Global Epidemiology of Urticaria: Increasing Burden among Children, Females and Low-income Regions

Gabrielle PECK[1], M. Jawad HASHIM[2], Cristin SHAUGHNESSY[3], Suraj MUDDASANI[1], Nourhan Ali ELSAYED[2] and Alan B. FLEISCHER JR[3]

[1]College of Medicine, [3]Department of Dermatology, University of Cincinnati, Cincinnati, OH, USA and [2]College of Medicine and Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates

Urticaria has a high socioeconomic burden worldwide. However, the global epidemiology of urticaria and its geographical and temporal trends are not well studied. Using the Global Burden of Disease dataset, the aim of this study was to analyse the age-standardized prevalence, incidence, years lived with disability, and mean duration of urticaria in 195 countries from 1990 to 2017. In addition, the relationship between socioeconomic development and urticaria was evaluated. The global prevalence of urticaria in 2017 was 86 million people. Females and children aged 1–4 years were more commonly affected than males and adults, respectively: these differences were outside the 95% uncertainty intervals. Regression analyses showed that a lower gross domestic product per capita was associated with a higher prevalence and incidence of urticaria ($p < 0.001$). The global prevalence of urticaria, incidence, and years lived with disability have remained stable from 1990 to 2017.

Key words: urticaria; epidemiology; gross domestic product; economics.

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Corr: Gabrielle Peck, College of Medicine, University of Cincinnati, 3230 Eden Ave, Cincinnati, OH 45267, USA. E-mail: peckgl@mail.uc.edu

Urticaria is a common condition that presents with transient, pruritic wheals, angioedema or both. It often leads to a reduced quality of life and significant socioeconomic burden (1–3). Despite the significant burden of disease, the global epidemiology of urticaria is not well documented. Most of the current epidemiological literature on urticaria has collected data from a single country (4–6). It is difficult to understand the global burden of urticaria throughout time due to the inconsistent methodology utilized in different studies. Since urticaria has a high socioeconomic burden, evaluation of the epidemiology of this condition could help direct healthcare resources to reduce its impact (1). One method by which these comparisons can be made is through analysis of the Global Burden of Disease (GBD) dataset (7).

The aim of this study was to evaluate the global patterns and trends for urticaria over the last 3 decades. In particular, this study aimed to assess the effect of socioeconomic development on the prevalence of urticaria.

SIGNIFICANCE

According to the Global Burden of Disease dataset for urticaria, its global prevalence, incidence, and years of life lived with disability, have remained stable between 1990 and 2017. Urticaria is more common in females than males, children than adults, and in regions with lower gross domestic product per capita. Clinicians should target appropriate healthcare resources for treatment of urticaria toward these demographic groups.

MATERIALS AND METHODS

The GBD dataset was developed by the Institute for Health Metrics and Evaluation at the University of Washington, Seattle, USA, as a systematic, comprehensive epidemiological database. The database provides epidemiological data on 354 diseases and injuries in 195 countries for each year between 1990 and 2017. The GBD dataset utilizes a substantial data repository in order to provide high-quality and up-to-date estimations for a range of indicators. The data repository includes raw input data from sources such as demographic and healthy surveys, census and claims data, or results from published literature. The data is then organized, filtered, and redistributed into intermediate data that can be used in the final modelling processes (7, 8).

The prevalence, incidence, years of life lived with disability (YLDs), and mean duration of urticaria were calculated as rates per 100,000 population. The mean duration of disease was calculated by dividing prevalence by incidence. YLDs are calculated by multiplying prevalence by the disability weight for the disease. Disability weights are developed through surveys of the general public and reflect the severity of health loss associated with a health state. The disability weights are measured on a 0–1 scale, where 0 is a state of full health and 1 is death. The Socio-demographic Index (SDI) is a composite measure developed by the GBD based on 3 variables: mean income per person, educational attainment, and total fertility rate. Countries were divided into 5 quintiles of SDI (8). The prevalence, incidence, YLDs, and mean duration of disease in the highest and lowest quintile of the SDI were evaluated. In addition, these same parameters were evaluated in 4 GBD-defined global regions (Africa, Asia, Europe, and the Americas). The relationships between sex, age, SDI, and gross domestic product (GDP) per capita were analysed with prevalence, incidence, YLDs, and mean duration of urticaria. These metrics were assessed and compared using age-adjusted values to account for differences in the age distributions across populations. The 95% uncertainty intervals were used to assess equivalence of estimates when comparing data values between cohorts.

