Original Paper

Epidemiological, Clinical and Biological Hemogram Features in a Cohort of Neuroendocrine Tumor Patients

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ABSTRACT: We conducted a retrospective study based on 55 patients diagnosed with gastroenteropancreatic neuroendocrine tumors (GEP-NETs)-gastric (G-NET), small bowel (SB-NET) and colonic (C-NET), hospitalized and evaluated within the Surgical, Gastroenterology and Internal Medicine Clinics, in The Clinical Emergency County Hospital Craiova, between May 2016 and April 2024. We aimed in this study to analyze the epidemiological aspects and clinical characteristics of patients with GEP-NETs. In our study group, the patients' ages were between 39-82 years, with a mean of 66.40 (±12.46) years. The incidence of GEP-NETs cases in young patients was insignificant low-1 case. 45.46% of all patients lived in urban areas. 16.36% were G-NET, 14,54 were SB-NET and 69.09% were C-NET. The GEP-NETs diagnosis was established by immunohistochemistry features. Also, we observed that the most frequency localization was on the ascending colon, while the rarest on the colon it is located on the transverse colon and the rarest is on the small bowel, in spite of the generally literature data. From the C-NET group, 49.09% have been presented arterial hypertension probable explained by serotonin and dopamine secretion an inflammatory through phenotype expression and just one patient has been presented an erythematous psoriasis, which could be also explained by the same neurotransmitter's involvement as a possible purposed mechanism. The results obtained in our study demonstrate that could be a common profile of GEP-NETs patients through epidemiological general information and clinical characteristics. Also, we demonstrate that, in the last years, the incidence increased for the GEP-NETs.

KEYWORDS: Digestive neuroendocrine tumors, epidemiological study, immunohistochemistry.

Introduction

Digestive cancers represent a public health problem and benefit from national screening programs.

Based on the clinical and epidemiological information communicated in the last decade, an increasing understanding of the molecular pathology of tumors has been reached.

According to GLOBOCAN 2022, which is the most recent world cancer data statistical analysis, of the 19.976.499 new diagnosed localization cancers, colorectal cancer was the fourth cause of neoplasm, followed by stomach localization [1].

These could be some arguments for the permanent common concern of the national and international health forums for prevention and earlier diagnostic campaigns.

In a comparison between GLOBOCAN 2020 and GLOBOCAN 2022, it is observed that colorectal cancer remains the third cause of incidence and the second in mortality for both sexes, while gastric cancer maintains the same position, respectively the fifth in incidence, and it descends in frequency, associated with a decreasing mortality [1,2].

Additionally, following the recent Coronavirus Infection (COVID-19 Disease) period, national medical screening campaigns, and the GLOBOCAN 2022 data, it is noteworthy that there is an increasing incidence of colorectal cancer and a decreasing trend in newly diagnosed gastric cancer.

By GLOBOCAN 2022 statistical analysis in cancer, in a top 15 most common types of cancers, it was observed the trends in incidence and mortality by the localization of the organs, on both sexes and grouped by sex, individual-males and females (Figures 1 and 2) [3].

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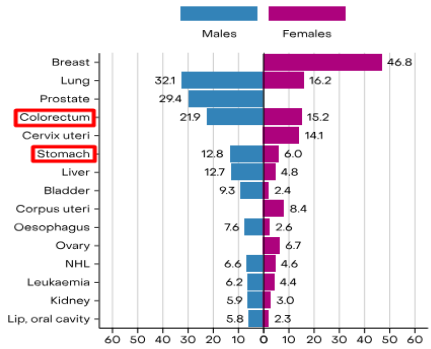

Figure 1. Top 15 most common cancer localizations by incidence and mortality [3].

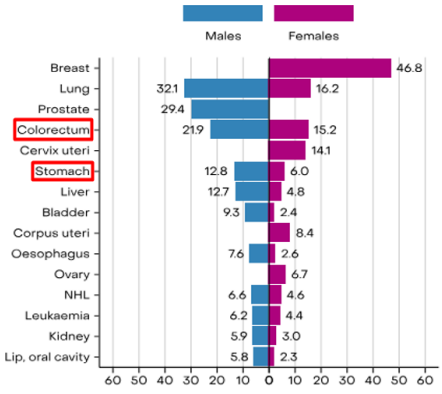

Figure 2. Top 15 most common cancer localizations by individual sexes [3].

