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Impact of Climate Variables on COVID-19 Pandemic in Asia: A Systematic Review

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Abstract

COVID-19 has become a global pandemic and threatens public health systems worldwide. Virus transmission can be influenced by several factors, one of which is climatic conditions. Temperature, humidity, precipitation, wind speed, and solar radiation play an important role in the transmission of infectious diseases and are variables that can determine the resistance of the SARS virus. This paper aimed to critically assess and provide evidence-based on the impact of climate variables on COVID-19 cases in Asia based on current knowledge to form the basis of guidelines for health care and prevention efforts. This systematic review used Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The articles were searched from ProQuest, Scopus, PubMed, and Springerlink databases. The reviewers had screened 2.784 abstracts, 103 full-text publications, and ultimately included 11 systematic reviews. The review found a consistently positive relationship between climate variables and COVID-19. Average temperature, maximum temperature, minimum temperature, and humidity (r = 0.83, 0.94, 0.93, 0.30) were significantly correlated with COVID-19 cases. Temperature, maximum humidity, and population density (adjusted R2 = 0.53, p<0.05), can be used as references in planning interventions during potential future pandemics. Linear regression framework, high humidity, and high temperature (p<0.05) significantly reduce the transmission of COVID-19. This systematic review shows that climate plays a role in the spread of the COVID-19 pandemic in Asia.

Keywords: climate change condition, COVID-19, humidity, precipitation, temperature

Introduction

Coronavirus Disease 2019 (COVID-19) has become a worldwide pandemic and threatens public health systems worldwide. There are many dynamics regarding the causative agent of COVID-19. Currently, SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) was determined to be the cause.¹ The COVID-19 is currently the third disease caused by the coronavirus transmitted from animals to humans. It was identified as a zoonotic coronavirus, similar to the SARS-CoV (Severe Acute Respiratory Syndrome Coronavirus) and MERS-CoV (the Middle East Respiratory Syndrome Coronavirus), which results in a severe respiratory syndrome after twenty years.^{2,3} As of August 31, 2020, a total of 24,854,140 confirmed cases were reported worldwide, with 838,924 deaths (CFR 3.4%) with cases reported in 216 countries/regions.⁴

Experts believe in the influence of seasons on viral epidemiology. Low temperature is the most optimal condition for viruses such as a respiratory syncytial virus (RSV), influenza virus, and human metapneumovirus (hMPV) to cause infection in humans. This season causes RSV and influenza cases to increase in winter, while hMPV cases occur most of the year and peak in winter and spring.⁵ The significant increase in the incidence of influenza at low temperatures and high humidity points to the potential impact of climatic conditions on the distribution and transmission of COVID-19, amid consideration of other non-climatic factors.^{6–9}

Climatic conditions are the essential factors that affect COVID-19 because they can be a direct cause of biological interactions between agents and humans. Climatic elements such as temperature, humidity, rainfall, wind speed, and sunlight are significant factors in disease transmission and are parameters that can determine the survival of the SARS virus.^{10–12} Therefore, this systematic review aimed to critically assess and provide evidence-based on the impact of climate variables on COVID-19 cases in Asia based on current knowledge to form the basis of guidelines for health care and preven-

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tion efforts.

Method

Search Strategy

For this review, articles were sourced from four science databases; ProQuest, Scopus, Pubmed, and Springerlink. The systematic review was adjusted using the PRISMA guidelines.¹³ The searching process utilized two main keywords, which include climate and COVID-19. The population was people diagnosed with COVID-19. The comparison was countries, study characteristics, climate variables, the outcome was COVID-19, and the type of research using qualitative methods.

The search **ProOuest:** strategy in climate AND covid-19 keywords. Full as text, peer review, the source is an academic journal, date of publication last 12 months, English language are included in the filter. In Scopus: TITLE-ABS-KEY climate AND covid-19 AND (LIMIT-TO (ACCESSTYPE(OA))) AND (LIMIT-TO(PUBYEAR, 2020)) AND (LIMIT- TO(DOCTYPE, "ar")). In Pubmed: (("climate"[All Fields]) AND ("covid-19"[All Fields]). Full text, type of article is a journal article, date of publication last one year, English language included filter. are in the The search strategy in Springerlink: climate AND covid-19 as a keyword.

