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Environmental and Behavioral Determinants of Septicemia Mortality in Türkiye: A Ten-Year Analysis

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ABSTRACT

This study examines the environmental and behavioral factors associated with variations in septicemia mortality rates across Turkish provinces. Province-level data spanning ten years were analyzed using ordinal logistic regression modeling to determine the predictors of septicemia mortality. Environmental factors such as humidity, temperature, and air pollutants, along with behavioral aspects including alcohol consumption, were evaluated. Analysis of the provided data revealed significant regional variations in septicemia mortality rates across areas with diverse environmental and social characteristics. Higher median humidity and stable environmental conditions (low variability in humidity and temperature) correlated with reduced mortality rates. Alcohol consumption was identified as a risk factor, moderately increasing the risk of septicemia mortality. The findings highlight the intricate relationship between environmental stability, personal behaviors, and septicemia outcomes. The study accentuates the need for targeted public health strategies and suggests that mitigating environmental risks and fostering healthy behaviors could effectively reduce septicemia mortality. Further studies should focus on individual-level data and explore the relationship between these factors in different climatic conditions.

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INTRODUCTION

Given the millions of cases reported annually and the persistently high mortality rate, Sepsis, a life-threatening condition resulting from the body's dysregulated response to infection, continues to pose a substantial global health challenge (World Health Organization [WHO], 2020). While the terms 'septicemia' and 'sepsis' are often used interchangeably, septicemia specifically refers to the presence of bacteria in the bloodstream, leading to blood poisoning and ultimately triggering sepsis. Sepsis can result in tissue damage, organ failure, and, if left untreated, death. The global and regional patterns of sepsis incidence and mortality are influenced by a myriad of factors, including environmental, meteorological, and behavioral agents.

A 2016 systematic review by Fleischmann et al. (2016) revealed an alarming upsurge in sepsis incidence and mortality worldwide, with a substantial burden observed in low- and middle-income countries (LMICs). These disparities are attributed to various factors, including limited access to healthcare, inadequate sanitation, and antimicrobial resistance (AMR) (Fleischmann et al., 2016; WHO, 2020).

There is a discernible correlation between sepsis incidence and mortality rates and the developmental level of a country. Data from the Global Burden of Disease Study (GBD) 2017 indicated that sepsis is a leading cause of death in sub-Saharan Africa and Southeast Asia, while developed countries like the United States and Europe have reported declining sepsis mortality rates due to improved healthcare infrastructure (GBD 2017 Risk Factor Collaborators, 2018; Angus & Van der Poll, 2013).

Recent studies have linked air pollutants, including Particulate Matter 10 (PM10), sulfur dioxide (SO_2), carbon monoxide (CO), nitrogen dioxide (NO_2), and ozone (O_3), with increased sepsis incidence and mortality. These pollutants are known to exacerbate respiratory and systemic infections, potentially leading to severe sepsis outcomes (Pope III et al., 2015; Yue et al., 2020).

Meteorological factors, such as air pressure, humidity, rainy days, temperature fluctuations, wind speed, sunlight exposure, and sun radiation, also play

a notable role in the epidemiology of sepsis. Such climatic elements influence pathogen survival, transmission, and human immunity, thereby having a marked correlation with sepsis rates (Wu et al., 2016; Kim et al., 2016; Reilly et al., 2023).

Behavioral factors, such as smoking, alcohol consumption, and exposure to second-hand smoke, have been identified as significant contributors to sepsis risk and fatality. These behaviors impair immune function and increase susceptibility to infections, affecting both the incidence and severity of sepsis (Lee et al., 2018).

To date, there is no literature discussing the impact of environmental and climatic characteristics and sepsis mortality in Türkiye; therefore, in this report, we aim to provide a comprehensive overview of the national and regional patterns of sepsis over a 10-year time window, investigating the interplay of environmental, meteorological, and behavioral factors in influencing its incidence and mortality. By identifying high-burden areas and vulnerable populations, and monitoring temporal trends, we seek to inform effective public health policy and intervention strategies. Reports like ours will also inform other similar geographies globally.

MATERIALS AND METHODS

Population-adjusted septicemia mortality rates were calculated for the 81 provinces of Türkiye (2010-2019), and their ordinal changes were used as the primary outcome variable. As for the environmental domain, represented by longitudinal data values, the following markers were obtained at the regional level: Particulate Matter 10 (PM10), sulfur dioxide (SO_2), Carbon Monoxide (CO), Nitrogen Dioxide (NO_2), and Ozone (O_3), air pressure, humidity, annual rainy days, maximum-average-minimum temperatures, wind speed as well as total sunlight, sun radiation, and electromagnetic field. These markers were further represented as the median values of the measurements collected between 2010 and 2019.