GDP per capita in US dollars was obtained from Worldometer (https://www.worldometers.info/gdp/), a data source that publishes statistics on economics and other fields (9). GDP per capita was used as an approximation of economic development and the study evaluated its relationship with prevalence, incidence, and YLD.

This relationship was analysed for 170 countries in 2017 which had reported data in both the GBD and Worldometer databases (7, 9). The data were analysed using multivariate regression analyses with SAS University Edition (SAS Institute Inc., Cary, NC, USA).

RESULTS

Prevalence of urticaria

The global prevalence of urticaria in 2017 was 86 million people; approximately 1.1% of the global population. Countries in the lowest quintile of SDI (1,170, 1,165) had a greater age-standardized prevalence rate than that of the highest quintile of SDI (885, 872) in both 1990 and 2017, respectively. This difference was outside the 95% uncertainty interval. Between 1990 and 2017, females had a higher age-standardized prevalence rate compared with males (Table SI; all supplementary Tables are available from: https://drive.google.com/file/d/1L1ktsnsevvUxeJvUnWEmvnEeo2nh-jP6/view?usp=sharing). This difference was also outside the 95% uncertainty interval. The age of highest prevalence per 100,000 was between 1 and 4 years, with an overlap in uncertainty with those between 5 and 9 years (**Fig. 1**, Table SIIa). Afghanistan (1,426) followed by Yemen (1,381) and Sudan (1,365), had the highest non-age-standardized prevalence rates in 2017 (Table SIIIa, **Fig. 2**). The Russian Federation (1,315), followed by the Ukraine (1,315) and Iran (1,280), had the highest age-standardized prevalence rates per 100,000 in 2017; however, the differences between the countries were within the 95% uncertainty interval (Table SIVa).

Incidence of urticaria

The global incidence of urticaria in 2017 was 160 million new cases annually. Countries in the lowest quintile of SDI had a higher age-standardized incidence rate (2,064, 2,054) than that of the highest quintile of SDI (1,564, 1,541) in both 1990 and 2017. This difference was outside the 95% uncertainty interval. Females had a higher age-standardized incidence rate compared with males between 1990 and 2017 (Table SIb). The sex difference was outside the 95% uncertainty interval. The age of greatest incidence per 100,000 was between 1 and 4 years, with an overlap in uncertainty with those between 5 and 9 years (Fig. 1, Table SIIb). Geographical patterns of incidence were similar to those for prevalence rates. The highest non-age standardized incidence rates in 2017 were in Afghanistan (2,542) followed by Yemen (2,450) and Sudan (2,420) (Table SIIIb). The age-standardized incidence rate for 2017 was highest in the Russian Federation (2,318) then the Ukraine (2,317), followed by Iran (2,257) (Table SIVb). The regional variations were within the 95% uncertainty interval.

Years lived with disability

The global YLD rate in 2017 was 68 per 100,000 population. Countries in the lowest quintile of SDI had a higher age-standardized YLD rate than that of the highest quintile of SDI in both 1990 and 2017; however, this difference was within the 95% interval of uncertainty. Between 1990 and 2017, females had a higher age-standardized YLD rate compared with males. This