A challenge for diagnosis and treatment in oncology are gastroenteropancreatic neuroendocrine tumors (GEP-NETs).

Neuroendocrine tumors (NETs) are a type of tumor that arises from neuroendocrine cells.

10-20% of NETs are neuroendocrine carcinomas, which are the most proliferative type of NET [4,5].

Also, the GEP-NETs represents the majority (over 50%) of the NETs, most frequently, in literature reviews being small bowel neuroendocrine tumors (SB-NETs), followed by rectal neuroendocrine tumors (R-NETs) at 20%, appendix (Apx-NETs) at 16%, colonic (C-NETs) at 11%, and gastric (G-NETs) at 7% [6].

In 2023, a new cross-sectional study was published, which was realized in four countries (France, Germany, Spain, and the United Kingdom) with the same frequencies as the general population, respectively SB-NETs, C-NETs, and G-NETs [7].

Regarding the risk factors for the development NETs, there are many studies that have proven that socioeconomic status, tobacco smoking, and alcohol consumption (>21 drinks per week) are important elements in NETs appearance.

Of course, type of diet (processed foods, red meat, and/or saturated fats) and the family history of cancer play an important role in NETs development, but there are many other factors besides these that are concerning in the medical history of our patients, like obesity, diabetes, a history of hepatobilliary diseases, and polyps. For SB-NETs, family history of colorectal cancer and breast cancer are important risk factors [8,9,10].

Furthermore, including drugs in statistical analysis, the use of aspirin is susceptible to a protective factor, results that could not be evidence for statins as protective drugs. The role of aspirin as a protective factor could be explained probably by the effect of blocking the isoform cyclooxygenase activity that could inhibit the carcinogenic process [10,11].

In NETs domain, there are few studies on general epidemiological information and associations between family and personal medical histories of others diseases and disorders and this tumor type, and more challenging in epidemiology, diagnosis, and treatment are synchronous types of adenocarcinoma and neuroendocrine tumors. The enshrined question, "Which came first, the egg or the chicken?" is here a central problem for starting relevant research.

Recent studies demonstrated that these forms, actually named mixed neuroendocrine and non-neuroendocrine neoplasms (MiNENs), have a molecular and genetic underlay, with almost a decade of diagnosis over the sixth, but especially within it [12,13].

Multiple retrospectives, prospective, cross-sectional studies, systematic reviews, and meta-analyses demonstrated that the incidence and prevalence of NET are increasing, so it is a mandatory necessity for growing up the epidemiology, biology, and molecular studies for identification of risk groups for every region. For this scope, we realized our epidemiological study would add to the specialty literature as new research for new establishments in the NETs.

Objective

The purpose of this study was to examine the epidemiological, clinical, and hemogram characteristics of GEP-NETs patients hospitalized in the Surgical, Gastroenterology, and Internal Medicine Clinics at the Clinical Emergency County Hospital Craiova between May 2016 and April 2024.

Through clinical, paraclinical, and hemogram information, we tried to realize a possible paradigm for the GEP-NETs (G-NET, SB-NET,

and C-NET) patients from our hospital for an earlier and properly diagnosed D-NET and a basic approach to monitoring for a rapid diagnosis process.

Materials and Methods

To establish epidemiological features of GEP-NETs, we carried out a retrospective study on 55 individuals who were hospitalized through epidemiological, properly pathological, clinical, and hemogram elements within the Surgical, Gastroenterology, and Internal Medicine Clinics in the Clinical Emergency County Hospital Craiova between May 2016 and April 2024.

The inclusion criteria established for study participants were: patients aged 18-90 years old with a confirmed diagnosis of GEP-NETs, supported by histopathological and immunohistochemical results. The exclusion criteria were represented by: patients with gastric, small bowel, or colonic benign tumor pathology; or patients for whom no pathological results were found.

Medical documentation consists of collecting and analyzing demographic and clinical data for NET patients. The initial exam for each subject included: contact information, age, gender, residence, smoking, alcohol and drug consumption, and possible associated comorbidities.

Permission was requested and gained from the Academic and Scientific Ethics and Deontology Commission of the University of Medicine and Pharmacy in Craiova for the study's implementation (No. 63/28.04.2021).

