Structure of comorbidity in urban population with essential hypertension in the clinical practice of a local general practitioner


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Abstract: Taking into account gender- and age-related features, to examine the structure of comorbidity in outpatients with essential hypertension residing in the city of Tambov.

Material and Methods — This research was an observational cross-sectional study based on data extracted from 47,113 electronic medical records (EMRs) of patients 20-99 years of age residing in Tambov. The study included 29,282 (62.2%) women and 17831 (37.8%) men.

Results — Essential hypertension is habitually associated with osteochondrosis (41.5% of patients with hypertension), cerebrovascular diseases (35.1%), artherosclerosis (28.3%), ischemic heart disease (IHD) (28.7%), menopausal disorders (17.5%), pancreatic diseases (15.4%), diabetes mellitus (14.7%), benign mammary dysplasia (14.2%), retinal diseases (12.9%), disorders of lipoprotein metabolism (12.4%), senile cataract (10.6%), gastritis and duodenitis (10.7%), varicose veins (10.1%), and thyroid diseases (10.0%). IHD is more common among men with hypertension, while other comorbidities are more characteristic for women. The most striking gender-related difference was associated with the finding that women with hypertension had varicose veins as a comorbidity (RR=1.398; 95% CI 1.376-1.422), while the smallest difference between genders related to retinal diseases (RR=1.065; 95% CI 1.038-1.092). IHD was strongly associated with the male gender (RR=1.148). Three diseases were more often associated with hypertension in the age range of 80-89 years (cerebrovascular disease, IHD, osteochondrosis); some of the diseases had the highest incidence in the age range of 60-69 years, and other disorders occurred in the age range of 40-59 years.

Conclusion — The gender- and age-related features of comorbid pathology associated with essential hypertension among urban residents revealed in this study are extremely important in the clinical practice of a local general practitioner for developing optimal patient-oriented treatment plans.

Keywords: essential hypertension, comorbidity, electronic medical records, cardiovascular diseases.


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Introduction

Essential hypertension (EH) is among the most common chronic diseases in many countries and a major risk factor for the development of cardiovascular diseases [1].

Local general practitioners encounter patients suffering from EH on a daily basis; however, the situation is complicated by the presence of comorbid pathology among such patients, which aggravates the course and outcome of the underlying disease, which constitutes a serious problem for primary care physicians.

To date, sufficient epidemiological data have been accumulated on diseases associated with EH among the population of the Russian Federation. Hence, according to the results of the RECVAZA population study, the structure of concomitant cardiovascular pathology and comorbidities among patients included in the registry of cardiovascular diseases was established [2]. According to the ESSE-RF multicenter observational study, the relationship between EH and cardiometabolic diseases was examined [3, 4]. There are also epidemiological data on the relationship of EH with individual specific diseases [5].

At the same time, there are differences in the design and results of conducted studies, while the literature does not provide epidemiological data on the most comprehensive profile of comorbid pathology associated with EH among the urban population, taking into account gender- and age-specific differences encountered by local general practitioners in their clinical practice.

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Since comorbid pathology is associated with a low level of compliance [6], more frequent visits for medical care [7], polypharmacy [8, 9], and higher patient costs for treatment [10], understanding the structure of comorbidity associated with EH would allow internists to choose the most optimal treatment plan for the patient, observing the principles of rational pharmacotherapy. Thus, the objective of our study seems quite relevant: taking into account gender and age characteristics, to examine the structure of comorbidity among outpatients with essential hypertension living in the city of Tambov.

Material and Methods

Study design

By design, our research was an observational cross-sectional study based on information extracted from electronic medical records (EMRs) of patients 20 to 99 years old living in Tambov and assigned to the city outpatient polyclinic for medical care. All medical appointments of city residents, covered by compulsory health insurance, in public health facilities were entered into the EMRs.

Overall, demographic data were extracted from 47,113 EMRs, regarding dates of seeking medical help and established diagnoses for the period from January 1, 2015, through December 31, 2019. In the studied cohort, there were 29,282 (62.2%) women and 17,831 (37.8%) men. The EMR diagnoses in the study cohort were coded in accordance with the 10th revision of the International Classification of Diseases. EH was coded as I10.X and I11.X and was identified in 21,514 EMRs. All diagnoses were subjected to primary analysis, and diagnostic pairs were subsequently selected, one of which was EH, and the other was a chronic disease with an incidence rate among patients with EH above 10%.

The personal data of patients extracted from EMRs were encrypted and anonymized, their further identification was impossible. During the study, the patients were not prescribed medical tests and treatment, clinical trials were not conducted: hence, the informed consent of the patient to participate in the study was not required.

