



Asthma mortality in Serbia: a 30-year analysis

Dragica P. Pesut^{a,b,*}, Milica V. Bulajic^c, Ljudmila M. Nagorni-Obradovic^{a,b}, Anita D. Grgurevic^d, Zorana B. Gledovic^d, Dimitrije R. Ponomarev^e, Ana Z. Blanka^b

^a School of Medicine University of Belgrade, Internal Medicine Department, Belgrade, Serbia

^b Teaching Hospital of Lung Diseases, Clinical Centre of Serbia, Belgrade, Serbia

^c Faculty of Organizational Sciences, Laboratory of Statistics, Belgrade, Serbia

^d School of Medicine University of Belgrade, Institute of Epidemiology, Belgrade, Serbia

^e Teaching Hospital Centre Zvezdara, Department of Allergology and Pulmonology, Belgrade, Serbia

KEYWORDS

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Summary

Introduction: The asthma mortality pattern differs among countries. No published evidence is currently available on asthma mortality in a European low-middle-income country in socioeconomic transition. We analyzed the trend of asthma mortality rate in Serbia during the period 1980-2009.

Materials and Methodology: a descriptive study; source of data: Republic of Serbia Institute of Statistics Death Registry. We analyzed asthma mortality data in the total population, including gender specific analysis, and in the selected ≥ 5 -34 year age group. The International Classification of Diseases codes for asthma 493 (1980-1996) and J45+J46 (1997-2009) were included. Population estimates were based on 1991 and 2002 census data, with extrapolation.

Results: The over-all average mortality rate was $7.27 \pm 2.14/100,000$ inhabitants. The mortality rate peaked in 1981 at $11.3/100,000$ but was $4.45/100,000$ in the last year of analysis. While both overall mortality rate, as well as gender specific rates, showed clear decreases over the observed 30-year period (average absolute annual decrease of $0.195/100,000$ inhabitants, $0.241/100,000$ men and $0.149/100,000$ women; $p < 0.001$) with corresponding relative annual decreases of 2.9% for the whole population, 3.0% for men and 2.8% for women, a stable trend of the rate was found in the age group ≥ 5 -34 years. Male-to-female ratio was 1.59 ± 0.186 , on average and it showed a stable trend over the observed period.

Conclusion: Although the failure of the health care system during the socioeconomic crisis of the 1990s might have transiently affected asthma mortality rates, the overall mortality rate for the disease shows a favorable decreasing trend.

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Introduction

Asthma is a major public health problem. The project Global Burden of Asthma showed variable burdens and trends of the disease worldwide.¹⁻³ The reasons for exacerbations of severe asthma are complex and include underestimation by

the patients or failure of health care. If not recognized and treated properly, these exacerbations can be fatal.^{4,5} Although asthma related deaths are rare and should be entirely avoidable, the mortality from this disease has even shown an increased tendency in the last few decades.³

Specific factors that have been identified as associated with a higher risk of asthma mortality include a previous history of life threatening acute attacks, hospitalization within the previous year, psychosocial problems, a history of intubations for asthma, recent reductions or cessation of glucocorticosteroid therapy and non compliance with rec-

* Corresponding author. Prof. Dragica Pesut, MD, PhD.
Teaching Hospital of Lung Diseases, Clinical Centre of Serbia,
11000 Belgrade, Visegradska 26, Serbia.
Tel.: 381 11 366 39 56; fax: 381 11 268 15 91.
E-mail: dragica.pesut@gmail.com (D. Pesut).

ommended therapy.^{4,6} Although with conflicting evidence, some drugs like long-acting β -agonists may also contribute to asthma related death.⁷ Individuals at risk of death from asthma are more likely to be non-Caucasian and young⁸ but African American patients are not at increased risk for death relative to Caucasian/Semitic ones.⁹ Some recent results support the existence of a genetic basis to the severe asthma phenotype, including asthma-related death.¹⁰

Several unfavorable trends and epidemics of fatal asthma have been registered in various developed countries of Europe, the United States of America and New Zealand over the last three decades.¹¹ International comparisons revealed some striking differences in the pattern of asthma mortality.^{8,12} Country-specific data on asthma mortality rates since 1960 in the 5- to 34-year-old age group were collated recently. Elevated asthma mortality rates were observed in the 1960s, with a mean increase of 53% from 0.55 per 100,000 in 1960 and 1961 to a peak of 0.84 in 1966 and 1967.¹¹ This trend was followed by a progressive decline to a nadir of 0.45 per 100,000 in 1974 and 1975. Asthma mortality rates then gradually increased again to a peak of 0.62 per 100,000 in 1985 and 1986, with a mean increase of 38%.^{3,8} Since the late 1980s, there has been a widespread and progressive overall 63% reduction in mortality rate down to 0.23 per 100,000 in 2004 and 2005.^{3,11}