Statistical analysis

We organized and processed data from all medical cases using Microsoft Excel. The information was statistically analyzed using the GraphPad Prism 5 trial edition (San Diego, CA, USA). Categorical data were reported as percentages and compared using the Chi-squared or Fisher's exact tests. The statistical significance level was set at $p \leq 0.05$. The existence of significant correlations between parameters was evaluated using Pearson's coefficients ($-1 < r < 1$).

Results

Anatomical location of the tumor

In the 8 years of the analyzed study, the following locations of GEP-NETS were diagnosed: 9 tumors located in the stomach, 8 small intestine tumors, and 38 tumors located in the colon. We did not diagnose any cases with rectal localization.

Examining the tumors' anatomical locations on the colon segments, we discovered several differences across the groups investigated: identified appendix and sigmoid colon tumors in each of the 10 patients, accounting for 52.63% of the total tumors. The prevalence of ascending colon tumors was 15.79% (6 cases); 5 cases (13.16%) had tumors at the hepatic flexure, 3 cases (7.89%) at the transverse colon, and 2 cases (5.26%) at the level of the splenic flexure.

We diagnosed only 2 cases at the rectosigmoid junction (7 cases, 5.26%).

Demographic characteristics of the group of patients

The group on which the present study was carried out includes 55 patients: 34 male (61.81%) and 21 female (38.19%). The patients' ages were between 39 and 86 years, with a mean age of 66.40 (for this median age, the single patient who was 39 years old at the moment of diagnosis was eliminated, being presented just like a rare and possible medical case) (Figure 3).

Male patients are aged between 40-82 years, with a mean±SD of 67.60±8.95 years, and female patients are aged between 39-86 years, with a mean±SD of 65.23±12.77 years, with no statistically significant differences between mean age ($p \geq 0.05$).

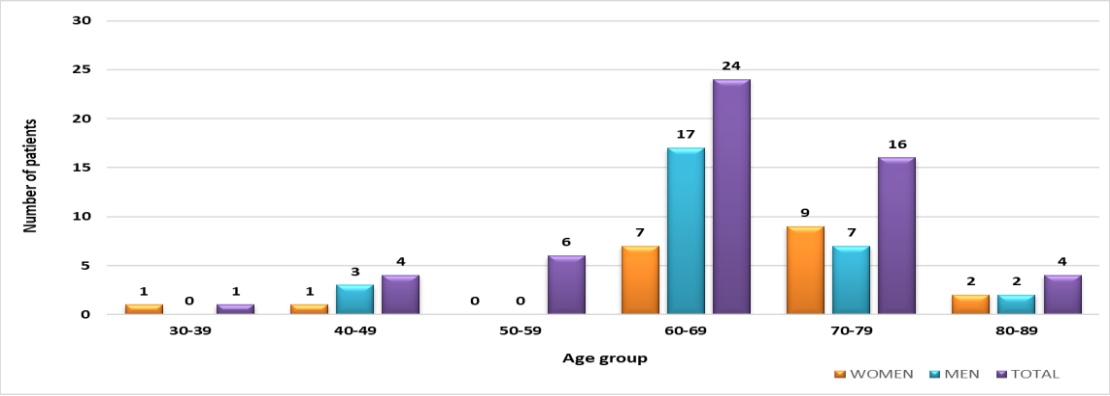

Figure 3. Patients from the current study grouped by age and gender.

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We identified 9 cases in the G-NET group, consisting of 7 males and 2 females (shown in red on the chart), demonstrating a remarkable trend of aggregation in the sixth to seventh decades of life: 1 patient in the 50-59 age decade, 3 patients in the 60-69 age decade, and 5 patients in the 70-79 age decade; the youngest patient was 58 years old and the oldest was 78 years old. We also noticed that G-NET appears after the age of 50 (Figure 4).

