

Abstract

Nataliia L. Tsyndrenko

ORCID: 0000-0001-6763-476X

Anatolii M. Romaniuk

ORCID: 0000-0003-2560-1382

Yana R. Nikolayenko

*Department of Pathology, Sumy
State University, Sumy, Ukraine*

**CLINICAL, MORPHOLOGICAL, AND EPIDEMIOLOGICAL
CHARACTERISTICS OF ENDOMETRIAL HYPERPLASTIC
PROCESSES IN SUMY REGION**

Endometrial hyperplastic processes take an important place among the gynecological diseases in women of various ages and are one of the most common reasons for admission at inpatient gynecology departments. The urgency of the pathology is due to the significant prevalence of endometrial hyperplastic processes, high incidence of malignancy, prolonged relapsing course, and decreased reproductive function, since these diseases are one of the most common causes of infertility in women of childbearing age. The statistics related to the incidence of endometrial hyperplastic processes in Ukraine is not available. An analysis of case histories and medical records showed that in 40% of cases, endometrial hyperplastic processes were asymptomatic. In 60% of cases, the clinical manifestations of endometrial hyperplastic processes were menstrual disorders, such as dysmenorrhea, oligomenorrhea, menorrhagia, and metrorrhagia. In 30% of cases, endometrial hyperplastic processes were recurrent. The most common concomitant pathologies of the pelvic organs were uterine leiomyoma and endometriosis; the most common concomitant extragenital diseases were hypertension and obesity. Our study and data analysis showed that there is an increasing trend in the incidence of endometrial hyperplastic processes in Sumy region in 2011–2020. The maximum incidence was in 2016. A correlation was found between hyperplasia incidence and age. Thus, the largest number of non-atypical and atypical endometrial hyperplasia cases was observed in women aged 45–55 years. The lowest number of non-atypical endometrial hyperplasia cases was registered in women aged 66+, while atypical hyperplasia cases – in women under 30 years of age. Glandular polyps of the endometrium were most often diagnosed at the age of 31–44; the lowest number of these was found in women over 66 years. Most glandular-fibrous endometrial polyps were observed in women aged 45–55 years, while women under 30 presented with the fewest cases. Fibrous endometrial polyps were most common in older age groups – 66+; the lowest number of such endometrial polyps was found in women under 30 years. We attributed the decreased incidence of endometrial hyperplastic processes in 2020 to the quarantine measures introduced, which, as a consequence, led to the decreased number of diagnosed cases, since they are often asymptomatic.

Keywords: endometrial hyperplasia, endometrial polyps, morbidity, classification, diagnostics, statistics.

Corresponding author: Nataliia L. Tsyndrenko, Department of Pathology, Sumy State University, Sumy, Ukraine

e-mail: nebesenko.n@ukr.net

Резюме

Наталія Л. Циндренко

ORCID: 0000-0001-6763-476X

Анатолій М. Романюк

ORCID: 0000-0003-2560-1382

Яна Р. Ніколаснко

*Кафедра патологічної анатомії,
Сумський державний університет,
м. Суми, Україна*