To assess the influence of environmental fluctuations on Septicemia incidence, we established the standard deviation (SD) and coefficient of variation (CV) of relevant environmental markers between 2010 and 2019 as indicators of variability. Additionally, our analyses incorporated established behavio-

ral risk factors, including tobacco smoking, alcohol consumption, and second-hand smoke exposure.

The TRAJ procedure developed by Jones, Nagin, and Roeder (2001) suggested three change-profiles for septicemia mortality based on the quality of fit diagnostics. To account for the ordered structure of these change profiles, (e.g., low, intermediate, high), an ordinal logistic regression model was utilized to evaluate the likelihood of transitioning to higher Septicemia trajectory categories with each unit increase in the univariate predictors. In this model, ordinal septicemia categories were treated as the response variable, and environmental and climatic variables were considered as independent univariable predictors. A total of 33 markers were investigated, with FDR correction (Benjamini & Hochberg, 1995) implemented to address the multiplicity of comparisons. To visualize the relationships between significant predictors, both the response variable and the independent variables were standardized to a mean value of zero and a variance of one. All analyses were conducted using SAS (R) Version 9.4 (Cary, North Carolina, USA).

RESULTS

Figure 1 presents a longitudinal analysis of septicemia mortality rates by region over time. The divergent trajectories by group suggest the heterogeneity of mortality patterns, influenced by the interplay of regional and temporal factors.

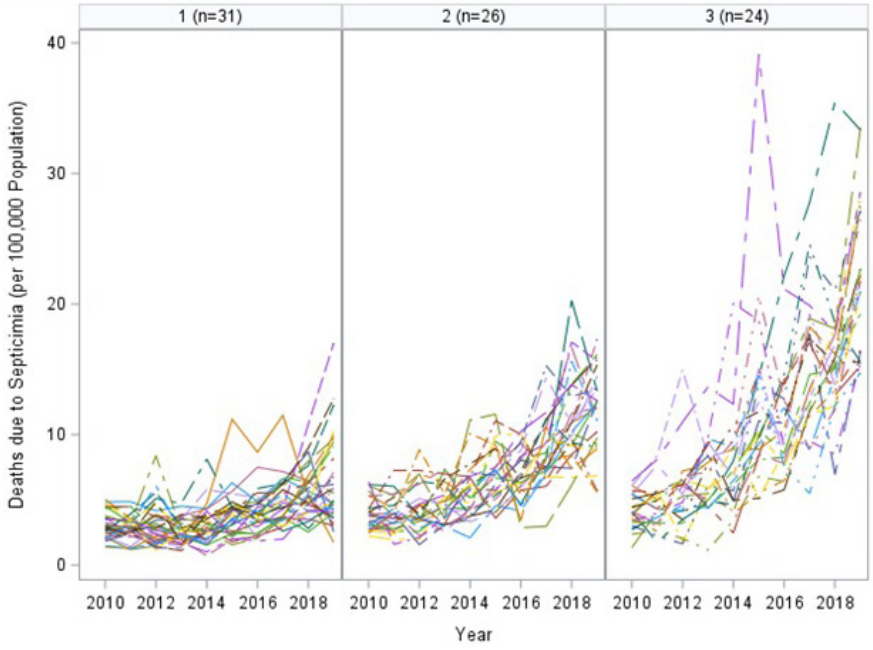

Figure 1. Septicemia Mortality Profiles by SAS TRAJ procedure

In alignment with the data in Table 1, we identified a positive association between median humidity and septicemia mortality (OR 1.08), implying that areas characterized by higher humidity levels may experience elevated mortality risks. Interestingly, increased variability in humidity, as quantified by the coefficient of variation (CV) and standard deviation (SD), demonstrated a protective effect against mortality (OR 0.90 and 0.81, respectively). These findings suggest that regions with greater fluctuations in humidity may experience lower mortality rates. Similar patterns were observed for temperature and precipitation. A higher degree of seasonal variation in both temperature and rainfall appeared to be inversely correlated with mortality risk.