We analyzed asthma mortality in Serbia between 1980 and 2009. The socioeconomic crisis in this South Eastern European country in the 1990s heavily affected the health care system and led to serious interruption of medical supplies, which could affect asthma mortality rates.¹³

Materials and methodology

We provided the data for this 30-year descriptive study from the Death Registry of the Republic of Serbia Institute of Statistics in Belgrade. The International Classification of Diseases (ICD) codes for asthma 493 (1980-1996) and J45+J46 (1997-2009) were included in the analysis. The existing ICD was replaced by ICD 10 in January 1997. While the earlier ICD included 493 as the only code for asthma, the new classification used both J 45 and J 46 to distinguish between more and less severe forms of asthma.

Apart from the asthma mortality rates for the whole population of Serbia (7,320,807 inhabitants in 2009), we separately analyzed the ≥ 5 -34 age group because the diagnosis of asthma mortality is firmly established for this latter one. Namely, it has been shown that in the ≥ 5 -34 years age group false-positive reporting (i.e. deaths from other causes falsely attributed to asthma) and false-negative reporting (i.e. asthma-related deaths falsely assigned to other categories) were extremely low.¹ However, the accuracy of this approach declines with increasing age, with false positive reporting rates of >30% in those aged 65 years or more.¹

Population estimates based on 1991 and 2002 census data with extrapolation were used to calculate asthma mortality rates in the observed period. A regression line was fitted to the annual age specific mortality rates for (a) all ages, for (b) the ≥ 5 -34 age group and (c) gender specific mortality to ascertain the probability (p) values. Mortality rates were expressed as number of asthma related deaths per 100,000 (No/100,000) inhabitants. Gender specific rates

were calculated as numbers of male or female asthma-related deaths per 100,000 male or female inhabitants, respectively. Linear, log-lin regression models and the least squares method were used to test trends and fit trend lines. For linear regression: value on the vertical axis = intercept \pm slope multiplied by the value on the horizontal axis + stochastic error term ($Y_t = \alpha_0 + \alpha_1 t + \varepsilon_t$). The slope α_1 represents the average absolute annual change of Y when the annual trend is tested. The log-lin model ($\ln Y_t = \beta_0 + \beta_1 t + \varepsilon_t$, where $\ln Y_t$ denotes natural logarithm of Y_t) was used in order to estimate and test the average relative annual change of Y, expressed as $(\beta_1 - 1)100\%$. The IBM SPSS (Statistical Package for the Social Sciences) Statistics, version 19 was used to estimate and test regression coefficients.

Results

The over-all average asthma mortality rate was 7.27 ± 2.14 /100,000 inhabitants (95% confidence interval [CI], 6.48-8.07). The rate peaked in 1981 with 11.3/100,000 and decreased to 4.45/100,000 in the last year of analysis. The average gender specific mortality rates were significantly different (3.32 ± 1.27 , $p < 0.001$). Thus, total mortality rate showed a clear decline over the observed 30-year period (absolute average annual decrease: 0.195; $p < 0.001$; 95%CI, -0.251; -0.139) with a relative annual decrease of 2.9% (Fig. 1). Gender related rates showed similar