Inclusion and Exclusion Criteria

All original articles in English, academic or research articles, ecological and time-series research, and the articles looking at the correlation between climate (temperature, humidity, precipitation, wind speed, and sunlight) and COVID-19 cases were included. The study about the relationship COVID-19 recovery rates, between climate and COVID-19 reproduction rates, and variables related to COVID-19 in addition to the number of cases, review articles, case reports, outbreak reports, and qualitative method were excluded.

Study Selection

Three reviewers selected the research based on the eligibility of the articles to be reviewed from the title, abstract, and full text. Three reviewers were selecting the articles based on their area of expertise.

Data Extraction

Data taken based on the conditions met, among

others, the author, the study period, the year of publication, the country carried out, the research design and research method, the research area, and the correlation between climate (temperature, humidity, precipitation, wind speed, and sunlight), and COVID-19 cases.

Data Synthesis

Data synthesis was carried out using narrative area included countries synthesis. The research in the Asian continent. The variables of climate reviewed were based on the local state meteorological and climatological agency. The number of COVID-19 cases was reviewed based on the diagnosis of COVID-19 cases recorded at the local state health department. To reduce the risk of bias, the three reviewers worked independently. It would be done through an online discussion process and reading all the selected articles if they have different opinions. The eligible articles were then analvzed qualitatively based the five variables: on temperature, humidity, precipitation, wind speed, sunlight exposure. The review and used а PRISMA guideline; a checklist has been carried out using the PRISMA Checklist 2020.

Results

The studies included in this review were 11 articles. From 11 studies, three studies were from India, two studies were from Turkey and Japan, and Bangladesh, Indonesia, Iran, China, and Gulf Countries each. The results were resumed in Table on studies reviewed, 1. Based temperature (average, minimum, maximum, ambient), humidity, wind speed, average precipitation, number sunny days with COVID-19. The Average of temperature was at 2 m (r = 0.83), maximum tempera-