Table 1: Summary of markers significantly associated with Septicemia Mortality Profiles (CV is Coefficient of Variance, SD is Standard Deviation)

Predictor	OR (95% CI)	p	FDR Corrected p
Ever Alcohol Use	1.06 (1.01,1.12)	0.0125	0.037392
Humidity (CV)	0.90 (0.85,0.94)	<.0001	0.000566
Humidity (Median)	1.08 (1.03,1.14)	0.0020	0.008801
Humidity (SD)	0.81 (0.73,0.90)	<.0001	0.001
Maximum Temperature (CV)	0.93 (0.88,0.98)	0.0071	0.023271
Maximum Temperature (SD)	0.63 (0.48,0.82)	0.0006	0.003868
Mean Temperature (SD)	0.42 (0.28,0.63)	<.0001	0.000566
Minimum Temperature (SD)	0.53 (0.35,0.79)	0.0022	0.008808
Particulate Matter-10 (SD)	0.89 (0.83,0.96)	0.0031	0.011009
Rainy Days (CV)	0.95 (0.91,0.98)	0.0012	0.00641
Sun Radiation (per 10-units)	0.92 (0.88,0.96)	0.0002	0.001777
Sunlight (per 10-units)	0.97 (0.96,0.99)	0.0005	0.0036

Elevated variability in particulate matter (PM10) concentrations, as measured by standard deviation, exhibited a protective association with septicemia mortality (OR=0.89), suggesting that increased PM10 variability may be instrumental in reducing mortality rates. Sun exposure metrics (solar radiation and sunlight per 10-unit increment) also demonstrated an inverse relationship with septicemia mortality, with odds ratios of 0.92 and 0.97, respectively, implying that increased levels of sun exposure are beneficial.

Figure 2 presents scatter plots that visualize the negative correlation between environmental stability (humidity and temperature) and septicemia mortality. This comprehensive analysis highlights the multifaceted nature of environmental and behavioral risk factors in determining Septicemia outcomes, suggesting the need for targeted public health interventions and personalized lifestyle modifications.

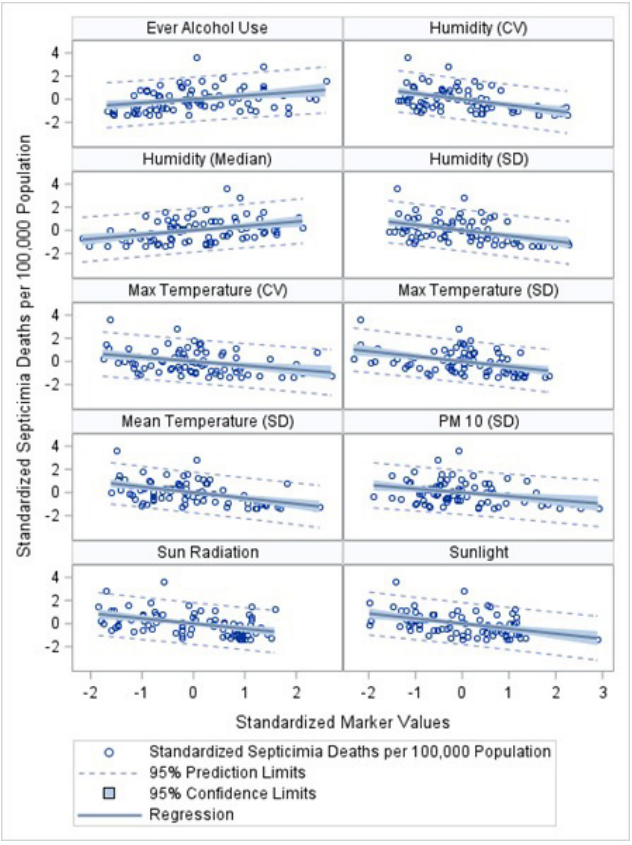

Figure 2. Significant markers indicative of an association with deaths due to Septicemia. CV: Coefficient of Variation, SD: Standard of Deviation

DISCUSSION AND CONCLUSIONS

Our decade-long analysis of septicemia mortality in Türkiye, depicted in Figure 1, suggests a temporal pattern potentially attributable to local environmental and behavioral influences on health outcomes. The significant predictors highlighted in Table 1, especially those associated with seasonal environmental variations in humidity and temperature, are consistent with contemporary research emphasizing the role of climate variables in infectious disease epidemiology (Lafferty, 2009). Each of the significant factors is discussed below in the light of the literature.

Ever Alcohol Use: Consistent with our findings, the literature indicates a correlation between alcohol use and increased risk of septicemia, potentially due to alcohol's immunosuppressive effects (Molina et al., 2010).