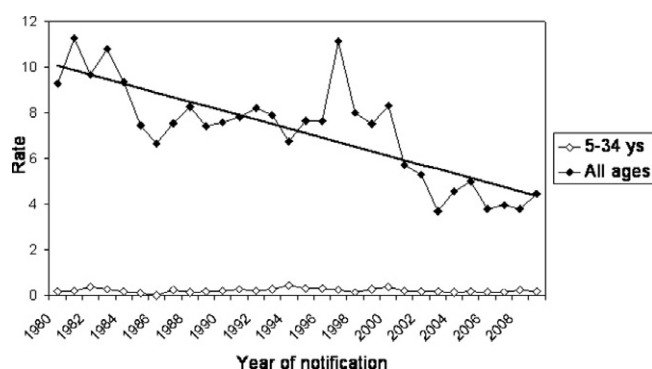


Fig. 1. Trend of asthma mortality rate in Serbia in the period 1980-2009. Total mortality rate decreased over the observed 30-year period ($y = 10.07 - 0.179x$; $p < 0.001$) while a slight non-significant increase of asthma mortality rate was seen in the age group ≥ 5 -34 years ($y = 0.203 + 0.001x$; $p = 0.744$). Mortality rate is expressed as case numbers per 100,000 inhabitants (No/100,000). Closed-rhombus line: asthma mortality rate in the total population (full line is the trend line); open-rhombus line: asthma mortality rate for ages ≥ 5 -34 years.

decreasing trends in both sexes but more expressed in men ($-0.241/100,000$ males or 3% annually; $p < 0.001$) than in women ($-0.149/100,000$ females or 2.8% annually; $p < 0.001$) (Fig. 2). Asthma mortality rate in the age group ≥ 5 -34 years was $0.21 \pm 0.09/100,000$ inhabitants, with a relatively stable trend during the analyzed period (Fig. 1). The male-to-female ratio showed that male asthma-related deaths predominated over female ones for all the years of the analysis (mean: 1.59 ± 0.186). The ratio trend was stable over the period, being the lowest in the last two years (Fig. 3).

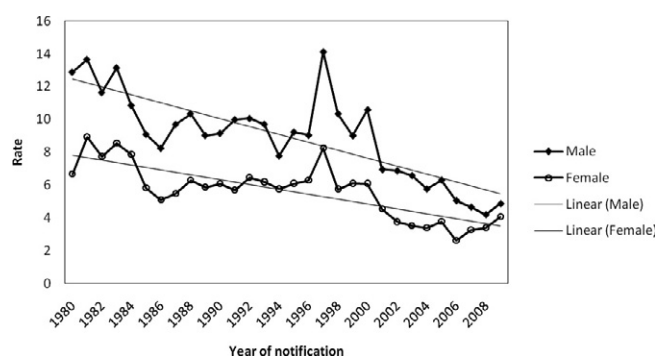


Fig. 2. Time trend of gender specific asthma mortality rates in Serbia, 1980–2009, No/100,000 inhabitants. Gender related rates showed similar decreasing trends in both sexes. This was more expressed in males ($-0.241/100,000$ men or 3%, annually; $p < 0.001$) than in females ($-0.149/100,000$ women or 2.8%, annually; $p < 0.001$).

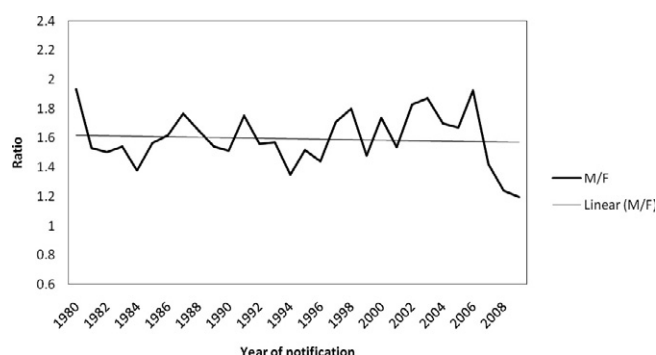


Fig. 3. Male-to-female ratio in asthma-related mortality in Serbia, 1980–2009. The male-to-female ratio (thick line) shows that male cases predominated over female ones for all the years of the analysis (mean value 1.59 ± 0.186). The time trend is stable.

Discussion

The overall asthma related mortality in our study showed a decreasing trend over the period 1980–2009. In Scandinavian countries, asthma mortality rates have declined markedly over the last ten years,¹ a trend attributed to improvements in asthma management, and similar findings were recently reported in France.¹⁴ Although the reduction in mortality rates generally was consistent among several countries, there was variation in the timing of its onset.¹¹ While our mortality rates peaked in 1981, this happened in England and Wales in 1987, with a progressive decline up to 2005, whereas in the United States, mortality did not peak until 1995, with a subsequent decline to 2005.¹¹ The decrease in our study was especially evident during the last few years, which were characterized with steadily improved treatment, as new generations of drugs¹ were both available and accessible for the majority of patients. The national adherence to globally accepted modern approaches in the diagnostics and management of asthma resulted in easy-to-access guidelines to facilitate health care workers' practice and education. General awareness about asthma symptoms, education of patients and implementation of self-management programs in asthma treatment¹⁵ could also improve early detection of instability and worsening of

the disease, prevent an unfavorable disease outcome and contribute to over-all reduction of asthma mortality.