Figure 1. Systematic Review Flowchart

Table 1. Journals in Review¹⁴⁻²⁴

Title	Author	Year of Publish	Variable	Analysis	Result	Suggestion
Correlation between weather and COVID- 19 pandemic in India: An empirical investigation	Prayas Sharma, Ashish Kumar Singh, Bharti Agrawal, Anukriti Sharma	2020	Temperature, Humidity	Pearson Product Moment Correlation Spearman's rank correlation	Minimum temperature (r = 0.93), maximum temperature (r = 0.94), average temperature (r = 0.83), and humidity (r = 0.30) were significantly correlated with cases of the COVID-19 pandemic with two-tailed 99% significance level.	The results of this study might use for further researchers in this field and formulate a policy in reducing the spread of COVID-19 in India.
Influence of Absolute Humidity, Temperature and Population Density on COVID-19 Spread and Decay Duration: Multi-Prefecture Study in Japan	Essam A. Rashed, Sachiko Kodera, Jose Gomez-Tames Akimas Hirata	2020	Population density, spread and decay duration, Maximum temperature, Absolute humidity	Rank correlation, A correlation matrix with partial correlation probabilities, Linear regression	Population density with social distance is one of the main factors influencing the distribution and damage pattern, with $R2 = 0.39$ (p < 0.05) and 0.42 (p < 0.05). Maximum humidity affected decay duration, which was normalized by population density ($R2 > 0.36$, p < 0.05). Based on multivariate analysis, it is known that the estimated duration of pandemic spread, maximum humidity, ambient temperature, and population density (adjusted $R2 = 0.53$, p-value < 0.05), is used to plan interventions during a potential future pandemic.	For similiar potential pandemics, especially a potential second wave COVID-19 pandemic, population density, spread and duration of decay, temperature, humidity should be considered, and multi- city comparisons to develop different protection policies.
The spread of COVID-19 virus through population density and wind in Turkey cities	Hamit Coşkun, Nazmiye Yıldırım, Samettin Gündüz	2020	Temperature, Humidity, Number of sunny days, Wind intensity	Regression analysis, Meditation analysis	Population density and wind are at risk of spreading the virus, with an estimated percentage of 94% Temperature, humidity, sun brightness, and air pollution did not affect the number of cases. The number of COVID-19 cases is affected by the influental population density and wind speed. The Sobel test showed a significant decrease (Sobel z=17.23, p=0.0001). There was a relationship between wind speed, density, and the case of COVID-19.	SARS-CoV-2, which is not visible in the air, spreads faster in windy weather, indicating that SARS-CoV-2 in the air is one factor that threatens humans with wind speeds that increase air circulation.
Association between temperature, humidity, and COVID-19 outbreaks in Bangladesh	Syed Emdadul Haque, Mosiur Rahman	2020	Temperature average, Humidity, Summer and rainy season	Linear regression test	The peak spread of COVID-19 occurred at an average temperature of 26 \circ C. A high temperature (p = 0.038) and high humidity (p = 0.005) significantly reduced COVID-19 transmission from the multiple linear regression results. This climate factor indicates that the hot season and rainy season in Bangladesh can reduce COVID-19 cases.	Social distancing as a community intervention aims to prevent the spread of the virus is still important. Further laboratory studies are needed to determine the mechanism.
Correlation between weather and COVID-19 pandemic in Jakarta, Indonesia	Ramadhan Tosepu, Joko Gunawan, Devi Savitry Effendy, La Ode Ali Imran Ahmad, Hariati Lestari, Hartati Bahar, Pitrah Asfian	2020	Minimum temperature, Maximum temperature, Temperature average, Humidity, Amount of rainfall	Spearman-rank correlation	Based on the analysis results, a significant relationship was found between the average temperature (°C) and COVID- 19 ($r = 0.392$; $p = 0.001$). Other variables such as minimum temperature, humidity, and rainfall were not significantly correlated with COVID-19.	The findings can be used as input for the government to reduce COVID-19 disease in Indonesia.
Investigation of effective effective climatology parameters on COVID-19 outbreak in Iran	Mohsen Ahmadi, Abbas Sharifi, Shadi Dorosti, Saei Jafarzadeh Ghoush Negar Ghanbari	2020 d chi,	Infected people with COVID-19, density, Intra-provincial movement, Infection days to end of the study period,	The Partial Corre- lation Coefficient (PCC), Sobol Jansen methods, Analyzing the effect and correlation of	The sensitivity analysis shows that population density, intra-provincial movement have a significant correlation with COVID-19. Areas with low humidity, wind	Researchers should pay attention to the presence of this type of virus every ten years by providing results based on previous experimen-

