Spatiotemporal analysis of environmental and physiographic factors related to malaria in Bareilly district, India

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ABSTRACT

Objectives: The aim of this study was to explore the spatiotemporal clustering of reported malaria cases and to study the effects of various environmental and physiographic factors on malaria incidence in Bareilly district, Uttar Pradesh, India.

Methods: Malaria surveillance data were collected from the state health department and cleaned into an analyzable format. These data were analyzed along with meteorological, physiographic, and 2019 population data, which were obtained from the Indian Meteorological Department, National Aeronautics and Space Administration web portal, the Bhuvan platform of the Indian Space Research Organization, and the 2011 Census of India.

Results: In total, 46,717 malaria cases were reported in Bareilly district in 2019, of which 25.99% were Plasmodium vivax cases and 74.01% were P. falciparum cases. The reported malaria cases in the district showed clustering, with significant spatial autocorrelation (Moran’s I value = 0.63), and space-time clustering (p < 0.01). A significant positive correlation was found between monthly malaria incidence and the monthly mean temperature (with a lag of 1–2 months) and rainfall (with a lag of 1 month). A significant negative correlation was detected between the elevation of blocks (i.e., intermediate-level administrative districts) and annual malaria reporting.

Conclusion: The presence of space-time clustering of malaria cases and its correlation with meteorological and physiographic factors indicate that routine spatial analysis of the surveillance data could help control and manage malaria outbreaks in the district.

Keywords: Cluster analysis; Geographical information systems; Malaria; Meteorological; Spatiotemporal; Surveillance
Introduction

Malaria, which is caused by mosquito bites, is among the most severe and fatal diseases worldwide. The disease is caused by a parasite that is transmitted to humans from infected female *Anopheles* mosquitoes. Various parasite species cause malarial infection, but *Plasmodium falciparum* and *P. vivax* are common organisms that cause the most severe cases of malaria. In particular, *P. falciparum* is the deadliest species.

Malaria is highly prevalent in poor tropical and subtropical areas worldwide, where it is known to be a major cause of mortality and illness. The most susceptible groups to malaria are young children and pregnant women [1]. The global burden of malaria in 2018 was estimated at 228 million cases and 405,000 deaths. *P. falciparum* cases accounted for 50% of estimated cases in the southeast Asian region, causing 8 million cases and 11,600 deaths [2].

In the Indian context, the National Vector Borne Disease Control Program reports from 2018 and 2019 showed that the total number of malaria cases in 2018 was 429,928, with 96 deaths. Similarly, there were 339,494 malaria cases in 2019 with 77 deaths, and the highest numbers of malaria cases were seen in Uttar Pradesh, Chhattisgarh, Jharkhand, Gujarat, Meghalaya, Odisha, and West Bengal [3]. The numbers of reported cases in Uttar Pradesh in 2018 and 2019 were 86,486 and 92,732, respectively, and Bareilly district had an annual parasitical incidence (API) of 7.32 per 1,000 population according to the 2018 report [3]. Bareilly district shares boundaries with Pilibhit and Shahjahanpur on the eastern side, Rampur on the western side, Badaun on the southern side, and Udham Singh Nagar (Uttarakhand) on the northern side, and it contains 2.23% of the total population of Uttar Pradesh. *P. falciparum*, which causes the deadliest malaria infections, accounted for 46.49% of the cases in Bareilly district in 2018 [3]. In 2018, Uttar Pradesh state was classified as category 2, meaning that the overall state has an API under 1 per 1,000 population, but multiple districts of the state have APIs of more than 1. In Uttar Pradesh, 3 districts have an API of more than 1, and Bareilly district had the highest API. The National Framework for Malaria Elimination in India 2016–2030 set a goal to eliminate malaria throughout the country by 2030 and reduce malaria incidence to an API of less than 1 by 2024.