Our study also showed a rather stable trend of asthma mortality rate of $0.21 \pm 0.09/100,000$ on average in the selected ≥ 5 –34 year age group. Among the twenty countries recently included in an analysis of asthma mortality rate per 100,000 inhabitants in the same age group, the lowest average rate of 0.14 was found in Finland, and the highest of 1.4 in New Zealand.¹¹ The average asthma mortality rate in this age group in our study is similar to values observed in Spain and the Netherlands during the same 30-year period¹¹ but lower than those found in Norway (0.26), Australia (0.3), Sweden (0.3), France (0.35), Canada (0.41), United States (0.42) and Germany (0.49). In Japan, the Republic of Ireland, England, Hong Kong and Austria, rates were higher than 0.5/100,000 inhabitants. The stable trend in this age group found here compared to the decreasing trend of overall mortality rate, could be explained by the younger age^{8,16} and possible influence of exposure to outdoor and indoor pollution, especially to environmental tobacco smoking,^{16–19} which is a serious problem in the local setting.^{20,21} There is overwhelming evidence that exposure to parental smoking has obvious adverse effects upon the respiratory health of young children.^{18,19} Gergen et al. found an increased odds ratio of 2–3 for asthma in children 2 months to 5 years old¹⁶ and some studies also included maternal smoking during pregnancy to show that the effects of exposure to tobacco smoke started before birth.²² Anti-tobacco policies and strengthening programs for prevention and cessation of tobacco smoking might have a considerable positive effect on disease severity and lethal outcome in a number of patients, especially in the younger age group.²²

Although a distinctive feature of asthma mortality is the low difference between the sexes,³ the results of our study show the Male/Female ratio 1.59 ± 0.186 . In a Japanese study based on the same methodology, asthma mortality rates were higher in men than in women during the entire study period between 1950 and 1997.²³

The validation studies have shown significant inaccuracies in certification of cause of death in older subjects, and probable underreporting of asthma deaths in some countries.⁸ These could explain some of the international differences noted and may be a limitation of our study as well. Our source of data was the National Institute of Statistics with a tradition of recording and reporting mortality from asthma and other diseases since 1947. Validity of data collected by National Institute of Statistics are further strengthened by the fact that Serbian data are close to regional lowest asthma prevalence in the Balkans with mean prevalence of clinical asthma 6.1% and prevalence in Albania 1.1%, Romania 1.5%, and Greece 1.9%.^{1,4,24} Asthma mortality rates are generally low in countries within this region, reflecting to some degree the low prevalence rates.⁴

One pattern seen in most regions of the world is an increase in asthma mortality rate with increasing age.¹ Even taking into consideration the decline in certification accuracy in older age groups, this does indicate a considerably greater risk of death in older asthmatics and the importance of care in this group.¹ Introduction of the ninth revision of the World Health Organization International Classification of Diseases brought a steep increase in reported asthma mortality rates in 1979.¹ Detailed analysis

of our mortality rate line revealed that the rate dropped only after the first few years of analysis (Fig. 1). However, the gradual increase in mortality rates in many countries during the 1980s and 1990s could not be explained by this change in code.⁸ After 1984, asthma mortality rates in Serbia showed rather stable rates below 8.3/100,000 except for 1998 when health care services failed and there was a serious shortage of medical supplies.¹³

It is still estimated that asthma accounts for about one in every 250 deaths worldwide.¹ Many of them are preventable, being due to suboptimal long term medical care and delay in obtaining help during the final attack.¹ This may also depend on the particular socioeconomic conditions, which influence access to health care and are different among countries.¹ Currently, new directions for novel asthma therapies have been proposed, which may influence asthma mortality in the future.²⁵

Conclusion

Although failure of the health care system during the socioeconomic crisis of the 1990s might have transiently affected asthma mortality rates in Serbia, the overall asthma-related mortality rate showed a favorable decreasing trend during the examined 30-year period. Nevertheless, asthma-related death remains a challenge, especially for treatment related investigations that could point to more effective therapy, leading to further mortality decrease and possibly primary prevention of the disease.

Conflict of interest statement

The authors declare that they have no competing interest.

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