Humidity (CV, Median, SD): The results of this study observed a non-linear relationship between humidity and septicemia risk, with higher median humidity associated with increased risk while humidity variability (CV and SD) demonstrated a protective effect. These findings corroborate previous research suggesting that fluctuations in humidity levels may support immune function, while prolonged exposure to consistently high humidity could have adverse health consequences (Johnson & Morawska, 2009).

Temperature (CV, SD): The observed protective effect of temperature stability (lower SD) is in line with research suggesting that extreme temperature fluctuations can exacerbate health vulnerabilities, especially in infectious diseases (Lee et al., 2018).

Particulate Matter-10 (SD): Fluctuating PM10 exposure, as indicated by a higher median and standard deviation (SD), may be more effective in stimulating the immune system than sustained exposure to elevated PM10 levels (Zhang et al., 2018).

Rainy Days (CV): As corroborated by Brown and Murray (2013), our results suggest that stable precipitation patterns may serve as a protective factor against the health impacts of climate variability, particularly in relation to infectious diseases.

Consistent with the conclusions of this study, the literature suggests that stable precipitation patterns can mitigate health risks associated with climate variability, including infectious diseases (Brown & Murray, 2013).

Sun Radiation and Sunlight: These results suggest a positive association between sun exposure and immune function, potentially attributable to the immunomodulatory effects of vitamin D (Holick, 2017).

The study's strengths include its comprehensive environmental domain and robust statistical methods. However, potential limitations arise from the inability to control for all behavioral confounders, such as dietary habits and exposure to tobacco, alcohol, and other substances. Furthermore, individual-level data, rather than aggregate data, would have provided a more granular perspective.

Public health interventions informed by these findings might focus on mitigating environmental exposures and fostering health-promoting behaviors to decrease Septicemia-related mortality. Further research should delve into the

underlying causal pathways of these observed relationships, with a potential focus on individual-level data to facilitate a more comprehensive understanding of the subject matter.

Future research approaches, based on the findings of this study, could include:

- Longitudinal Individual-Level Studies: To further understand the causal pathways, future studies should investigate individual-level data over time, including genetic, lifestyle, and environmental risk factors.
- Interventional Studies: Evaluating the efficacy of public health initiatives aimed at mitigating environmental hazards and fostering health-promoting behaviors may contribute to a reduction in septicemia mortality rates.
- Climate Change Impact Assessment: Exploring the potential implications of climate variability on septicemia and formulating adaptive healthcare interventions to enhance resilience and reduce mortality.
- Technological Integration: This initiative seeks to leverage advanced analytics to develop sophisticated machine learning algorithms and robust predictive models, capable of predicting the onset of septicemia outbreaks by utilizing individual-level big data encompassing environmental and behavioral factors.
- Global Comparative Studies: Extending our study to various geographic and climatic contexts to explore the consistency of our findings beyond the Turkish population.

These investigative goals aim to elucidate the complex interplay between environmental and behavioral factors in the pathogenesis of septicemia, and to devise evidence-based preventative strategies to mitigate the incidence and severity of the disease.

In conclusion, our investigation elucidates the multifaceted nature of septicemia mortality in Türkiye for the first time in the literature by providing compelling evidence of the synergistic relationship between environmental factors and alcohol consumption in influencing patient outcomes. The study emphasizes the vital necessity for public health initiatives to consider regional climatic variations and take into account the individual behavioral influences. To advance our understanding, future research efforts must focus on granular individual-level examinations and engage in cross-cultural comparisons. By

elucidating these complex relationships, we can inform and empower healthcare systems to enhance management and prevention efforts at the regional level, ultimately mitigating the burden of septicemia mortality. This specific report on Türkiye also informs other similar geographies and paves the way for similar association studies for other regions and countries in the world.

Ethical Approval: Our research protocol was approved by Istanbul Medipol University Ethics Committee (Application number: 10840098-604.01.01-E.53819). The Ethics Committee waived the need for Informed Consent as there is no human subject involved in this research. Data is simply province-level mortality data provided by the Turkish Statistical Institute per year.

Authors' Contributions: HGK generated the research idea, carried out the literature search, wrote the initial and final draft of the manuscript; MT helped with the literature search, manuscript writing, and detailing the discussions; MK acquired the research data, carried out the data analyses and modeling, provided the materials and methods section of the manuscript, and approved the final manuscript.

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