This study will provide useful data for predicting malaria outbreaks so that malaria control activities and resource allocation can be planned early. Routine monitoring and surveillance for malaria will reduce the transmission of malaria. In geographical information system (GIS)-based studies, geo-coded data are captured, stored, analyzed, retrieved, and depicted for analysis and planning in healthcare. Although some studies using GIS have been conducted in northern Uttar Pradesh [4], no GIS-based research has been conducted previously in Bareilly district; therefore, the present study will improve the surveillance quality of the district. GIS technology was used to perform malaria mapping, identify associations between malaria incidence and environmental factors, locate malaria hotspots. Geospatial analysis was used to point out different regions of the map within a defined area. The aim of the study was to explore the spatiotemporal clustering of reported malaria cases in Bareilly district and to study the effect of environmental and physiographic factors on malaria incidence in 2019. As mentioned above, the API of Bareilly district was 7.32 per 1,000 population in 2018, and *P. falciparum* accounted for 46.49% [3]; these data indicate a critical problem, so this study will be helpful for predicting malaria outbreaks and planning malaria control activities and resource allocation in advance.

Materials and Methods

The study was conducted in Bareilly district, which belongs to Uttar Pradesh, as shown in Figure 1. Bareilly district is located between latitudes 28°10’ to 28°54’ N and longitudes 78°58’ to 79°47’ E. The total area of Bareilly district is 4,120 km², with a population of 4,448,359 as per the 2011 census of India. Bareilly is divided into 6 *tehsils* (townships), namely Bareilly, Aonla, Baheri, Faridpur, Meerganj, Nawabganj. Bareilly have 17 block *panchayats* (intermediate-level councils) and 1,007 *gram panchayats* (village councils) in the district. The total number of community health centers (CHCs) is 15. The climate of Bareilly district is mainly humid subtropical. In May and June, the warmest months, the temperature fluctuates between 30°C and 40°C, while from September to January, the temperature goes down and fluctuates between 8°C and 15°C. January is considered the coolest month in Bareilly district, while July and August are considered monsoon months. The main river that flows from the west to southeast region of the district is the Ramganga. The northern area of Bareilly, which shares a border with Uttarakhand state, has a higher elevation than other regions. Sugarcane, cereals, cotton and wood are the main products of Bareilly district. Annual surveillance data of reported malaria cases at the block level are collected by the District Malaria Office at the district hospital of Bareilly. On a monthly basis, block-wise incidence data of reported malaria cases are collected from by the District Malaria Office at the district hospital of Bareilly. Lists of reported malaria cases at the village level in 2019 were collected by
block CHCs of Bareilly district. Daily meteorological data for 2019 of Bareilly district on temperature and rainfall were bought from the Indian Meteorological Department (regional center: Lucknow, Uttar Pradesh) for research purposes. Daily meteorological parameters at the block level for 2019 were collected by MERRA-2 (Modern-Era Retrospective Analysis for Research and Applications, version 2) from the National Aeronautics and Space Administration (NASA). Data on the normalized difference vegetation index (NDVI) for Bareilly district were collected from the Bhuvan geo-platform of the Indian Space Research Organization (ISRO), with a spatial resolution of 8 km and a radiometric resolution of 8 bits per pixel [5]. Elevation data for Bareilly district were collected from the NASA earth science data portal. Village and block-level population data and area data were obtained from the 2011 Census of India. Simple linear growth was assumed for projections of the population density in 2019 [6]. The Uttar Pradesh village-level shape file was downloaded from the Socioeconomic Data and Application Centre of the NASA web portal. The Uttar Pradesh administrative and block-level shapefile for Bareilly district was collected from the geospatial resources at Achutha Menon Centre for Health Science Studies at our institute. Choropleth mapping was done for the block level shapefile of Bareilly district using the latitude and longitude coordinates from the shapefile for each block. Maps were created for malaria indicators, such as the API, the annual falciparum incidence (AFI), slide positivity rate (SPR), the annual blood examination rate (ABER), and the percentage of P. falciparum cases (Pf%). Maps of the population density and literacy rate of Bareilly district were also created. R software (https://www.r-project.org/) version R-4.0.3 was used for data cleaning and analysis of secondary data, to extract the Bareilly district shape file for the block and village level, and to extract daily meteorological parameters at the block level for 2019 using the centroid of each block.
Latitude and longitude finder software was used to convert centroid coordinates values into the decimal format using an online resource (https://www.latlong.net/). R software was used to perform a spatial autocorrelation analysis, and both global and local measures were analyzed. The Moran's I-test was used to analyze spatial autocorrelation. The global Moran's I estimation was done to test the null hypothesis that there would be complete spatial randomness (CSR) of malaria prevalence in the whole area of Bareilly district. The range of Moran’s I is between −1 and +1, with a value close to 0 meaning that there is CSR, a positive value showing positive spatial autocorrelation, and a negative value showing negative spatial autocorrelation [7]. Moran’s I lags were also analyzed to study the range of autocorrelation. To identify hotspot areas at the local level, the local indicator of spatial association (LISA) model was used to evaluate the existence of clusters in the spatial arrangement by using a neighbors list based on regions with contiguous boundaries (i.e., sharing 1 or more boundary points). To evaluate the significance of the Moran’s I value, the Monte-Carlo permutation test was performed with the hypothesis that the malaria prevalence in Bareilly district is spatially random. A cluster map was also produced with local Moran’s I estimates, the Getis Ord Gi* statistic, which were categorized as high-high, low-low, high-low, and low-high. A high-high cluster means that there is a higher incidence of malaria in neighboring regions, whereas a low-low cluster means there is a low incidence of malaria in neighboring regions. Both high-low and low-high clusters were observed as outliers. The permutation test was done to check the significance level of the Moran’s I-test (i.e., to check whether spatial autocorrelation was significant). The associations between meteorological factors and malaria incidence were analyzed using monthly means of temperature and rainfall and the total number of malaria cases for each month. Pearson correlation analysis was performed at the block level. The total number of blocks was 17, so 34 Pearson correlation tests were performed for associations: 17 tests to check the association of monthly average temperature with monthly total malaria cases, as well as 17 tests for associations of monthly rainfall with total monthly cases of malaria. Raster data and metadata were obtained from the ISRO Bhuvan portal. Half-monthly data were available, and the total number of files downloaded was 24 for 2019. For analysis, data were aggregated quarterly. Using the R software, the average values for the NDVI index were obtained. NDVI values lie between −1 to +1, with values near +1 indicating high vegetation. Using the R software, the components of NDVI were determined using the average values at the block level. The components of the NDVI extracted were grass/cropland, forest, and agroforestry. The grass/cropland values ranged from 0.20579 to 0.37035; similarly, the agroforestry values lay between 0.37036 and 0.51073 [8]. Pearson correlation tests were performed using data categorized at quarterly intervals for NDVI components individually and relative to the corresponding reported malaria cases. For elevation data, 5 tiles of raster files covering the extent of Bareilly district coordinates were downloaded in the TIFF format. All raster files were merged, the shapefile of Bareilly district was overlaid with raster data, and the average mean elevation of each block of Bareilly district was estimated using the R software. The average elevation data were combined with the reported malaria data.

