IMPACT OF CLIMATE ON VARICELLA DISTRIBUTION IN BULGARIA (2009–2018)

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SUMMARY

Objectives: Temperature is the most important environmental variable associated with the varicella frequency across the world. The present study compares the incidence of varicella in the districts of Bulgaria against some climatic factors and tries to find environmental variables which account for the differences in the varicella distribution observed among the Bulgarian districts.

Methods: The 28 Bulgarian districts were used as units of observation and their average 10-year varicella incidence (2009–2018) was tested for correlation with the standard bioclimatic variables of WorldClim, version 2.

Results: The WorldClim estimates for the annual mean temperature, the maximal temperature of the warmest month, the minimal temperature of the coldest month, the mean temperature of the coldest quarter, and the solar radiation inversely and not significantly correlated with the average 10-year varicella frequency. The precipitation of the warmest quarter and the wind speed correlated positively and also not significantly. Only the mean temperature of the driest quarter correlates significantly with the incidence at district level (Spearman's rank correlation coefficient of −0.45, p = 0.02). The mean of average 10-year varicella incidence rates among districts with driest quarter during the winter (January, February, March) was 387.6 ± 114.1, while among districts with driest quarter during the summer/autumn (July, August, September or August, September, October) 283.3 ± 102.1 (p = 0.02, ANOVA test).

Conclusions: Dry winter and/or wet summer appear as significant determinants for the fluctuant spread of varicella infection in Bulgaria.

Key words: chickenpox, WorldClim, communicable diseases, epidemiology, notifiable infectious diseases

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INTRODUCTION

Varicella (chickenpox), a usually benign childhood infection, is a disease of contrasts. First, the extremely high morbidity contradicts with relatively low mortality. Second, despite its ubiquitous presence in all inhabited areas of the world, the infection shows distinct locality. It attacks different age groups in temperate and tropic regions (1, 2), it has distant seasonal peaks of incidence in different countries (3–5), and consists of several circulating strains of the causative agent, the varicella-zoster virus (VZV) across the geographic regions (6). The vaccination policies across the world (7–9) also contribute to the varicella particular locality. Curiously, even regarding the massive immunization, two polar approaches are often present – some countries apply vaccination on a wide basis and almost the whole population is protected, while others do not have any immunization regulation regarding varicella and the population is exposed to the natural infection.

Although demographic factors remain most important for varicella epidemiology (10), the local singularity of the infection distribution suggests that climatic and meteorological factors also play a crucial role in the regional spread of the disease. Various environmental factors have been shown to correlate in a divergent way with the varicella incidence, seroprevalence and hospitalization rates – relative humidity is negatively associated with the number of paediatric varicella hospitalizations in Hong Kong (11), as well as with the incidence rate in Mexico (12), and in Jinan, China (13); the temperature inversely affected varicella risk in Taiwan (14), and in China (13, 15, 16), but positively correlated to the number of cases in Mexico (17), Hong Kong (16), or with the level of seropositivity – in Iran (18). Atmospheric pressure correlated positively with the weekly incidence rates and daily hospitalizations for varicella in Jinan (China) and in Hong Kong, respectively (13, 16). In the same studies, sunshine, rainfall and the Southern Oscillation Index were also positively associated with the chickenpox spread. In Thailand, the mean of the extreme minimum temperature was shown to be the most important for the chickenpox distribution – regions with higher extreme minimum temperature were with lower seroprevalence (19). The most detailed data exist for Japan, where the varicella incidence was shown to increase at the temperature range of 5–20° C and to decrease at < 5 °C and > 20 °C (4, 20).

Whether such kind of association exists in most of the European countries is less clear. Only the hospitalization rates among Greek children were inversely linked to the mean monthly air temperature and positively to the wind speed (21) and varicella cases in Mallorca (Spain) have been shown to increase with the decrease in water vapour pressure and with the increase of solar radiation (22). Also, temperature appeared as the most significant contributor to the pattern of varicella seasonality in Northern Europe (Finland and Denmark) (3). But whether is there any connection between the varicella dynamics and the climate in the central continental part of Europe, between the North extremities and the Mediterranean region, is currently unknown. To answer this question (at least partially), the present study compares the average 10-year incidence of chickenpox in the districts of Bulgaria against a number of climatic factors. It tries to find environmental variables which account for the differences in the varicella distribution observed among the Bulgarian districts.