КЛІНІКО-МОРФОЛОГІЧНА ТА ЕПІДЕМІОЛОГІЧНА ХАРАКТЕРИСТИКА ГІПЕРПЛАСТИЧНИХ ПРОЦЕСІВ ЕНДОМЕТРІЯ У СУМСЬКОМУ РЕГІОНІ

Гіперпластичні процеси ендометрія посідають вагоме місце серед гінекологічної захворюваності жінок різних вікових груп та є однією з найбільш частих причин госпіталізації до гінекологічного стаціонару. Актуальність патології зумовлена значним поширенням гіперпластичних процесів ендометрія, високою частотою малігнізації, тривалим рецидивуючим перебігом та зниженням репродуктивної функції, адже вони є однією з найчастіших причин непліддя у жінок репродуктивного віку. Статистичні дані щодо захворюваності на гіперпластичні процеси ендометрія в Україні відсутні. Виконаний аналіз історій хвороб та медичних карт показав, що у 40 % випадків гіперпластичні процеси ендометрія були безсимптомними. У 60% випадків клінічними проявами гіперпластичних процесів ендометрія були порушення менструального циклу у вигляді менорагії, метрорагії, дисменореї та олігоменореї. У 30 % випадків гіперпластичні процеси ендометрія були рецидивуючими. Найчастішою супутньою патологією зі сторони органів малого тазу були лейоміома матки та ендометріоз, а екстрагенітальною патологією – гіпертонічна хвороба та ожиріння. Виконане нами дослідження та аналіз даних показав, що на сьогодні спостерігається тенденція до зростання захворюваності на гіперпластичні процеси ендометрія у Сумському регіоні у період 2011–2020 років. Пік захворюваності припадав на 2016 рік. Відмічається певний взаємозв'язок частоти гіперплазій з віковими категоріями. Так, найбільша кількість неатипових та атипових гіперплазій ендометрія спостерігається у жінок віком 45–55 років. Найменша кількість неатипових гіперплазій ендометрія виявлена у жінок віком 66 і більше років, а атипових гіперплазій – у жінок віком до 30 років. Залозисті поліпи ендометрія найчастіше діагностуються у віці 31–44 роки; найменша ж кількість залозистих поліпів ендометрія виявлена у жінок після 66 років. Найбільша кількість залозисто-фіброзних поліпів ендометрія спостерігається у жінок віком 45–55 років, а найменша – у жінок до 30 років. Фіброзні поліпи ендометрія найчастіше зустрічаються у старших вікових групах – 66 і більше років; найменша кількість таких поліпів ендометрія виявлена у жінок до 30 років. Зменшення захворюваності на гіперпластичні процеси ендометрія у 2020 році нами пояснюється введеними карантинними заходами, і, як наслідок, зменшенням кількості діагностованих випадків гіперпластичних процесів ендометрія, адже останні часто перебігають безсимптомно.

Ключові слова: гіперплазія ендометрія, поліпи ендометрія, захворюваність, класифікація, діагностика, статистика.

Автор, відповідальний за листування: Наталія Л. Циндренко, Кафедра патологічної анатомії, Сумський державний університет, м. Суми, Україна

e-mail: nebesenko.n@ukr.net

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Introduction/Вступ

Endometrial hyperplasia (EH) is a pathological condition characterized by hyperplastic changes in the glandular and stromal structures of the endometrium in the uterine cavity [1]. This is a histological diagnosis often made by morphologists and clinical gynecologists.

Clinicians and pathologists pay special attention to endometrial hyperplastic processes (EHP) due to the increasing incidence of this pathology (more than 200,000 new cases registered in developed countries per year) and the high risk of malignant transformation in untreated patients [2].

According to foreign authors, EHP developing in peri- and postmenopausal women leads to malignant transformation in 80% of cases. The frequency and timing of malignant transformation depend on the type of EHP [3]. Although there is no screening tool available for endometrial cancer, EHPs are recognized as prognostic markers for it, and thus, timely detection of EHP will help prevent the development of malignant processes [4]. Despite the high frequency of endometrial hyperplastic processes in the premenopausal period (up to 60–76%), there is an increasing trend of young women diagnosed with this disease. Due to anovulation secondary to chronic hyperestrogenemia, EHP became one of the causes of infertility in women of reproductive age [5]. The prevalence of endometrial polyps (EP) in women is about 7.8%. But in women over 30, it reaches 9.2%. In most cases, the polyps are benign. Estimation of endometrial cancer risks secondary to polyps varies depending on age groups and amounts to 1.1–4.9%. In older age groups, the risk of malignancy is higher [6]. The malignant potential of polyps is understudied [7].

There is no statistics available on the incidence of endometrial hyperplasia in Ukraine [8].

According to the International Statistical Classification of Diseases and Related Health Problems (10th Revision, Australian Modification, 2017), EHPs include:

N84 Polyp of female genital tract

N84.0 Polyp of corpus uteri

N85 Other noninflammatory disorders of uterus, except cervix

N85.0 Endometrial glandular hyperplasia: cystic, glandular-cystic, polypoid

N85.1 Endometrial adenomatous hyperplasia
Hyperplasia of endometrium, atypical [9].

According to 2014 WHO classification, non-atypical hyperplasia and atypical hyperplasia are distinguished [10].

In 2000, a group of gynecologists suggested a classification of endometrial intraepithelial neoplasia (EIN) based on computerized morphometric analysis. Morphological D-score is calculated as stromal volume over total tissue volume. The total tissue volume includes the epithelium, stromal volume, and gland lumen. The endometrial tissue is considered benign if $D > 1$ and EIN if $D < 1$ [10].

The diagnostic criteria for EH are based on the assessment of the balance of glandular and stromal endometrial components, as well as the presence or otherwise of atypical epithelial cells. EHPs are characterized by endometrial glands proliferation, which leads to an increase in the gland to stroma ratio $> 50\%$, in contrast to normal proliferative endometrium (gland to stroma ratio $< 50\%$) [11].