IRB/IACUC Approval
Ethical clearance for the study was provided by the Institutional Ethical Committee of Sree Chitra Institute of Medical Sciences and Technology (SCIMIT), Thiruvananthapuram (IEC No: IEC /1581 on November 20, 2020).

Results
The total number of reported malaria cases for 2019 was 46,717, out of which 25.99% were P. falciparum and 74.01% were P. vivax cases. Slightly more than half (52.3%) of total cases were in male inhabitants, and 47.7% were in female residents of the district. The distribution of cases by age, as determined using line list data, was as follows: 23.7% of cases were under 10 years of age, 38.8% of cases were 11 to 24 years of age, 23.8% of cases were 25 to 49 years of age, 6.41% of cases were 50 to 63 years of age, and 1.2% of cases were ≥64 years of age. The largest proportion of cases was found in the age category of 11 to 24 years.

Figure 2 shows the block level distribution of the number of reported malaria cases. There were more cases in the southern block than in other regions. Table 1 gives the epidemiological profile of the reported cases of malaria. Figure 2 shows the occurrence rate of reported malaria cases per 1,000 population at the block level, revealing that Majhgawan, Bhamora, Aonla, and Ramnagar blocks had higher incidence rates than other blocks. Figure 3 presents a choropleth map showing the distribution of the API at the block level; blocks situated in the southern region of the district had APIs between 40–60, for which reason they can be considered higher-transmission areas. The choropleth map for Pf% at the block level indicates that the Pf% was higher in the blocks situated in the southern region than in other blocks, meaning that the risk of malaria from P. falciparum was higher (Figure 3). The choropleth map in
Figure 3 shows that the AFI was higher among the blocks situated in the southern and western regions. Mainly in the southern region, many blocks had AFIs >20, indicating a higher transmission of *P. falciparum* cases and showed similar trends for slide falciparum rate (SFR), indicating that the southern region blocks had higher SFRs than other regions (Figure 3). In Figure 4, the choropleth map shows that the SPR in blocks situated in the southern region was higher than in other regions. Figure 4 also shows that the ABER was >10% in Majhgawan, Bhamora, and Aonla blocks, which lie in the southern region of Bareilly district, whereas other blocks had ABER values <10%, which is a concern.