Statistical analysis

Quantitative parameters are presented as M±SD (95% CI of M), where M is the mean value of the parameter, SD is the standard deviation, CI is 95% confidence interval with a confidence level of 95%. For parameters characterizing qualitative features, the absolute number (n) and the relative value as a percentage were indicated. The study of age differences between groups (having a normal distribution sensu Kolmogorov-Smirnov test) was carried out via Student’s t-test (t_{st}), with a preliminary check of the distribution normality of quantitative characteristics using the Lilliefors test. The analysis of differences in the incidence of comorbidity in the compared groups was carried out using the contingency tables, with the calculation of Pearson’s Chi-squared test ($\chi^2$) and the achieved level of statistical significance. Statistical significance was assumed at $p<0.05$.

The incidence rate of a disease associated with EH was calculated using the following formula:

$$P = \frac{A}{B} \times 100\%$$

(1) where $P$ is the ratio of the number of patients with EH-associated disease ($A$) to the total number of patients with EH ($B$).

The relative risk (RR) was calculated as:

$$RR = \frac{a/(a+b)}{c/(c+d)}$$

(2) where $a$ is the number of women with the analyzed disease associated with EH, $b$ is the number of men with the analyzed disease associated with EH, $c$ is the number of women with EH without the analyzed concomitant disease, and $d$ is the number of men with EH without the analyzed concomitant disease.

For the analysis, comorbid chronic diseases were selected with an incidence rate among individuals with EH exceeding 10%. Statistical analysis was performed using Microsoft Excel–2016, IBM SPSS Statistics 23.0.

Table 1. Rank structure of incidence rate of chronic comorbidities associated with essential hypertension (EH)

<table>
<thead>
<tr>
<th>Concomitant diseases</th>
<th>Incidence rate, n (%)</th>
<th>Significance level of differences (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal osteochondrosis</td>
<td>8,926 (41.5)</td>
<td>7,360 (28.8)</td>
</tr>
<tr>
<td>Cerebrovascular diseases</td>
<td>7,548 (35.1)</td>
<td>1,074 (4.6)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>6,184 (28.7)</td>
<td>1,101 (4.3)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>6,079 (28.3)</td>
<td>1,921 (7.5)</td>
</tr>
<tr>
<td>Menopausal disorders and other perimenopausal disorders</td>
<td>3,757 (17.5)</td>
<td>459 (1.8)</td>
</tr>
<tr>
<td>Other diseases of the pancreas</td>
<td>3,320 (15.4)</td>
<td>1,529 (6.0)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3,171 (14.7)</td>
<td>438 (1.7)</td>
</tr>
<tr>
<td>Benign mammary dysplasia</td>
<td>3,049 (14.2)</td>
<td>2,054 (8.0)</td>
</tr>
<tr>
<td>Other diseases of the retina</td>
<td>2,780 (12.9)</td>
<td>479 (1.9)</td>
</tr>
<tr>
<td>Lipoprotein metabolism disorders and other lipidemias</td>
<td>2,665 (12.4)</td>
<td>1,401 (5.5)</td>
</tr>
<tr>
<td>Gastritis and duodenitis</td>
<td>2,367 (10.7)</td>
<td>1,890 (7.4)</td>
</tr>
<tr>
<td>Senile cataract</td>
<td>2,270 (10.6)</td>
<td>183 (0.7)</td>
</tr>
<tr>
<td>Varicose veins of the lower limbs</td>
<td>2,180 (10.1)</td>
<td>682 (2.7)</td>
</tr>
<tr>
<td>Thyroid diseases</td>
<td>2,149 (10.0)</td>
<td>885 (3.5)</td>
</tr>
</tbody>
</table>

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Chronic diseases were detected in 82.7% of EH patients, and 14 chronic diseases concomitant in patients with EH had an incidence rate of 10.0% or more (Table 1).

The collected data confirmed that the listed chronic diseases occurred significantly more often in patients with EH, compared with patients without EH.

The results of the analysis of gender-based differences in the incidence of chronic pathology associated with EH made it possible to establish that both female and male cohorts in most cases were accompanied by spinal osteochondrosis. Top second and third ranks in terms of the comorbidity frequency in women with EH belonged to cerebrovascular diseases and arthritis. Among men with EH, ischemic heart disease (IHD) ranked second, while and cerebrovascular diseases ranked third (Table 2).

Also, among the studied chronic diseases associated with EH, IHD was associated with men, and RR of developing IHD in the male cohort was 1.101 (95% CI 1.056-1.148) times higher vs. female cohort.