Given the urgency of this problem, the goal of our study was to evaluate the prevalence of endometrial hyperplastic processes in Sumy region in 2011–2020 and to perform an analysis of the data.

Materials and methods

Data were collected and analyzed at MI of Sumy Regional Council "Sumy Regional Pathoanatomical Bureau" and at Department of Pathology of Medical Institute of Sumy State University in 2011–2020. The treated cases of endometrial hyperplastic process were analyzed using the data provided by Municipal Non-Profit Enterprise of Sumy Regional Council "Sumy Regional Clinical Oncological Dispensary", Municipal Non-Profit Enterprise of Sumy Municipal Council "Blessed Virgin Mary Clinical Maternity Hospital", and Municipal Non-Profit Enterprise of Sumy Regional Council "Regional Clinical Perinatal Center" in 2011–2020. Histological specimens were studied using morphological methods. Methods of statistical analysis were used to process the obtained results.

Results and discussion

An analysis of case histories and medical records showed that in 60% of cases, EHPs were accompanied by menstrual disorders, such as dysmenorrhea, oligomenorrhea, menorrhagia, and metrorrhagia. In 40% of cases, endometrial hyperplastic processes were asymptomatic. Analysis of histological material revealed that glandular hyperplasia of the endometrium is characterized by glands of various shapes and sizes (small to large and cystic). The latter were lined with high prismatic epithelial cells with multiple rows of nuclei and clearly defined apical sides of cells. The nuclei were oval and rich in chromatin. The cytoplasm was basophilic, usually with no secretion, although sometimes there was some

mucus in the lumen of the glands. Stromal cells were slightly enlarged and had acidophilic cytoplasm. In glandular and stromal cells, mitotic figures were often observed, which indicated active proliferation of glandular and stromal elements [12].

According to the results of the analysis, it was found that the largest number of EHP cases in Sumy region over the past 10 years was registered in 2016 (2020 cases of which 1679 EH cases (83.1%) and 341 EP cases (16.9%)), and the lowest number of EHP cases – in 2020 (1317 cases of which 899 EH cases (68.3%) and 418 EP cases (31.7%)) (Fig. 1). The latter might be due to the COVID-19 pandemic and related quarantine measures which led to a reduction in the number of diagnosed EHP cases.