MATERIALS AND METHODS

Bulgaria is a country in South-East Europe situated on the Balkan Peninsula. Its population of 7,364,570 (as of 1 February 2011, the last census) and its territory of 110,994 square kilometres are divided into 28 administrative districts. In this relatively small territory, the climate conditions are highly variable mainly as a result of the continental and Mediterranean influence and the mixed landscape (23). More information about the climate profile of the country is discussed in details elsewhere (23).

For the purposes of the current study, the standard bioclimatic variables for WorldClim version 2, a spatial resolution of 2.5 minutes (annual mean temperature, mean diurnal range, isothermality, temperature seasonality, max. temperature of the warmest month, min. temperature of the coldest month, temperature annual range, mean temperature of the wettest quarter (1/4 of the year), mean temperature of the driest quarter, mean temperature of the warmest quarter, mean temperature of the coldest quarter, annual precipitation, precipitation of the wettest month, precipitation of the driest month, precipitation seasonality, precipitation of the wettest quarter, precipitation of the driest quarter, precipitation of the warmest quarter, precipitation of the coldest quarter) were used (24). They are average estimates for the years 1970–2000 and represent long-term summary of climatic trends and seasonality rather than precise weather measurements. In addition, the monthly data for precipitation (in mm), solar radiation (in kJ m^{-2} day^{-1}) and wind speed (m s^{-1}) were also obtained. All data were extracted with the R project software for statistical computing (version 4.0.4/2021-02-15) using the raster package and the coordinates (latitude and longitude) of the main city of each district. This approximation was considered to avoid the effect of the meteorological data from stations in mountainous and other non-inhabited areas of the districts.

Varicella is a compulsorily notifiable disease in Bulgaria – all medical practitioners should report possible, probable and confirmed cases on daily basis to the Regional Health Inspectorate of the corresponding district. Cases are then summarized and reported to the national bodies. The National Centre of Public Health and Analyses (NCPHA), Ministry of Health, aggregates the data and publishes the monthly and annual incidence rates at district and country level. The annual publications "Public Health Statistics" (2010–2019) of the NCPHA (25) served as a source for the annual varicella incidence rates (cases per 100,000 population estimate) at national and district level in Bulgaria. The average 10-year incidence was then calculated and used in the analysis.

A set of regional socio-demographic characteristics (total population, population density and proportion of urban population) was obtained from the National Statistical Institute database (2011 census data).

To test the possible association between the average 10-year varicella incidence rates and the bioclimatic variables, the Spearman's rank correlation coefficients and linear regression models were calculated using the R project software. The possible difference between the group means/medians was analysed either with ANOVA test in the case of normally distributed variables or with the Wilcoxon test in the case of non-normally distributed variables. The accepted significance was set at $p < 0.05$.

RESULTS

Figure 1 shows the annual varicella incidence rates in Bulgaria for the last ten years (2009–2018). On a national scale, the lowest incidence was in 2010 – 261.8 and the highest one was in 2013 – 530.2 cases per 100,000 inhabitants. The mean of the annual incidences for the 10-year period was 373.64 ± 74.16 cases per 100,000, the median was 361.15 and the interquartile range was 42.8.

District annual frequencies varied widely both among the districts and among the years of interest (in some cases more than 30 times) (Table 1). The effect of these severe fluctuations

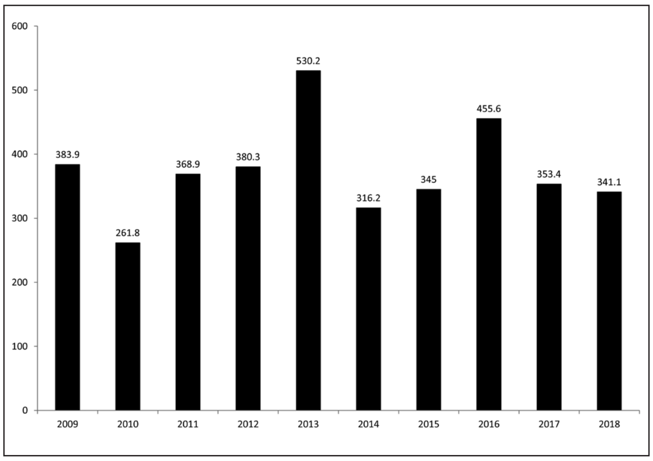

Fig. 1. *Annual incidences of varicella in Bulgaria (2009–2018).*
Cases per 100,000 inhabitants