Other analyzed diseases were associated with women. For instance, in female cohort, EH was associated with an increased RR of developing thyroid diseases (RR=1.398; 95% CI 1.376-1.422), varicose veins of the lower limbs (RR=1.244; 95% CI 1.204-1.285), arthritis (RR=1.126; 95% CI 1.103-1.157), spinal osteochondrosis (RR=1.126; 95% CI 1.106-1.147), gastritis and duodenitis (RR=1.121; 95% CI 1.093-1.150), senile cataract (RR=1.095; 95% CI 1.067-1.124), diabetes mellitus (RR=1.231; 95% CI 1.204-1.258), and other diseases of the pancreas (RR=1.114; 95% CI 1.113-1.154).
mellitus (DM) (RR=1.078; 95% CI 1.053-1.103), and other retinal diseases (RR=1.065; 95% CI 1.038-1.092).

We established that the structure of chronic pathology concomitant with EH changes with age. E.g., three most common chronic diseases associated with EH in the study group of people aged 20-39 years were spinal osteochondrosis, other diseases of the pancreas, along with gastritis and duodenitis (Table 3).

In the studied cohort of patients with EH at the age of 40-59 years old, the first three ranking places in terms of incidence rate fell on spinal osteochondrosis, arthrosis and cerebrovascular diseases. The cohorts of people with EH, aged 60-79 and 80-99 years, were characterized by the highest incidence of cerebrovascular diseases, IHD and spinal osteochondrosis, but the frequency of their association varied with age.

Comparative analysis of age-related differences in the incidence rate of comorbidities typical for patients with EH demonstrated that some chronic diseases tended to increase in incidence with age, while others were characterized by a multidirectional trend: first increasing in occurrence, then declining.

E.g., cerebrovascular diseases were concomitant with EH in the studied group of 20-39 years old patients only in 3.2% of cases, whereas at the age of 80-99 years, already over a half of them suffered from cerebrovascular diseases. The similar trend of age-related increasing incidence rate was observed for IHD as a concomitant disease for EH. For varicose veins of the lower limbs, arthrosis, DM, thyroid diseases, other diseases of the pancreas, menopausal disorders, senile cataract, and other retinal diseases, an increase in their incidence rates as concomitant pathologies for EH by the age of 60-79 years was quite characteristic, followed by a decline in frequency by the age of 80-99 years old. Osteochondrosis, DLP, and benign mammary dysplasia were characterized by the maximum incidence in EH patients at the age of 40-59 years, followed by a decrease by the age of 80-99 years. Gastritis and duodenitis were detected in EH patients with different incidence rate depending on age, with a peak occurrence at 60-79 years and a minimum at the age of 80-99 years.

We discovered that nearly all analyzed chronic diseases had significant differences in the incidence rate between the groups of people aged 40-59 years vs. 60-79 years.

Meanwhile, not all compared age groups were characterized by significant differences in the incidence of chronic diseases associated with EH. For example, the incidences of other pancreatic diseases, gastritis and duodenitis, and other retinal diseases did not differ significantly between individuals 20-39 and 40-59 years of age. The incidence rate for varicose veins of the lower limbs did not differ significantly between people aged 60-79 and 80-99 years, and the incidence of DLP did not differ between the ages of 40-59 and 60-79 years.

In all analyzed age groups, we observed significant gender-based differences in the incidence of chronic pathology associated with EH: specifically, for IHD, associated with men, and thyroid disease, associated with female gender (Table 4).

In the age groups of 20-39 years, 40-59 years and 60-79 years, statistically significant gender-related differences in the incidence rates of pathologies concomitant with EH were typical for varicose veins of the lower limbs, and for gastritis and duodenitis. It is worth noting that these conditions were more typical for women.

The incidence of arthrosis associated with EH was significantly higher in the female cohort, compared with the male cohort, at the age of 40-59 years, 60-79 years, and 80-99 years.

In two age groups (40-59 years and 60-79 years), we observed significant gender-based differences in the incidence of cerebrovascular diseases, osteochondrosis, DLP, other pancreatic diseases, and senile cataract, as concomitant with EH, with their predominance in the female cohort.

For DM and other retinal diseases, concomitant with EH, significant gender-related differences in the incidence of cases were established only for the age group of 60-79 years old, with statistically significant prevalence in women.

Discussion

Our study presented new data on gender- and age-related patterns of the incidence of comorbid pathology associated with EH in outpatients living in urban areas. Our results are consistent with the data of other studies, indicating a high prevalence of comorbid pathology among patients with EH [11, 12].