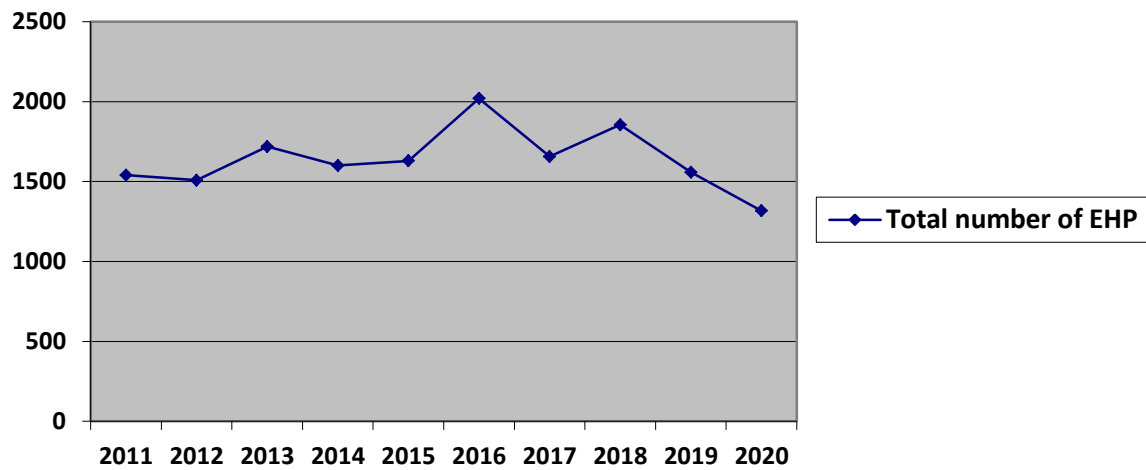


Figure 1 – Changes in the total number of EHP in Sumy region in 2011–2020

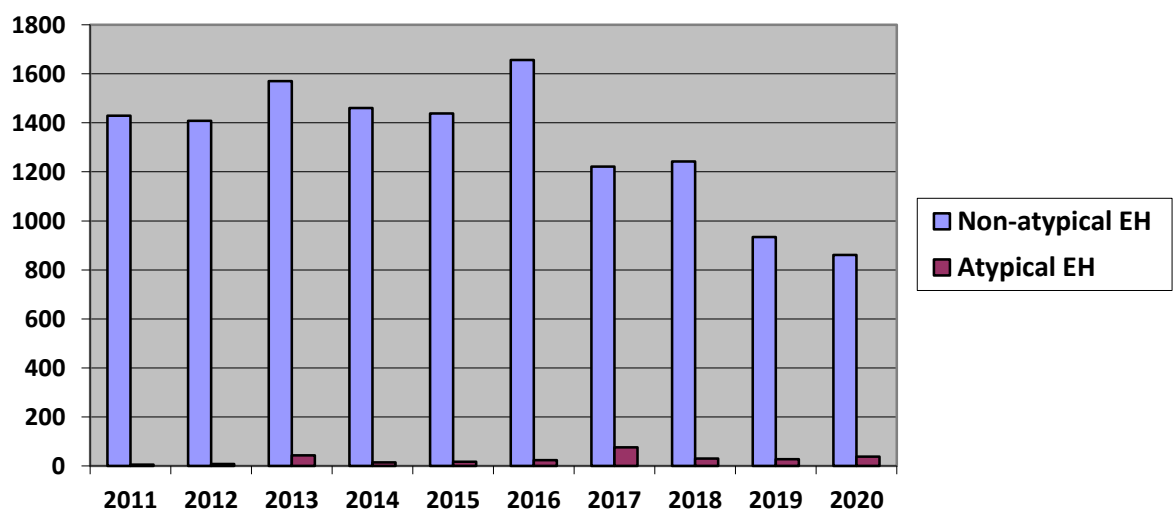


Figure 2 – Number of non-atypical EH and atypical EH cases in Sumy region in 2011–2020

According to the study results, the most of non-atypical EH cases were registered in 2016 (1656 cases – 98.6% of the total number of diagnosed EH cases in 2016), while the minimum number was reported in 2020 (861 cases – 95.8% of the total number of diagnosed EH in 2020). Atypical EH cases were most prevalent in 2017 (75 cases – 5.8% of the total diagnosed EH cases in 2017), while the fewest atypical EH cases were reported in 2011 (5 cases – 0.35% of the total diagnosed EH cases in 2011) (Fig. 2).

Analysis of the frequency of diagnosed EH during 2011–2020 showed an age-dependent correlation. Thus, the largest number of simple non-atypical EH was observed in women aged 45–55 years (a total of 6965 cases over 10 years in women of this age group, i.e. 52.7% of the total diagnosed non-atypical EH cases in 2011–2020). The minimal number of simple non-atypical EH was registered in women aged 66+ (a total of 181 cases over 10 years in women of this age group, i.e. 1.4% of the total diagnosed non-atypical EH cases in 2011–2020) (Fig. 3).

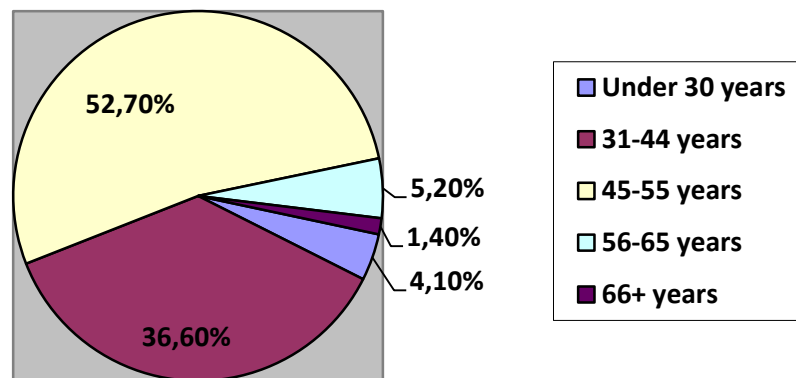


Figure 3 – Age structure of simple non-atypical EH in Sumy region in 2011–2020

The most of atypical EH cases were also observed in women aged 45–55 (a total of 132 cases over 10 years in women of this age group, i.e. 47.1% of the total diagnosed atypical EH cases in 2011–2020). The minimal number of atypical EH

was reported in women under 30 (a total of only 7 atypical EH cases over 10 years in women of this age group, i.e. 2.5% of the total diagnosed atypical EH cases in 2011–2020) (Fig. 4).

