seto WH. The Effects of Temperature and Relative Humidity on the Viability of the SARS Coronavirus. https://doi.org/10.1155/2011/734690

Currie D. 2012. National Public Health Week celebrated nationwide: Health departments, schools, communities hold events. The Nation's Health, **42(5),** 18-31.

Darnell MER, Subbarao K, Feinstone SM, Taylor DR. 2004. Inactivation of the coronavirus that induces severe acute respiratory syndrome, SARS-CoV. Journal of Virological Methods **121(1),** 85-91. https://doi.org/10.1016/j.jviromet.2004.06.006

Du L, Yang Y, Zhou Y, Lu L, Li F, Jiang S. 2017. MERS-CoV spike protein: a key target for antivirals. Expert opinion on therapeutic targets **21(2),** 131-143.

Gorbalenya A, Baker S, Baric R, de Groot R, Drosten C, Gulyaeva A, Neuman B. 2020. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nature Microbiology.

Gralinski LE, Menachery VD. 2020. Return of the Coronavirus: 2019-nCoV. Viruses **12(2),** 135.

Grossoehme NE, Li L, Keane SC, Liu P, Dann III CE, Leibowitz JL, Giedroc DP. 2009. Coronavirus N protein N-terminal domain (NTD) specifically binds the transcriptional regulatory sequence (TRS) and melts TRS-cTRS RNA duplexes. Journal of molecular biology **394(3),** 544-557.

Khan S, Siddique R, Ali A, Bai Q, Li Z, Li H,. Nabi G. 2020. The spread of novel coronavirus has created an alarming situation worldwide. Journal of infection and public health.

Letko MC, Munster V. 2020. Functional assessment of cell entry and receptor usage for lineage B β-coronaviruses, including 2019-nCoV. bioRxiv.

Menachery VD, Yount Jr, BL, Debbink K, Agnihothram S, Gralinski LE, Plante JA, Donaldson EF. 2015. A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence. Nature medicine **21(12),** 1508.

Organization WH. 2020a. Coronavirus disease 2019 (COVID-19): situation report, 92.

Organization WH. 2020b. Coronavirus disease 2019 (COVID-19): situation report, 72.

Raymondos K, Molitoris U, Capewell M, Sander B, Dieck T, Ahrens J, Corrado A. 2012. Negative- versus positive-pressure ventilation in intubated patients with acute respiratory distress syndrome. Critical Care **16(2),** R37. https://doi.org/10.1186/cc11216

Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. 2020. COVID-19 infection: origin, transmission, and characteristics of human coronaviruses. Journal of Advanced Research.

Tang B, Bragazzi NL, Li Q, Tang S, Xiao Y, Wu J. 2020. An updated estimation of the risk of transmission of the novel coronavirus (2019-nCov). Infectious disease modelling **5,** 248-255.

Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D. 2020. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. Cell.

Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Peng Z. 2020. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA, **323(11),** 1061-1069. https://doi.org/10.1001/jama.2020.1585

Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, Pei YY. 2020. A new coronavirus associated with human respiratory disease in China. Nature, **579(7798),** 265-269.

Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, Zhou Y. 2020. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. International Journal of Infectious Diseases.

Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Huang CL. 2020. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature **579(7798),** 270-273.

Zhou Y, Yang Y, Huang J, Jiang S, Du L. 2019. Advances in MERS-CoV vaccines and therapeutics based on the receptor-binding domain. Viruses, **11(1),** 60.