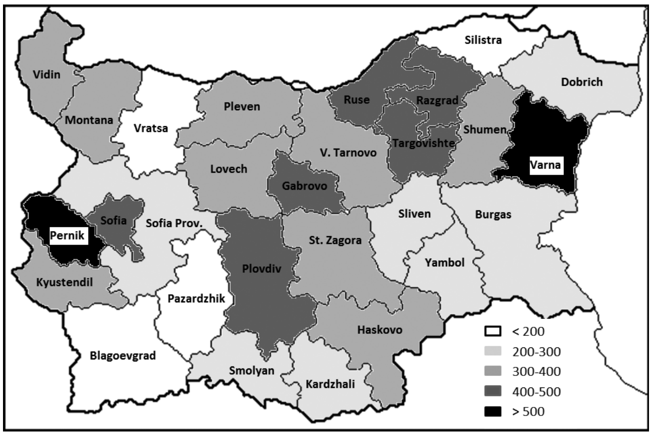

Fig. 2. *Map of Bulgarian districts with the corresponding 10-year average incidence rates of varicella (2009–2018).*
Cases per 100,000 inhabitants

__Table 1.__ Average 10-year varicella incidence rates[a] in Bulgarian districts (2009–2018)

Districts	Incidence 2009–2018	SD	Range
Blagoevgrad	176.14	33.79	141–261.6
Burgas	220.86	86.21	112.4–400.6
Varna	589.49	219.13	312.1–1010.5
Veliko Tarnovo	323.20	167.37	132–672.1
Vidin	340.74	140.28	71.7–561.2
Vratsa	183.42	68.38	93.4–347.9
Gabrovo	409.82	176.40	166.2–705.2
Dobrich	281.21	112.93	127–516.3
Kardzhali	202.36	142.44	29–454.6
Kyustendil	304.34	186.91	53.4–624.6
Lovech	357.13	229.27	117–948.0
Montana	363.34	236.10	76.4–798.6
Pazardzhik	120.85	53.65	42.5–204.4
Pernik	505.11	369.12	128.3–1259.9
Pleven	389.32	199.72	109.8–852.3
Plovdiv	470.79	123.18	260.5–668.7
Razgrad	427.17	141.13	225.3–643.0
Ruse	488.53	257.49	148–881.6
Silistra	184.84	114.30	59.8–387.1
Sliven	279.56	96.60	169.9–459.0
Smolyan	276.23	162.53	110.8–593.6
Sofia City	495.94	151.65	330–867.2
Sofia Province	210.91	65.43	93.7–330.1
Stara Zagora	381.59	108.49	147.2–533.1
Targovishte	476.29	209.50	245.5–880.1
Haskovo	393.63	105.99	256.5–584.1
Shumen	371.34	136.13	163.2–624.3
Yambol	273.10	164.27	37.9–608.7

[a]Cases per 100,000 individuals; SD – standard deviation

could be minimized when using the average of incidences for longer periods (26). However, as shown in Table 1 and Figure 2, although averaged for ten years, the varicella incidence rates among the districts of Bulgaria still significantly differed – the lowest 10-year average incidence was reported in district Pazardzhik – 120.85, and the highest one – in Varna, 589.49 cases per 100,000 inhabitants.

To see if this difference depended on the climate of each district, a correlation analysis between the average 10-year varicella incidence rates of Bulgarian districts and bioclimatic variables had been performed. The Spearman's rank correlation coefficients between varicella frequency and most of the standard WorldClim bioclimatic variables were almost negligible (less than |± 0.2|). Six factors showed a weak to moderate correlation with the varicella incidence at district level in Bulgaria (Table 2). All temperature-related factors correlated inversely with the chickenpox distribution while the precipitation of the warmest quarter correlated positively. Only one of these six variables – the mean temperature of the driest quarter was associated significantly with $p = 0.02$ (Fig. 3).