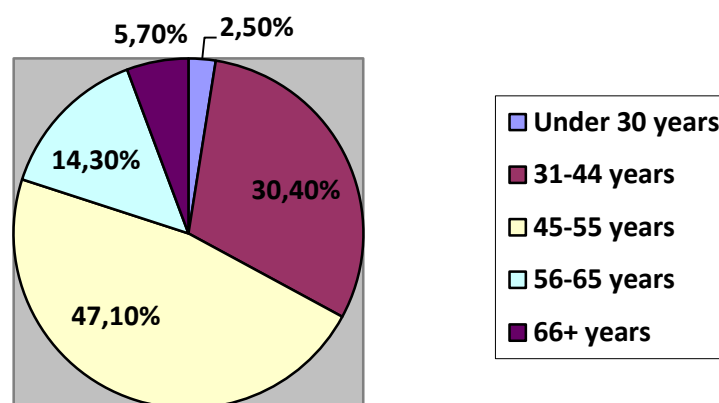


Figure 4 – Age structure of atypical EH in Sumy region in 2011–2020

Analysis of clinical data of the patients diagnosed with EHP showed that in 40% of women, EHPs manifested with menopause and metrorrhagia, in 15% – with oligomenorrhea, in 5%

of cases – with dysmenorrhea; 40% of EHPs were asymptomatic. In 30% of cases, endometrial hyperplastic processes were relapsing. Concomitant pathologies of female genital tract were: in 50% of

cases – uterine leiomyoma, in 40% of cases – endometriosis, in 25% of cases – cervical erosion, in 15% of cases – mastopathy; in 10% of cases – chronic adnexitis, in 5% of cases – ovarian cysts. 85% of women had pregnancies and deliveries. 15% of women had a history of infertility. Concomitant extragenital pathologies were: in 35% of cases – obesity and hypertension, in 20% of cases – gastrointestinal diseases, in 15% of cases – pathologies of the nervous system, in 10% of cases – diabetes mellitus, in 5% of cases – respiratory and urinary tract diseases.

A study of the histological material related to endometrial polyps showed that the polyps were localized elevations of endometrial glands and stroma protruding from the endometrium (focal endometrial hyperplasia) [13]. Most polyps were benign, although malignant transformation was observed in 0 to 13% of cases. We noted that polyp malignant potential was determined by the patient's age and menopausal status. These data were consistent with the literature data [14]. According to the histological structure, we distinguished glandular, glandular-fibrous, and fibrous polyps of the endometrium. Glandular polyps were usually formed from the basal layer and contained stroma and glands. Glandular-fibrous EP consisted of connective tissue stroma and a limited number of glands. Fibrous polyps derived from connective tissue and were often collagenized, with a few or no glands. We

noted that the hyperplasia of the endometrium and the surrounding stroma formed broad-based polypoid vegetations, which later developed a stalk. We found that EP could be single or multiple (in 26% of cases). We noted that with a long-term and favorable course, glandular polyps sometimes reversed by replacing glandular elements with fibrous tissue. According to some authors [15], this was usually accompanied by a decrease in the primary focus size.

According to the study results, the most EP cases were registered in 2019 (597 cases – 38.3% of the total number of diagnosed EP cases in 2019), while the minimum number of EP cases was reported in 2012 (92 cases – 6.5% of the total number of diagnosed EP in 2012). According to the analysis of EP histological structure, the most of glandular EP cases were registered in 2018 (475 cases – 81.2% of the total diagnosed EP cases in 2018), while the minimum number of glandular EP cases was reported in 2012 (73 cases – 79.3% of the total diagnosed EP cases in 2012). Glandular-fibrous EPs were most prevalent in 2019 (180 cases – 30.1% of the total diagnosed EP cases in 2019), while the fewest glandular-fibrous EP cases were reported in 2011 (4 cases – 3.8% of the total diagnosed EP cases in 2011). Fibrous EPs were most prevalent in 2019 (13 cases – 2.2% of the total diagnosed EP cases in 2019), while there were no fibrous EP cases diagnosed in 2011 and 2016 (Fig. 5).