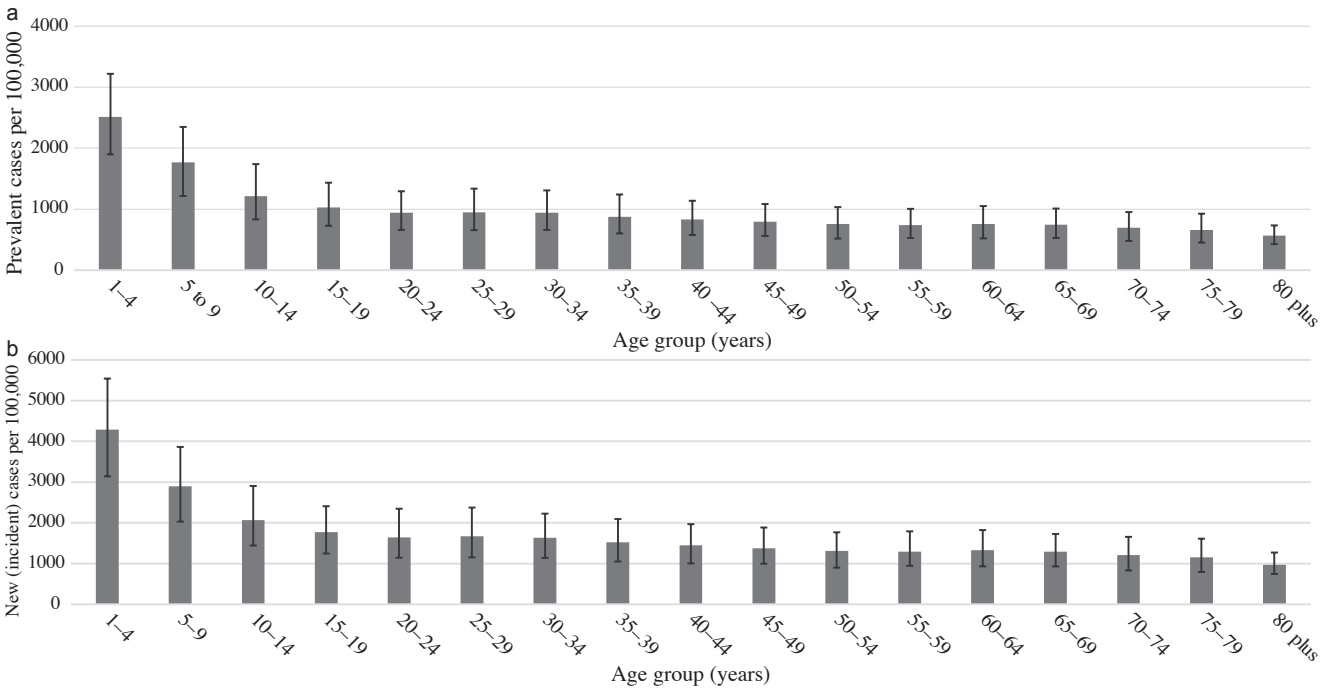

Fig. 1. Age-standardized global incidence and prevalence by gross domestic product (GDP) in US dollars per capita in 2017, with linear trend line and R^2.