Table 1. Journals in Review¹⁴⁻²⁴

Title	Author	Year of Publish	Variable	Analysis	Result	Suggestion
			temperature, precipitation, Humidity, Wind speed, Average solar radiation	variables with the COVID-19 spreading rate	speed, and solar radiation can support the viability of the virus, causing high infection rates.	tal and observational studies and considering how these factors may affect the spread of COVID-19. In addition, a long-term study of the world's climate can anticipate the possibility of a similar pandemic occuring.
					Provinces with a high population density, intra-provincial movement, and high humidity levels in Tehran, Mazandaran, Alborz, Gilan, and Qom are more susceptible to infection.	
Impact of weather on COVID-19 pandemic in Turkey	Mehmet Şahin	2020	Temperature, Dew point, Humidity, Wind speed, Population	Spearman's correlation test	Temperature associated with the number of COVID-19 cases.	The results of this study can be a guide for authorities and decision- makers in taking specific steps for pandemic control
					on the day of the COVID-19 cases.	
					Wind speed correlates with COVID-19 cases.	1
					The population is a prominent indicator of determining or estimating COVID-19 cases.	g
Effect of temperature on the infectivity of COVID-19	Mugen Ujiiea, Shinya Tsuzukib, Norio Ohmagari	2020	Temperature, Number of COVID-19 cases	Poison regression analysis	The old-age dependency ratio, visitors arriving from China in January 2020, and the average temperature in February 2020 associated with the cumulative number of COVID-19 cases as of March 16, 2020	There may be a link between low temperatu- res and an increased risk of COVID-19 infection. Further evaluations will be carried out at the global level.
Effect of temperature and humidity on the dynamics of daily new cases and deaths due to COVID-19 the outbreak in Gulf countries in Middle East Region	S.A. Meo, A.A. Abukhalaf, A.A. Alomar, N.M. Alsalame, T. Al- khlaiwi, A.M. Usmani	2020	The mean temperature and humidity were recorded from the appearance of the first case of COVID-19 in the region. The ratio by which quantity overcomes itself overtime; it is the same as the daily cases divided by the cases on the previous day	The data were recorded and analyzed; Mean and Standard Error of Mean (SEM) were calculated. A correlation calculated between meteorological factors and daily new cases and deaths of COVID-19. The growth factor, in which the quantity beats itself over time, was calculated.	The daily basis mean temperature was 29.20±0.30°C, and humidity was 37.95±4.40%.	These findings can be used to reference policy makers and health officials based on the epidemiological trends of the impact of temperature and humidity of daily new cases and deaths from COVID-19.
					There was a negative correlation in the number of daily cases and deaths with the increase of the humidity in Oman, Kuwait, Qatar, Bahrain, United Arab Emirates, and Saudi Arabia.	
					There was a correlation between increasing the temperature and the increase in daily cases and deaths due to COVID-19.	
					The growth factor result for daily cases were 1.09±0.00, and daily deaths were 1.07±0.03 for COVID-19. This result showed the declining trends in the GCC region.	
Association of Environmental Parameters with COVID-19 in Delhi, India	Nikhilesh Ladha, Pankaj Bhardwaj, Jaykaran Charan, Prasenjit Mitra, Jagdish Prasad Goyal, Praveen Sharma, Kuldeep Singh, Sanjeev Misra	2020	The number of tests, temperature, relative humidity on the number of COVID-19	Daily maximum temperature, mean temperature, and average relative humidity data were entered into excel and cross-checked. Then a linear regression test was performed to model the data using SPSS 21.	This model was significantly able to predict the number of COVID-19 cases, F (4.56) = 1213.61, p = 0.001, with a value of 99.4% of the variation of COVID-19 cases with adjusted R2 = 98.8%. Maximum temperature, temperature, and average relative humidity did not show statistically significance.	This research indicates that the COVID-19 , pandemic may not be suppressed by increasing temperatures and humidity. However, it is critical to increase testing capacity to achieve epidemiological understanding and guide policy determination for COVID-19.

Table 1. Journals in Review¹⁴⁻²⁴

Title	Author	Year of Publish	Variable	Analysis	Result	Suggestion
Significance of geographical factors to the COVID-19 outbreak in India	Amitesh Gup, Sreejita Banerjee, Sumit Das	2020	Air temperature, Rainfall, Actual evapotranspirator ion, Solar radiation Specific humidity, Wind speed with topographic altitude, The population density at the local level to investigate the spatial relationship with the number of COVID-19 infections	Pearson product- moment correlation Partial least square regression Generalized additive model	The spatial distribution of COVID-19 cases in India shows that maximum transmission occurs in countries with fewer wet conditions. However, provinces with the wet and very wet categories were less likely to be infected by the transmission. The bivariate analysis found no significant relationship with the number of infected cases in 36 provinces in India. The Variable Importance Projection (VIP) through the Partial Least Square (PLS) technique signifies the higher importance of SR, T, R, and AET. However, a general additive model that is equipped with the log transformation values input variables and applying spline fix to PD and E, there is a very high prediction accuracy (R2 = 0.89); therefore, there is a well-explained complex heterogeneity among parameter associations in the region with COVID-19 cases in India.	The positive relationship with SR and temperature and the negative relationship with humidity and rainfall indicate that areas with high temperatu- re and arid in lowland areas are advised to be more stringent in following up on emergency precautions.

ture at 2 m (r = 0.94), minimum temperature at 2 m (r =(0.93), and humidity at 2 m (r = (0.30)) were significantly correlated with cases of the COVID-19 pandemic with two-tailed 99% significance level. Ambient temperature, maximum absolute humidity, and population density (adjusted R2 = 0.53, p-value<0.05), proved useful for planning interventions during potential future pandemics, including the second COVID-19 outbreak. Average temperature (°C) correlated significantly with the COVID-19 pandemic (r = 0.392; p < 0.01). Linear regression framework, high humidity (p = 0.005) and high temperature (p = 0.038) significantly reduce the transmission of COVID-19. These results show that the arrival of the hot summer and rainy season in Bangladesh can effectively reduce the transmission of COVID-19. In Iran, regions with low wind speed values, average precipitation, humidity, and solar radiation exposure to a high infection rate support the virus's survival.