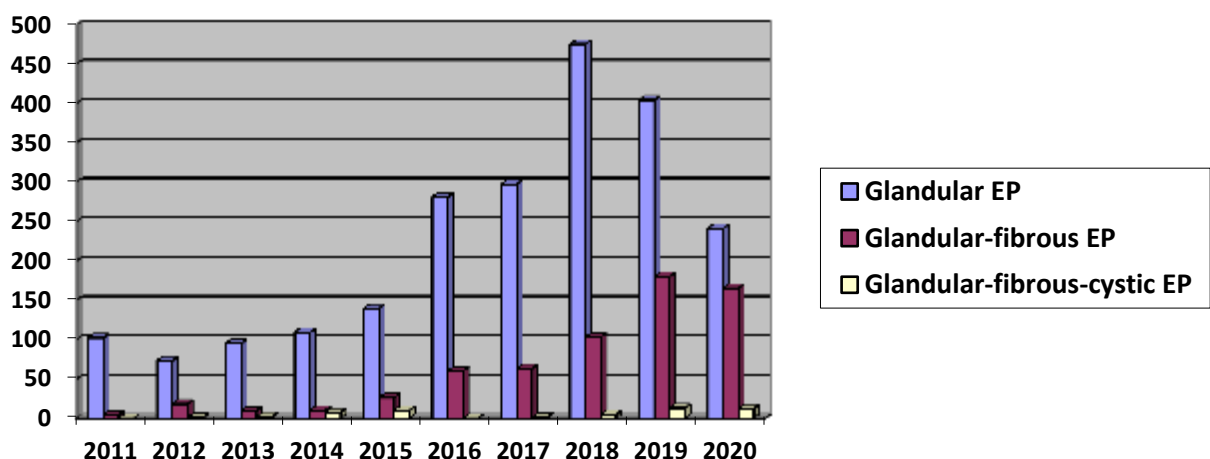


Figure 5 – Number of different histological EP types in Sumy region in 2011–2020

Analysis of EP-related age structure revealed a correlation with age. Thus, glandular polyps of the endometrium were most often diagnosed at the age of 31–44 (a total of 907 cases over 10 years in women of this age group, i.e. 40.9% of the total diagnosed glandular EP cases in 2011–2020); the

lowest number of glandular EP cases was observed in women over 66 years (a total of 113 cases over 10 years in women of this age group, i.e. 5.1% of the total diagnosed glandular EP cases in 2011–2020). Glandular-fibrous polyps of the endometrium were most often diagnosed at the age

of 45–55 (a total of 237 cases over 10 years in women of this age group, i.e. 37.1% of the total diagnosed glandular-fibrous EP cases in 2011–2020); the lowest number of such EP cases was observed in women under 30 years (a total of 31 cases over 10 years in women of this age group, i.e. 4.9% of the total diagnosed glandular-fibrous EP cases in 2011–2020). Fibrous polyps of the

endometrium were most often registered in older patients – 66+ years (a total of 23 cases over 10 years in women of this age group, i.e. 45.1% of the total diagnosed fibrous EP cases in 2011–2020); the fewest fibrous EP cases were observed in women under 30 years (a total of only 2 cases over 10 years in women of this age group, i.e. 3.9% of the total diagnosed fibrous EP cases in 2011–2020).