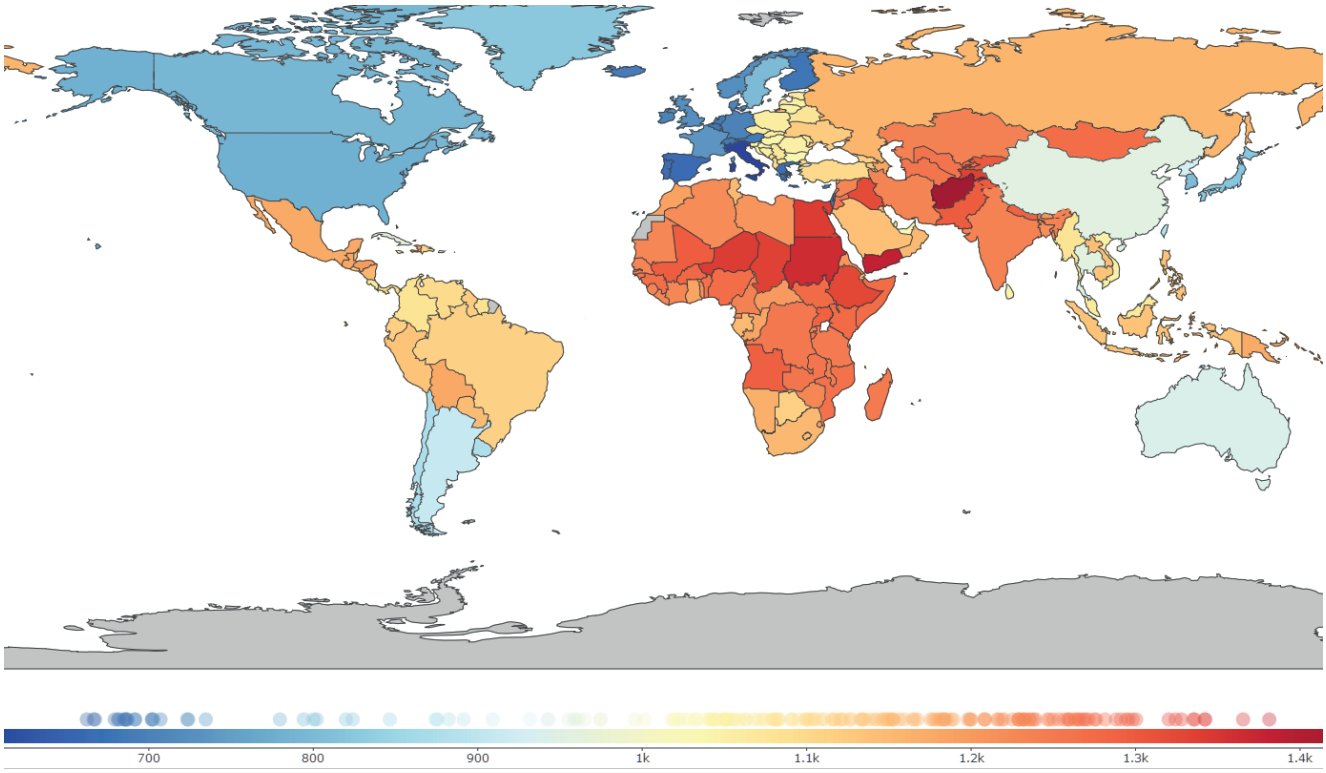

Fig. 2. Global distribution of urticaria. Prevalence of urticaria per 100,000 population in 2017. *Source:* Global Burden of Disease, Institute of Health Metrics and Evaluation (IHME), University of Washington. https://vizhub.healthdata.org/gbd-compare/.

difference was within the 95% uncertainty interval (Table SIc).The countries with the highest non-age-standardized YLD rates in 2017 were Afghanistan (86), followed by Sudan (82) and Yemen (82) (Table SIIc). For 2017 age-standardized YLD, the Russian Federation (79) and the Ukraine (79), followed by Iran (77) had the highest rates (Table SIIIc). However, these variations were within the 95% uncertainty interval.

Mean duration of disease

The current global mean duration of disease in 2017 was 0.57 years. The mean duration of disease in 1990 and 2017 in both the lowest and highest quintile of the SDI was 0.57 years. The mean duration of disease in 1990 and 2017 for both females and males was 0.57 years (Table SId). Similarly, there were no significant differences in the mean duration of disease by age or country in 1990 and 2017, and values ranged between 0.57 and 0.61 years (Tables SIIc, SIIId, and SIVd).

Trends from 1990 to 2017

The age-standardized global prevalence, incidence, YLD, and mean duration of disease rates per 100,000 population between 1990 and 2017 remained relatively

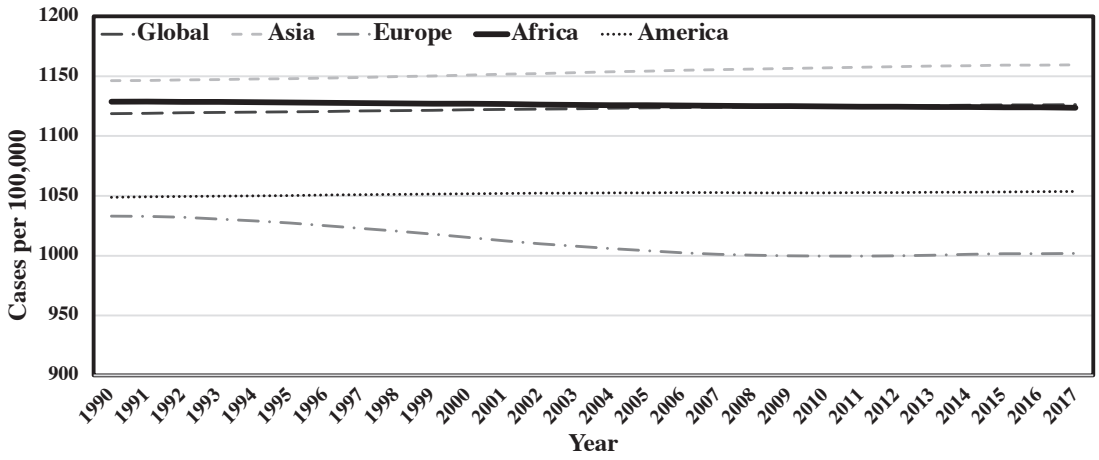

Fig. 3. Trends in prevalence of urticaria from 1990 to 2017.