Table 4. Gender-based differences in the incidence of chronic diseases associated with essential hypertension in different age groups

<table>
<thead>
<tr>
<th>Concomitant diseases</th>
<th>40-59 years</th>
<th>59-79 years</th>
<th>60-80 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>female (%)</td>
<td>male (%)</td>
<td>female (%)</td>
</tr>
<tr>
<td>Cerebrovascular diseases</td>
<td>20.3 (5.3)</td>
<td>14.3 (3.0)</td>
<td>1,114 (23.2)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>11.1 (4.9)</td>
<td>11.4 (4.1)</td>
<td>568 (11.8)</td>
</tr>
<tr>
<td>Arteriosclerosis</td>
<td>24.2 (38.3)</td>
<td>2,404 (50.0)</td>
<td>919 (36.2)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>60.10 (4.4)</td>
<td>1,432 (29.9)</td>
<td>421 (16.6)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>50.3 (5.2)</td>
<td>16.3 (3.4)</td>
<td>784 (16.3)</td>
</tr>
<tr>
<td>Thyroid diseases</td>
<td>67 (11.6)</td>
<td>8 (1.7)</td>
<td>667 (13.9)</td>
</tr>
<tr>
<td>Menopausal disorders</td>
<td>74 (12.8)</td>
<td>53.1 (11.2)</td>
<td>814 (16.9)</td>
</tr>
<tr>
<td>Benign mammary dysplasia</td>
<td>80 (13.9)</td>
<td>52.9 (8.9)</td>
<td>575 (12.0)</td>
</tr>
<tr>
<td>Other diseases of the pancreas</td>
<td>54 (9.4)</td>
<td>50 (10.6)</td>
<td>540 (11.2)</td>
</tr>
<tr>
<td>Gastritis and duodenitis</td>
<td>1 (0.2)</td>
<td>0</td>
<td>239 (5.0)</td>
</tr>
</tbody>
</table>

* – gender-based differences within the age group are significant at p <0.05 according to the χ²-Pearson’s test; ** – gender-based differences within the age group are significant at p <0.01 according to χ²-Pearson test; *** – n (%) – data are presented as absolute value and percentage.
For instance, in a study conducted on the data from RECVAZA registry, it was shown that the incidence of cardiovascular pathology concomitant with EH was 79.7%, while IHD was comorbid with EH (in combination with, or without, other cardiovascular diseases), in more than 68% of cases, which significantly exceeded our results (28.7%) [13, 14]. The data on the incidence of DM were almost comparable (19.1% vs. 14.7%), whereas erosive gastritis accompanied patients with cardiovascular diseases in 4.1% cases, which was significantly lower than in our study. Our study confirmed that comorbid chronic diseases were found in 82.7% of EH patients. However, given the differences in the methodology and design of the compared studies, there was some discrepancy in the nosology and frequency of established comorbidities.

According to the results of the study [15], based on the analysis of over 6 million case histories of patients with EH, 20% of the most common comorbitides were identified, of which the incidence of three diseases was somewhat comparable to our data: IHD (21.7% vs. 28.6%), DM (16.0% vs. 14.7%), and lipid metabolism disorders (13.8% vs. 12.4%). However, the frequencies of gastritis (2.26%) and artheros (2.0%) in that study were significantly lower than in the present study (10.7% and 28.3%, respectively). Besides, in the compared studies, there were no chronic lung diseases and oncological diseases due to their low incidence rates.

The most common comorbidity in individuals with EH in the study [16], in addition to DM (38.4%) and lipid metabolism disorders (19.6%), was bronchial asthma (11.0%), absent from our study due to the low detection rate in EH patients (below 10% of cases).

In a multicenter study of multimorbidity [17], EH was ranked as the most common chronic disease (63.1%), significantly exceeding other diseases in its occurrence, followed by IHD (35.2%), DM (27.6%), cataract (23.5%), acute cerebrovascular accident (18.1%), osteoarthritis (15.9%), and gastrointestinal tract diseases (15.5%); while despite slight differences in frequency, there was almost a close match with the obtained data on nosology. In addition, the incidence of chronic obstructive pulmonary disease was 10.4%, of chronic kidney disease 10.1%, of cancer 6.4%, which, however, was not confirmed in the present study.

In our study, the highest incidence rate in patients with EH was characteristic of spinal osteoarthritis (41.5%), and the incidence of artheros was 28.3%. These findings were partially consistent with the results of the study [17] that established the incidence rates of chronic low back pain and osteoarthritis at the levels of 34.4% and 26.2%, respectively, among 17,128 EH patients ≥ 20 years old.