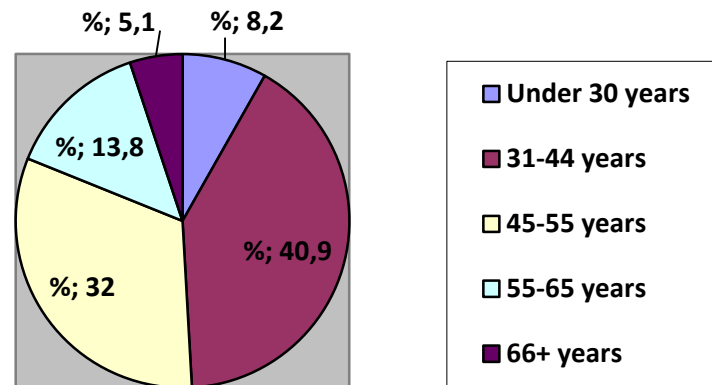


Figure 6 – Age structure of glandular EP in Sumy region in 2011–2020

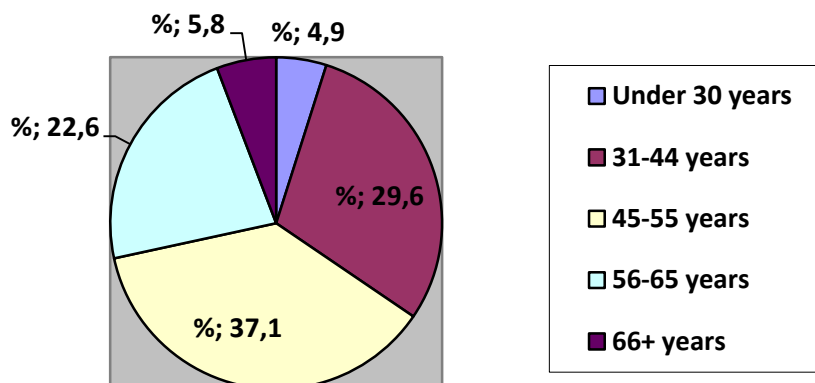


Figure 7 – Age structure of glandular-fibrous EP in Sumy region in 2011–2020

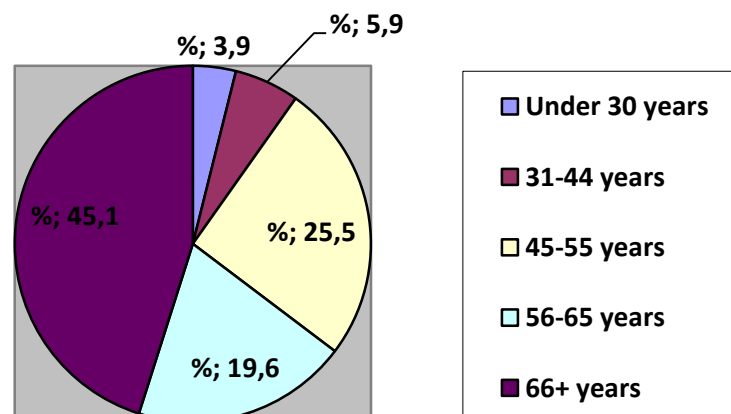


Figure 8 – Age structure of glandular-fibrous-cystic EP in Sumy region in 2011–2020

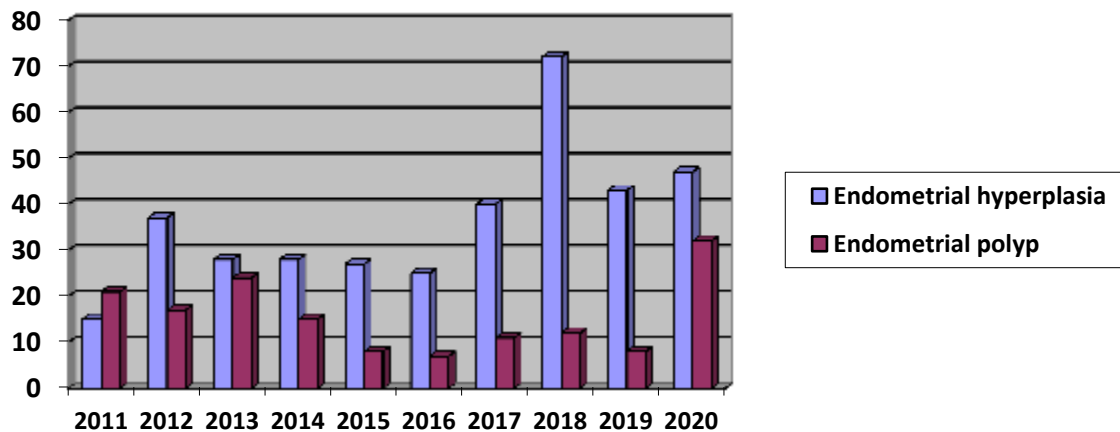


Figure 9 – EHP cases treated at Municipal Non-Profit Enterprise of Sumy Regional Council "Sumy Regional Clinical Oncological Dispensary" in 2011–2020

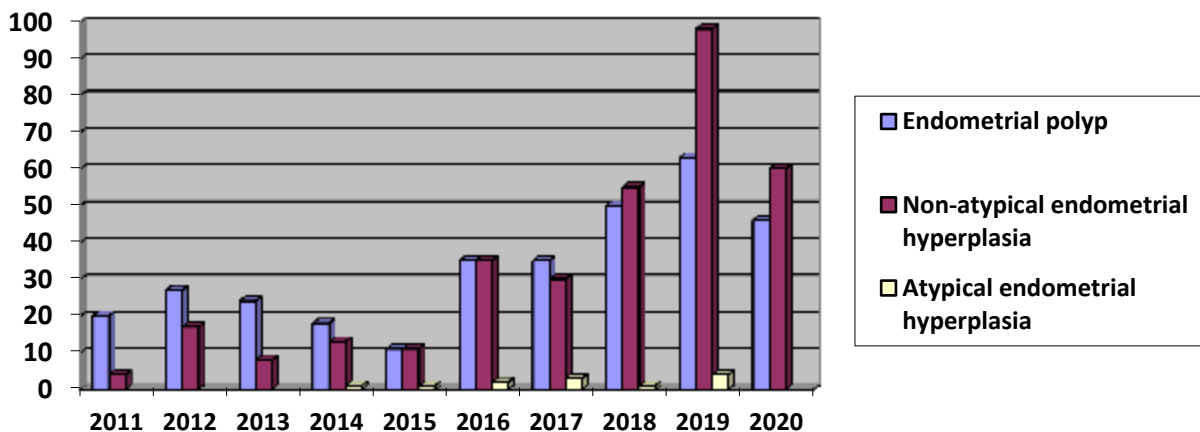


Figure 10 – EHP cases treated at Municipal Non-Profit Enterprise "Blessed Virgin Mary Clinical Maternity Hospital" in 2011–2020