unchanged, both globally and in the 4 GBD-defined regions. The differences from 1990 to 2017 were within the 95% uncertainty intervals (**Fig. 3**).

Multivariate analysis with gross domestic product

Regression analysis showed that, in 2017, for every 1 US dollar increase in GDP per capita, there was a small decrease of 0.0035 (95% uncertainity interval 0.0017–0.0050) prevalent cases per 100,000, 0.0062 (95% uncertainity interval 0.0031–0.0093) incident cases per 100,000, and 0.0002 (95% CI 0.0010–0.00031) YLDs per 100,000 ($p < 0.001$) (**Fig. 4**). Regression analysis controlled for age differences in the respective populations.

DISCUSSION

This study found that countries with lower socioeconomic development have higher age-standardized incidence, prevalence, and YLD rates of urticaria. Children have higher disease morbidity than adults, and females have a greater burden of disease than males. The age-standardized prevalence, incidence, and YLD rates of urticaria per 100,000 remained relatively unchanged between 1990 and 2017. Age, sex, and geographical location had no impact on the mean duration of the disease.

The finding that paediatric patients have increased disease morbidity compared with adults is in contrast to previous studies suggesting that urticaria is less common in children (4, 5, 10, 11). Specifically, the prevalence of urticaria in paediatric patients was previously thought to be approximately one-tenth that in adults (12). However, the current results show that urticaria is more common in children, especially ages 1–4 years, compared with adults (Fig. 1). The reason for this difference between the current results and previous studies is unclear. A possible explanation could be that most of these studies were completed in high-income countries (4, 5, 10, 11). There is insufficient evidence to explain why urticaria may be more common in children, and further research is needed. The current study showed that urticaria has a greater burden of disease in low-income regions; thus, further studies on the paediatric epidemiology of this condition in low-income regions may offer insight into the reasons for this finding.

The higher morbidity of urticaria amongst children is clinically important, because this disease imposes a notable burden on children. Paediatric patients with urticaria have higher rates of inpatient and outpatient healthcare visits and cost, mean of US$2,090 more per year on total healthcare compared with healthy children (13). Adding to the socioeconomic burden of urticaria, many children with urticaria have additional comorbidities. One study found that 70% of children with urticaria have comorbid psychiatric disorders and vitamin D deficiency (14). Atopy, thyroid conditions, and *H. pylori* infection are other common comorbidities (14, 15). Despite this considerable burden of disease, there is a lack of published guidelines for clinical management of urticaria, or studies on the pathogenesis of the disease, and the burden of disease amongst children (16). Further research and resources dedicated to improving the clinical management of urticaria in children are necessary.

Countries with a lower GDP per capita often have less access to healthcare resources and physicians, which may result in suboptimal management of urticaria. This may contribute to our finding of higher prevalence of urticaria in areas with lower socioeconomic development. This is particularly notable because of the high disease burden associated with urticaria. Urticaria has quality of life scores similar to ischaemic heart disease or moderate-to-severe psoriasis (17, 18). In both adults and children, urticaria has been shown to lead to absenteeism, lower