Discussion

Temperature In the studie

In the studies reviewed, the temperature was significantly associated with the incidence of daily COVID-19 with and without time lag. Therefore, it was concluded that temperature drives the spatial and temporal correlation of the COVID-19 outbreak in China. It should be considered the optimal climate predictor for the incidence of COVID-19.²⁵ Several flu viruses that occur in northern states are caused by flu viruses of the same family type. This flu has a cyclic pattern of events known

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as "flu season." The flu virus was widespread during fall and winter and reached its peak between December and May.²⁶ Worldwide, cases of human morbidity and mortality from COVID-19 continue to increase in the "flu season," but COVID-19 was not the flu. Data obtained from the China National Meteorological Center and the Hong Kong Observatory, China, shows that the COVID-19 outbreak occurred during winter, similar to the previous SARS epidemic outbreak.⁹

Research conducted in 122 cities in China found a significant relationship between average temperature and the number of positive cases of COVID-19.²⁷ Also, the relationship between temperature and COVID-19 covering all countries affected by COVID-19, showed the result of an increase in daily temperature by an average of one degree Fahrenheit reduced the number of cases by about 6.4 cases/day. There is a negative correlation between the average temperature per country and the number of SARS-CoV-2 infection cases. This association remains strong even incorporating additional variables and controls (maximum temperature, average temperature, minimum temperature, and precipitation) and fixed state effects.¹⁰

The study explained that temperature was significantly associated with daily COVID-19 incidence with and without lag time. In addition, the researchers also found that the rate of transmission decreased as the temperature increased and that the increase in temperature contributed to a further decrease in infection rates and outbreak size. Therefore, it is concluded that temperature drives the spatial and temporal correlation of the COVID-19 outbreak in China and should be considered as the optimal climate predictor for the incidence of COVID-19.²⁵ A research conducted by Bashir *et al.* (2020) in New York, USA, confirms that there are significant results between the mean temperature and the total cases and deaths from COVID-19.²⁸ **Humidity**

High humidity, associated with low temperature, is an essential factor in influenza virus transmission, either by maintaining virulence or weakening the host by cooling the body or drying out the respiratory tract.²⁹ The literature shows that SARS-CoV transmission is similar to the influenza virus in terms of climate fluctuations.³⁰ The relationship between humidity and COVID-19 cases can be proven by the research conducted by Liu et al. (2020) in 30 provincial capitals in China that show a statistically significant relationship between absolute humidity and the number of COVID-19 cases. In addition. the association increased with the accumulated time duration up to 14 days. The study concluded that meteorological factors, particularly absolute humidity, played an independent role in the transmission of COVID-19 after controlling for population migration. Local weather conditions with low temperatures, mild diurnal temperature ranges, and low humidity tend to favor transmission.³¹

A similar study was conducted by Oliveiros et al. (2020) in 31 provinces in Mainland China, whose results show that humidity has a negative correlation with the doubling time of COVID-19 cases. This result means that, when humidity is low, the doubling time of COVID-19 cases will be longer, so the rate of progression of COVID-19 is expected to be slower. However, humidity and temperature variables only contributed up to a maximum of 18% of the variation. comparison, In the remaining 82% was related to other factors such as controlling population mobilization, public health policies, population density, transportation, and cultural aspects.8

Precipitation

Precipitation was one of the climatic factors which seem to be an essential factor to consider. Based on research conducted by Sobralet al. (2020), covering all countries affected by COVID-19 showed a positive correlation between precipitation and transmission of SARS-CoV-2. Countries with higher rainfall measurements show increase disease an in transmission. For every inch of increase in mean/day rainfall, there was an increase of 56.01 cases/day.¹⁰

In contrast to research conducted by Menebo (2020) which examined the relationship between temperature and precipitation with daily new cases of COVID-19 in Norway, it was shown that among the seven weather variables studied, maximum temperature and the normal

temperature had а positive and significant correlation with COVID-19. On the other hand, the rainfall measured at 7.00 a.m. has a negative and significant correlation with COVID-19, which means that the higher the rainfall, the lower the cases of COVID-19. Various arguments can be given for the negative relationship between rainfall and new cases. One of them was the hypothesis that people will avoid going out if it rains. On the other hand, people are more prone to breaking the 'stay at home' rule when the sun is shining outside, thus becoming exposed to the virus.³²