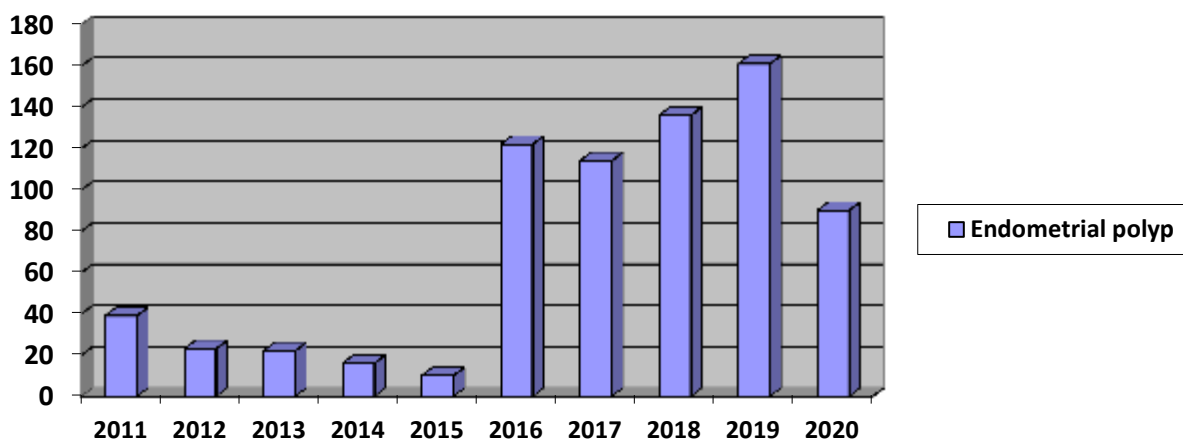


Figure 11 – EHP cases treated at Municipal Non-Profit Enterprise of Sumy Regional Council "Regional Clinical Perinatal Center" in 2011–2020

According to the results of the analysis, the largest number of EH cases treated at Municipal Non-Profit Enterprise of Sumy Regional Council was registered in 2018 (72 cases), and the largest number of endometrial polyps – in 2020 (32 cases). EH and EP cases treated at Municipal Non-Profit Enterprise of Sumy Municipal Council "Blessed Virgin Mary Clinical Maternity Hospital" were most prevalent in 2019 (98 and 63 cases, respectively). The most EP cases treated at Municipal Non-Profit Enterprise of Sumy Regional Council "Regional Clinical Perinatal Center" were reported in 2019 (161 cases).

Conclusions/Висновки

Statistical data analysis showed an increasing trend in the incidence of EHP in Sumy region in 2011–2020. We attributed the decreased incidence of EHP in 2020 to the quarantine measures, since EHP often has an asymptomatic course and patients do not seek medical attention. Therefore,

Data analysis showed that there was an increasing trend in the incidence of endometrial hyperplastic processes in Sumy. We attributed the decreased incidence of endometrial hyperplastic processes in 2020 to the quarantine measures introduced with relation to the COVID-19 pandemic, which, as a consequence, led to the decreased number of diagnosed cases, since they often have asymptomatic course. In older age groups, local EHP with a fibrous component predominated.

mandatory outpatient follow-up of such patients should be introduced. The maximum EHP incidence was observed in 2016. There is a correlation between EHP incidence and age, which requires appropriate attention from family physicians and gynecologists.

Prospects for future research/Перспективи подальших досліджень

Study of the morphological and immunohistochemical features of different types of endometrial hyperplastic processes and investigation of the role of genetic polymorphisms in the development of endometrial hyperplastic processes.

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Information about the authors/Відомості про авторів

Nataliia Leonidivna Tsyndrenko, postgraduate student, Department of Pathology, Sumy State University, Sumy, Ukraine.

E-mail: nebesenko.n@ukr.net

ORCID: 0000-0001-6763-476X

Anatolii Mykolaiovych Romaniuk, DMedSc, Prof., Head of the Department of Pathology, Sumy State University, Sumy, Ukraine.

E-mail: pathomorph@gmail.com

ORCID: 0000-0003-2560-1382

Yana Romanivna Nikolayenko, 4th year student of the Medical Institute, Sumy State University, Sumy, Ukraine.

E-mail: nijana001@gmail.com