__Table 2.__ Correlation between 10-year varicella incidence rates in Bulgarian districts and some bioclimatic variables[a]

Bioclimatic factor	Spearman's rank correlation coefficients
Annual mean temperature	−0.25
Max. temperature of warmest month	−0.20
Min. temperature of coldest month	−0.31
Mean temperature of driest quarter	−0.45*
Mean temperature of coldest quarter	−0.28
Precipitation of warmest quarter	0.23

[a]WorldClim version 2, a spatial resolution of 2.5 minutes
Only correlation coefficients > |± 0.2| are listed; *p < 0.05

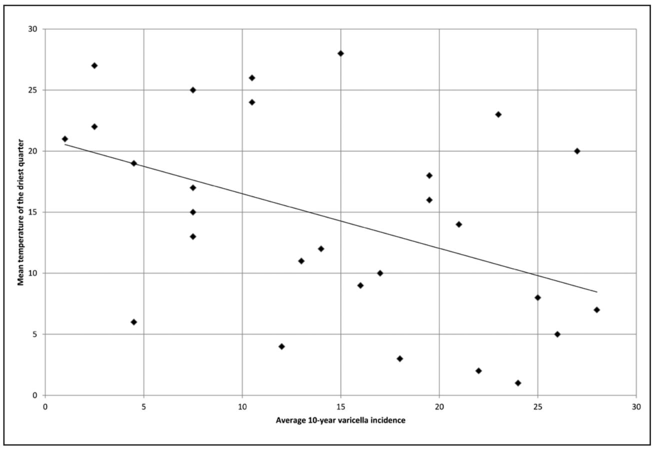

***Fig. 3.** Correlation between the mean temperature of the driest quarter of each district and the 10-year average incidence rates of varicella.*

Line fit plot of Spearman's rank coefficients

A simple linear regression model with the mean temperature of the driest quarter as an independent predictor yielded the following equation: Y (average 10-year varicella incidence) = 396.10 – 6.13 X (mean temperature of the driest quarter) with R squared = 0.19 and $p = 0.02$. In other words, when the mean temperature of the driest quarter increases by one, the value of the varicella incidence decreases by 6.13. Previous analyses (10) showed socio-demographic factors to be significant predictors of varicella incidence. The proportion of the urban population strongly associated with the incidence of varicella at the district level in Bulgaria (27). Accordingly, this variable was included in a multiple regression model: $Y = 46.61 - 5.10\ X^1$ (mean temperature of the driest quarter) + $513.17\ X^2$ (proportion of the urban population) with R squared = 0.44, adjusted R squared = 0.40, coefficient of multiple correlation = 0.67, and $p = 0.001$. Other socio-demographic variables were also tested in regression analyses but the obtained models did not yield better equations.

When the monthly precipitation data for each district were analysed in details, two patterns were observed: 15 out of 28 Bulgarian districts (Varna, V. Tarnovo, Dobrich, Gabrovo, Kyustendil, Lovech, Pernik, Pleven, Razgrad, Ruse, Silistra, Sofia, Sofia province, Targoviste, Shumen) had lowest precipitation rate in the winter (driest quarter: January, February, March) and 13 – in the summer/autumn (either driest quarter of July, August, September or August, September, October). The mean of average 10-year varicella incidence rates in the first group was 387.6 ± 114.1, while in the second one 283.3 ± 102.1 ($p = 0.02$, ANOVA test).

The wind speed and the solar radiation also seemed to be weakly and not-significantly correlated to the varicella incidence rates – the average of the monthly wind speeds in each district was positively associated with chickenpox frequency (Spearman's rank correlation coefficient of 0.27, $p = 0.16$) and the average of the monthly solar radiation was negatively correlated (Spearman's rank correlation coefficient of −0.24, $p = 0.23$). Interestingly, the wind speed and the solar radiation differed significantly in the two groups of districts – in the group with dry winter and high varicella incidence the median wind speed was 2.56 m s^{-1} and the mean solar radiation was 13,200.04 kJ m^{-2} day^{-1}, while in the group with wet winter and low varicella frequency, it was 2.11 and 13,501.31, respectively ($p = 0.003$, Mann-Whitney U test and $p = 0.03$, ANOVA test).