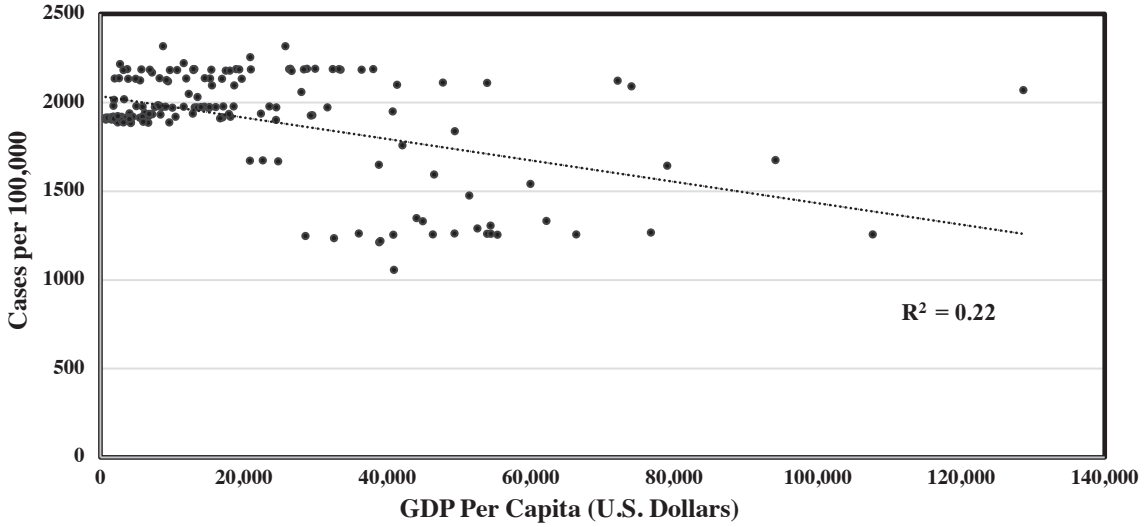

Fig. 4. Global prevalence and incidence of urticaria by age. (a) Global prevalence by age in 2017. (b) Global incidence by age in 2017.

productivity, and increased incidence of depression, anxiety, and other autoimmune diseases (2, 6).

The higher morbidity of urticaria in lower income regions may also be explained by the higher burden of infectious disease and environmental pollution in these regions (19, 20). A causal relationship between urticaria and infections (especially parasitosis) and pollution is well established (4, 21, 22). Infections are the most commonly identified cause of urticaria, and eradication of the infectious disease has been shown to reduce the likelihood of developing urticaria (21). In addition, countries with some of the highest urticaria morbidity rates are also ranked amongst the top countries for worst air quality indices; for example, Afghanistan, Ukraine, Iran, Sudan and Russia are all ranked amongst the top 20 countries for low air quality index (23). Increased rates of infectious disease and poor air quality may contribute to the increased morbidity of urticaria amongst low-income regions.

Study limitations

The principal limitation of this study is its reliance on secondary data. The GBD utilizes estimation models based on multiple sources in order to derive its dataset (8). With fewer physicians in certain geographical locations, there is a lack of accurate coding of data in these global regions. The GBD interpolates information from nearby countries and regions in order to derive the data estimates for these particular countries and regions. A further limitation of the GBD is that the data do not differentiate between acute and chronic urticaria (8, 24). In addition, in the GBD, skin disease disability is characterized only by physical symptoms, and the impact on other aspects of a patient's life, such as mental health, is not considered (25, 26). However, despite these limitations of the data, the GBD is a resource that allows us to quantify global epidemiological data over time (8).

Conclusion

Understanding the global prevalence, incidence, mean duration of disease, and YLDs of immunological diseases, such as urticaria, is important for developing a sustained and concerted response to reducing the burden of disease (25–27). Much of the existing epidemiological literature has utilized data from a single country to predict burden of disease on a global scale, a method that lacks global external validity and produces incongruity in the literature (1, 5, 6, 28, 29).

To our knowledge, one study has used the GBD 2016 results to evaluate the relationship of geographical distribution and age with disability-adjusted life years (DALYs) for urticaria (30). However, by extending the evaluation of the GBD's data on urticaria, the current study was better able to define the global epidemiology of urticaria and establish that individuals living in lower income regions, females, and children aged 1–4 years are more commonly impacted worldwide. The demographic characterization of urticaria globally can aid clinicians in diagnosing the disease, and public health officials in predicting future disease trends in order to allocate resources appropriately. Overall, this study suggests that future healthcare initiatives to reduce the burden of urticaria should be directed at low-income regions, women, and young children.

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Conflicts of interest. ABF is a consultant for Boerhringer-Ingelheim, Incyte, Qurient, SCM Lifescience, and Syneos. He is an investigator for Galderma and Trevi. The other authors have no conflicts of interest to declare.

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