Spatial autocorrelation estimates are done to explore the geographical clustering of data. The global Moran’s I performed for the data found an autocorrelation of 0.630, which was significant at the level of <0.001. Figure 5 shows a Moran’s I scatter plot with high-high clusters in the upper right column and low-low clusters in the lower left column. The significant high-high clusters were mainly present in the southern region of Bareilly district. An analysis at the block level showed clusters in the Majhgawan, Bhamora, Aonla, and Ramnagar blocks. The blocks shaded in red in Figure 5 are hotspot areas. The darkness of the colours represents the intensity of the Getis Ord Gi* statistic values, which is the indicator of LISA. A cluster analysis was conducted using line list data, and the villages that formed the primary clusters are shown on the map.

In the Pearson correlation analysis, a significant positive relationship was found between monthly rainfall and monthly malaria incidence with a 1-month lag in most blocks (p<0.01), as shown in Table 2. High-malaria-burden blocks (mainly Majhgawan, Aonla, and Ramnagar) showed a very strong association between monthly malaria incidence and monthly rainfall with a 1-month lag, as shown in Table 2. Similarly, Table 3 indicates that the 3 blocks (Majhgawan, Bhamora, and Aonla) that accounted for more than 50% of all cases showed a high correlation between the monthly mean temperature and monthly malaria incidence with a lag of 2 months. The peak burden of malaria cases in 2019 was mainly reported in August to October, just after the monsoon rainfall. The maximum rainfall occurred from July to August in 2019.

The Pearson correlation test was carried out to determine

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**Table 1.** Epidemiological indicators of malaria incidence in Bareilly district in 2019 (based on line list data collected from Bareilly district)

| Parameter                              | Value     |
|----------------------------------------|-----------|
| Population                             | 5,007,329 |
| Blood samples+rapid diagnostic test    | 294,432   |
| Total positives                        | 46,717    |
| Pf%                                    | 25.99     |
| Pv%                                    | 74.01     |
| Annual blood examination rate%         | 5.88      |
| Annual parasital incidence             | 9.3297    |
| Slide positivity rate                  | 15.9      |
| Slide falciparum rate                  | 4.124     |
| Annual falciparum incidence            | 2.42      |

Pf%, percentage of cases caused by *Plasmodium falciparum*; Pv%, percentage of cases caused by *P. vivax*.

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**Figure 2.** Choropleth map showing the distribution of annual reported malaria cases and incidence rate of malaria cases in Bareilly district 2019.

**Figure 3.** shows the AFI was higher among the blocks situated in the southern and western regions. Mainly in the southern region, many blocks had AFIs >20, indicating a higher transmission of *P. falciparum* cases and showed similar trends for slide falciparum rate (SFR), indicating that the southern region blocks had higher SFRs than other regions (Figure 3). In Figure 4, the choropleth map shows that the SPR in blocks situated in the southern region was higher than in other regions. Figure 4 also shows that the ABER was >10% in Majhgawan, Bhamora, and Aonla blocks, which lie in the southern region of Bareilly district, whereas other blocks had ABER values <10%, which is a concern.

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The Pearson correlation test was carried out to determine
the statistical significance of the relationship between the mean elevation of blocks in Bareilly district and the reported malaria incidence. A negative correlation (−0.494) was found between the mean elevation of blocks in Bareilly district and block-level malaria incidence ($p < 0.05$). The Pearson correlation test was also used to evaluate the association of the quarterly mean NDVI value and quarterly malaria incidence, and the average correlation was 0.36. The correlation analysis between monthly rainfall and monthly cases showed a strong and significant association with a lag of 1 month, with coefficients lying between 0.61−0.80.

**Discussion**

The study explored the spatial distribution of the reported malaria cases in Bareilly district in 2019 to identify hotspot areas. The malaria burden increased to 46,717 cases in 2019 from 37,387 cases in 2018. Significant positive spatial autocorrelation was found (0.63), showing that malaria incidence was clustered. Space-time clusters were mainly found in the southern and southwest regions covering 3 blocks of Bareilly district (Majhgawan, Bhamora, and Aonla). This information will be useful for the surveillance unit of the district as monitoring activities and surveillance can be strengthened in hotspots to prevent further outbreaks. Disease control activities and awareness programs regarding malaria should be increased.