DISCUSSION

Varicella incidence in Bulgaria (at district level) seems to depend on temperature. The annual mean temperature, the maximal temperature of the warmest month, the minimal temperature of the coldest month, the mean temperature of the driest quarter and the mean temperature of the coldest quarter inversely correlate with the average 10-year varicella frequency. To summarize this relationship someone can speculate that the warmer the weather in the district the smaller the varicella incidence. This conclusion although simplified is reasonable as the temperature was shown to be the most important negative climatic factor for varicella incidence in several temperate and subtropical climates (3, 4, 21, 28). However, the correlation for Bulgaria is weak/moderate and seems statistically significant only for the mean temperature of the driest quarter – varicella is more frequent in districts with the winter as the driest season. A similar finding exists for the Hong Kong population, where children and adolescent hospitalizations for varicella were inversely correlated with the mean relative humidity and total rainfall in cool seasons (11). Interestingly, the precipitation of the warmest quarter also plays a role (at least weak) for the number of varicella cases among Bulgarian districts. This suggests that more than one climatic factor participates in varicella epidemiology in a complex and intercorrelated manner.

Climatic factors may affect both survival in the nature and effective transmission of viruses among people. The character of this influence on VZV is currently unknown. On molecular level, the temperature might affect the replication and the reactivation of VZV – the speed of viral replication at a lower temperature is slightly faster than at 37 °C (29). On the community level, the traditional epidemiological explanation for the increased number of social contacts in closed areas in winter and lighter clothing in summer is also relevant. Regarding the humidity and the precipitation as factors for varicella distribution, Yang et al. (13) hypothesized that in dry air conditions, the aerosols would be smaller in size and more persistent in the air, as well as skin scratching would be more significant.

A possible explanation of the results in the current study could be the better survival and/or transmission of the virus in the regions with dry winters. Winter is the leading season in the epidemiology of varicella in Bulgaria – not only the highest proportion of cases is registered during the winter but the districts which contribute the most to the number of cases have a clear winter dominance (30). So, it is reasonable to speculate that dry winter weather is favourable for chickenpox spread in the community. The alternative hypothesis – that the increased precipitation might improve the survival in critical summer months when the incidence is the lowest – is also possible or even more logical, as the bioclimatic variable "precipitation of warmest quarter" (which in all Bulgarian districts is July, August and September) has a weak to moderate correlation with the varicella incidence. However, the exact mechanism remains to be defined. This will be a difficult task, as disagreement about the main way of chickenpox transmission still exists (31). Spreads by the mean of lesions and by aerosols are broadly accepted as the most important but which one is dominant in different climates is not fully understood.

Also, the role of wind speed and solar radiation merits discussion. While solar radiation is more studied than wind velocity, its effect is less clear: in Mallorca, Spain and Jinan, China, the correlation is positive, while in Poland, where only the UV radiation has been measured – the association is inverse. An inverse correlation was also detected for the Bulgarian districts but it was not statistically significant. The role of solar radiation could be in both directions – the sunlight, especially its UV component may suppress the cell-mediated immunity of the host but also may affect the viral survival and transmissibility (31). Which one of these events will dominate might depend on the geographic location of the studied area. The wind velocity as a factor for varicella incidence was already studied only in Greece (21), and the association is positive as for Bulgaria. Data are not available for other regions, and it remains to be determined if this association is a typical Balkan phenomenon or exists in other parts of the world.

The current study has one major limitation – the diverse climate across the territory of Bulgaria and the districts. It is clear that the administrative division is not the same as the climatic one, and it is difficult to assign all specific climate factors in such a way to reflect completely the administrative districts. As stated above, one point (the main town of the district) was assigned as a geographic location for the bioclimatic variables' projection. This allows for avoiding the impact of the meteorological stations in non-inhabited areas but predicts missing some possible associations. Also, the study deals with summarized data that may help avoiding local and temporary noising but may miss significant short-term associations. The work uses bioclimatic average estimates which represent a long-term summary of climatic trends rather than precise measurements. This approach could not consider the lag between the moment of climate action and its effect on the disease incidence due to the relatively long incubation period of varicella (up to 21 days).

CONCLUSION

In conclusion, this is one of the few studies discussing the importance of the climate for the varicella incidence in Europe – an impact that will continue to grow with the widely observed climatic changes. In addition to the demographic factors, the climatic variables also play a significant role in the fluctuant incidence of varicella among the Bulgarian districts. The mean temperature of the driest quarter seems to have the dominant importance, and the dry winter and/or wet summer appear as significant determinants for the spread of varicella infection in Bulgaria.

Conflicts of Interest

None declared

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