Indeed, the frequency of comorbidity increased with age, reaching maximum values in old age [18]. The results of this analysis implied that there was an increase in the occurrence of cardiovascular diseases, comorbid with EH, with age, in contrast to younger people, among whom musculoskeletal system diseases were most common. Gender-specific features of the incidence of comorbidity in EH were also revealed. E.g., IHD was more common among men with EH, whereas all other chronic diseases prevailed among women with EH; and the most significant differences were found for varicose veins of the lower limbs.

The issues of comorbidity is most relevant for primary care physicians, due to the lack of a comprehensive strategy for medical care for patients with multiple chronic diseases.

E.g., DM is quite common among patients with EH, which is confirmed in the present study. Despite the high level of comorbidity of DM with EH, published sources point out an insufficient degree of control over both pathological conditions, treated by different specialists [19], which confirms the need for an individual approach to each patient.

Some associations of EH with chronic diseases are characterized by the coincidence of the principles of therapy and prevention. For example, EH and associated cardiovascular diseases are part of a single pathophysiological process and have a partial overlap in the methods of medicamentous treatment and prophylactic effects, which allows the doctor prescribing or correcting the treatment of both the underlying disease and concomitant diseases on same visit. In contrast, the association of EH with musculoskeletal diseases does not make it possible to fully implement therapeutic and preventive measures for both diseases, due to the fact that the active lifestyle required for EH would be constrained by limitation of movements in the joints with osteochondrosis or artheros, and nonsteroidal anti-inflammatory drugs prescribed for artheros exhibit cardiotoxicity.

On the other hand, despite the common pathophysiological mechanism of development between two associated diseases, such as EH and senile cataract [20, 21], the treatment of such patients is carried out by entirely different specialists, which requires an integrated approach.

Thus, the results of the present study and literature review show that comorbidity among patients with EH is the rule rather than the exception. Considering that the majority of patients with EH have comorbilities, local general practitioners most often contact them, and therefore they should have a clear understanding of the comorbidity structure, taking into account age-related and gender-based differences; and also be able to coordinate the efforts of various specialists to provide high quality medical care. It is essential for specialists to determine the best coordinated, consistent and continuous model of care that is focused on the patient with comorbidity.

Also, our study provided a compelling case for the public healthcare system to rethink primary health care provisioning in order to focus on patients with multiple diseases, as a response to the increased workload for local general practitioners.

Advantages and limitations of the study

The main advantage of our study is the use of a large amount of data extracted from EMRs for analysis. EMRs constitute a researcher-friendly source of coded data on diseases, given its low cost and fast data, collection. All instances of the patient seeking medical assistance in any public healthcare institution in the region are recorded in the EMR. Errors and biased attitude of the researcher, which could be present during the mechanical selection of outpatient records, are nonexistent.

However, it should be noted that the study has several limitations. For instance, the results obtained using the approach based on the analysis of information from EMRs obviously depended on the quality of collected data, in particular, on whether the diagnoses extracted from EMRs were confirmed by instrumental and laboratory studies, along with consultations of
relevant specialists. Within the framework of this study, the verification of diagnoses was not carried out; however, it should be noted that the data in EMRs were the basis for payments for medical services administered by insurance organizations and the territorial compulsory health insurance, the employees of which constantly monitor the volume, timing, quality and conditions for the provision of medical care by healthcare institutions. The second limitation, in our opinion, was the difficulty in extracting information from the EMRs and its subsequent processing for analysis. The third limitation was related to the fact that medical information about the patient was not reflected in the anamnesis before the introduction of EMR into practice.

Conclusion

The results of EMR analysis demonstrated that concomitant chronic diseases were revealed in 82.7% of patients with essential hypertension, whereas 14 chronic diseases were detected with an incidence rate of 10.0% or more. Most often, patients with EH had concomitant cardiovascular diseases, which included cerebrovascular diseases (35.1%), IHD (28.7%), varicose veins of the lower limbs (10.1%); musculoskeletal system diseases, which included osteoarthritis (41.5%) and arthrosis (28.3%); as well as diseases of the endocrine system, which included diabetes (14.7%), DLP (12.4%) and thyroid disease (10.0%). The incidence of most analyzed chronic diseases among people with EH increased with their age, reaching the highest values at 60-79 years, except for cerebrovascular diseases and IHD, the frequency of which was highest in the age range of 80-99 years. Gender-related differences in the incidence rate of concomitant chronic pathology were caused by a higher incidence of IHD in the male cohort with EH; for other compared chronic diseases, their incidence was higher in the female cohort with EH.

The gender and age characteristics of EH-associated comorbid pathology uncovered in this study appear extremely important in the clinical practice of a local general practitioner in terms of developing the optimal patient-oriented treatment plan.

Conflict of interest

The authors declare no conflicts of interest.

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