The malaria burden in Bareilly district increased from 2018 to 2019. *P. vivax* and *P. falciparum* were responsible for malaria incidence [9]. Most cases were found to be concentrated in the southern region of Bareilly district. The annual API for the district was 9.32 per 1,000 inhabitants.
Figure 4. Choropleth maps of the slide positivity rate (SPR) and annual blood examination rate (ABER) in Bareilly district at the block level.

Figure 5. Moran's I scatterplot and map of significant clusters at the block and village levels.
Table 2. Correlations between monthly malaria incidence and monthly rainfall in 2019 for each block

| Block name          | M1   | M2   | M3   | M4   |
|---------------------|------|------|------|------|
| Shergarh            | 0.608*| 0.738**| 0.430|      |
| Bhamora             | 0.508| 0.715**| 0.535|      |
| Meerganj            | 0.555| 0.800**| 0.545|      |
| Fatehganj West      | 0.543*| 0.404| 0.243|      |
| Nawabganj           | 0.570*| 0.528| 0.201|      |
| Kuandanda           | 0.750**| 0.520| 0.171|      |
| Bithi Chainpur      | 0.332| -0.003| -0.030|      |
| Bhadpura            | 0.516| 0.378| 0.165|      |
| Baheri              | 0.726**| 0.040| -0.157|      |
| Mundia Nabi Baksh   | 0.742**| 0.670*| 0.363|      |
| Majhgawan           | 0.416| 0.759**| 0.620*|      |
| Aonla               | 0.204| 0.753**| 0.721*|      |
| Ramnagar            | 0.638*| 0.742**| 0.334|      |
| Faridpur            | 0.838*| 0.614*| 0.085|      |
| Bhojipura           | 0.765**| 0.264| -0.014|      |
| Kyara               | 0.614*| 0.635*| 0.449|      |
| Bareilly Urban      | 0.664*| 0.558| 0.228|      |

M1, M2, and M3 are months.

* < 0.05, ** < 0.01.

Table 3. Correlations between monthly malaria incidence and monthly temperature in 2019 for each block

| Blocks name          | M1   | M2   | M3   | M4   |
|---------------------|------|------|------|------|
| Shergarh            | 0.538| 0.731**| 0.779**| 0.720**|
| Bhamora             | 0.266| 0.407| 0.523| 0.657*|
| Meerganj            | 0.255| 0.386| 0.526| 0.659*|
| Fatehganj West      | 0.643*| 0.834**| 0.797**| 0.597*|
| Nawabganj           | 0.594*| 0.787**| 0.824**| 0.648*|
| Kuandanda           | 0.492| 0.728**| 0.811**| 0.707**|
| Bithi Chainpur      | 0.658*| 0.836**| 0.702*| 0.339|
| Bhadpura            | 0.646*| 0.833**| 0.796**| 0.572|
| Baheri              | 0.398| 0.690*| 0.674*| 0.467|
| Mundia Nabi Baksh   | 0.297| 0.619*| 0.819*| 0.840*|
| Majhgawan           | 0.260| 0.416| 0.520| 0.661*|
| Aonla               | 0.044| 0.179| 0.318| 0.581*|
| Ramnagar            | 0.497| 0.688*| 0.759**| 0.706*|
| Faridpur            | 0.485| 0.703*| 0.829**| 0.715**|
| Bhojipura           | 0.506| 0.766**| 0.788**| 0.588*|
| Kyara               | 0.452| 0.696*| 0.776**| 0.752**|
| Bareilly Urban      | 0.565*| 0.774**| 0.799**| 0.684*|

M1, M2, M3, and M4 are months.