Wind Speed

The wind was implied as a critical climatic factor for the transmission of COVID-19. However, studies on this factor were still minimal.³³ Based on research conducted by Rosario *et al.* (2020), who conducted a study on the relationship between weather and COVID-19 cases in tropical countries showed that wind speed had a negative correlation (p<0.01). Therefore, high temperatures and wind speed were potential factors to reduce the spread of COVID-19.³⁴

Research conducted by Coşkun *et al.* (2020) has had a different result. Research conducted by collecting climate values (temperature, humidity, number of sunny days, wind intensity) from 81 provinces in Turkey in March 2020 shows that population density and wind effectively spread the virus. These two factors explain 94% of the variance in the spreading virus. In addition, population density mediates the effect of wind speed (9%) on the number of COVID-19 cases. The finding that the invisible COVID-19 virus in the air spreads more in windy weather suggests that airborne viruses threaten humans with wind speeds that increase air circulation.¹⁶

Sunlight Exposure

The results of research conducted by Rosario *et al.* (2020) in Rio de Janeiro, Brazil, showed a strong negative correlation between solar radiation and the incidence of COVID-19 (r = 0.609, p < 0.01). This result means that high solar radiation can reduce the incidence of COVID-19.³⁴ This research is in line with the study conducted by Ratnesar-Sumate *et al.* (2020), who proved that sunlight could kill SARS-CoV-2 on the surface. This study also demonstrated the effectiveness of natural sunlight as a disinfectant for contaminated non-permeable surfaces.¹¹

Based on research conducted by Asyary and Veruswati (2020), it was found that a higher duration of sunlight exposure was also associated with more case recovery from COVID-19 in patients. Sunlight can maintain the health condition of COVID-19 patients so that they have a chance to recover. Sunlight boosted the immune system, which slows down the development of influenza and SARS agents in the human body.^{35,36}

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Limitations

This systematic review had some limitations. There were only 11 articles that met the inclusion criteria, and most of the articles did not examine the climate element thoroughly, thus affecting the results of the analysis. Due to the lack of controlled studies, a meta-analysis was not performed. This study could only see the relationship/ correlation and did not analyze the causal relationship. In addition, this study used secondary data so that the level of bias is less controllable.

Conclusion

This systematic review found a positive association between temperature (average, minimum, maximum, ambient), humidity, wind speed, average precipitation, number of sunny days with COVID-19. This systematic review shows that climate plays a role in the spread of the COVID-19 pandemic in Asia. The results of this review might be used as a reference for researchers to conduct further research. In addition, it can also be used as input for policymakers as a reference for the preparation of the COVID-19 pandemic prevention program.

Abbreviations

AET: Actual Evapotranspiration; T: Temperature; COVID-19: coronavirus disease 2019; hMPV: Human Metapneumovirus; MERS-CoV: Middle East Respiratory Syndrome Coronavirus; PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analyses; PCC: Partial Correlation Coefficient; PLS: Partial Least Square; PD: Population Density; R: Rainfall; RSV: Respiratory Syncytial Virus; SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; SR: Solar Radiation; SH: Specific Humidity; SEM: Standard Error of Mean; VIP: Variable Importance Projection; WS: Wind Speed.

Ethics Approval and Consent to Participate

This study was approved by the Research and Community Engagement Ethical Committee, Faculty of Public Health, Universitas Indonesia, No. 210/UN2.F10.D11/PPM.00.02/2021.

Competing Interest

The authors declare that there is no competing interest.

Availability of Data and Materials

For this review, articles were sourced from four science databases: ProQuest, Scopus, Pubmed, and Springerlink.

Reporting Guidelines

The PRISMA Flowchart has a temporary link https://doi.org/10.6084/m9.figshare.14977866.v1³⁷ and the PRISMA Checklist in the link https://doi.otg/10.6084/m9.figshare.14977926.³⁸

Authors' Contribution

DS contributed substantially to the concept, work design, acquisition of the funding, and submitting the reporting guidelines to Figshare.com. YAS conducted data analysis, data interpretation, and drafting of the manuscript. VYS revised it critically for the important intellectual content of YAS, DS, and final approval of the version to be published.

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