* < 0.05, ** < 0.01.

in 2019, which is higher than 2018, and 7 blocks had APIs of more than 10 per 1,000 inhabitants, indicating that these were highly endemic regions. Pf% declined to 25.9 in 2019 compared to the previous year [3]. The ABER was 5.88% for the district; however, as per guidelines, ABER should be >10% (i.e., more than 10% of the population should receive blood slide examinations and rapid diagnostic tests) [3]. The study found significant positive spatial autocorrelation (0.63), showing that malaria incidence was clustered. Another study in Zimbabwe presented a spatial analysis of reported malaria cases from 2011 to 2016 and found significant positive spatial autocorrelations in all years [10]. A significant negative correlation was found between the elevation of blocks and annual malaria cases of the block. In other words, there was a decrease in the cases with an increase in elevation. Bareilly district is not a high-altitude area, and the difference in elevation between the northern and southern regions of Bareilly is merely 30 to 40 meters; however, the district has several rivers, such as the Ramganga (a tributary of the holy river Ganga) and rivers of local importance passing through the southern region of district. Therefore, it is possible that when rainfall occurs, water comes to the southern region from the northern region and the consequent waterlogging might create congenial conditions for the development of vector population to build up its density above the critical level required for active transmission of malaria [10]. This could explain the much higher number of reported malaria cases in the southern region than in the northern region.

Furthermore, the Bareilly district is agricultural and cropland has a high likelihood of undergoing waterlogging. A positive correlation was found between the NDVI and malaria incidence, with a correlation coefficient of 0.36. The major vegetation cover of Bareilly district is agricultural/cropland. Studies have found that grass/cropland has a significant influence on changing the trends of malaria incidence [11]. A previous study found that cropland and agricultural land provided a suitable environment for malaria vectors, subsequently increasing malaria transmission [12].

In a study in the Philippines, a spatial analysis of malaria incidence for 2016 showed spatial autocorrelation of 0.45 and 0.44 by using the queen and rook criteria [13]. Another study in Zimbabwe showed that spatial analysis with reported malaria cases from 2011 to 2016 had significant positive spatial autocorrelations in all years [14]. A study in China showed a clear significant positive spatial correlation from 2004 to 2011 [15].

A study in Sri Lanka showed a similar association between monthly average rainfall and monthly malaria incidence with the lag of 1 to 3 months [16]. Another study in Dehradun, India showed an association between monthly average rainfall and monthly malaria incidence with a 1-month lag [17]. The study also found that the average mean temperature had a substantial influence on malaria incidence with a lag of 1 to 3 months

\[ p < 0.05, \quad * < 0.01. \]
A low mean average monthly temperature provides a suitable environment for mosquitos to breed so that they can transmit the infection to humans. A study in Tibet also showed that the monthly average temperature played an important role in malaria transmission, with a lag time of 2 months [18]. Another study in Iran showed a positive association between the monthly mean temperature and malaria incidence and a rise in malaria cases with a 1-month lag [19]. A study in Bhutan also showed a rise in temperature with a 1-month lag, and the temperature was found to have a large influence on malaria incidence [20]. Cases increased due to rainfall with a lag of 1 month, indicating that rainfall is followed by the development of temporary water bodies, which provide a suitable environment for malaria mosquitos to breed and infect humans. Data on the lag period between meteorological variables and malaria incidence will be helpful for the authorities to plan malaria control strategies as early as possible to control further malaria outbreaks.

**Conclusion**

Overall, the malaria burden in Bareilly district predominantly observed from July to October, with a peak in malaria incidence in September. Malaria occurrence at the block level was spatially clustered in the district, and all clusters were located in the southern region of Bareilly district. A statistically significant association was also found between reported monthly malaria cases and monthly mean temperature with a lag of 2 months. A positive association between rainfall and malaria incidence with a lag of 1 month was found in most blocks, which is a highly significant finding. Vegetation coverage was also associated with malaria incidence, showing that areas covered with cropland influenced the pattern of malaria incidence. The presence of space-time clustering of malaria cases and its correlation with meteorological and physiographic factors indicate that routine spatial analysis of surveillance data could help control and manage malaria outbreaks in the district.

**Limitations**

The disease surveillance data used in the study were obtained from the health department of Uttar Pradesh and might not reflect the actual occurrence of malaria in the state, especially from the private sector. Point pattern analysis was not possible as the exact incidence locations of the cases were not traceable; therefore, an area-based data analysis was conducted.

**Notes**

**Ethics Approval**

The Institutional Ethics Committee of Sree Chith Institute of Medical Sciences and Technology (SCTIMST), Trivandrum approved this study (Order IEC/1581 on November 20, 2020).

**Conflicts of Interest**

The authors have no conflicts of interest to declare.

**Funding**

None.

**Availability of Data**

The datasets were obtained from the state health authorities under a non-disclosure agreement. However, any legitimate requests for data would be considered positively and acted upon.

**Additional Contributions**

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