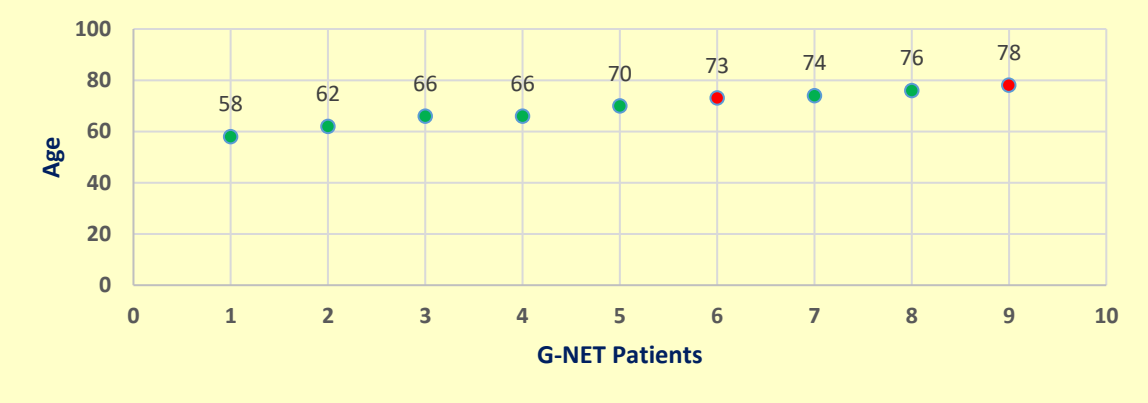

Figure 4. The distribution of G-NETs patient by the age of diagnosis.

For the SB-NET group, we found 8 cases: 6 males and 2 females (red color in the chart).

We observed a remarkable aggregation in the 60-69 age decade. 2 patients in the 50-59 age decade, 5 patients in the 60-69 age decade, and 1 patient was 86 years old. The youngest patient was 57 years old, and the oldest was 86 years old (Figure 5).

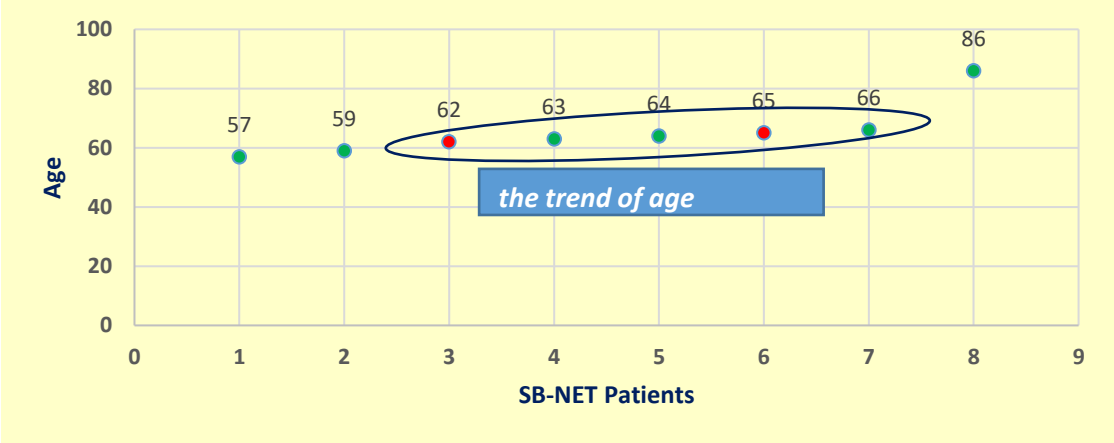

Figure 5. The distribution of SB-NETs patient by the age of diagnosis.

In the C-NET group, we found 38 cases, 21 males and 17 females, with statistically significant differences (p <0.05) (Figure 6).

We observed the same aggregation in the 60-69 age decade.

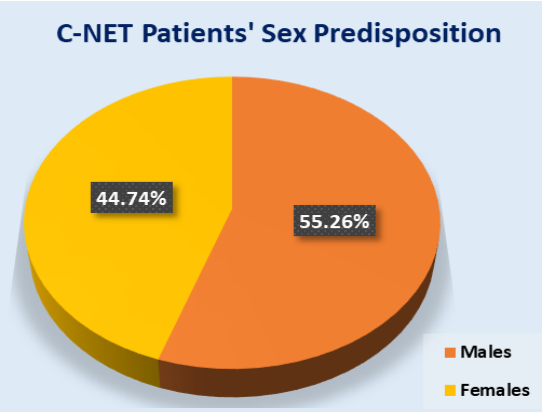

Figure 6. Distribution on both sexes for C-NETs.

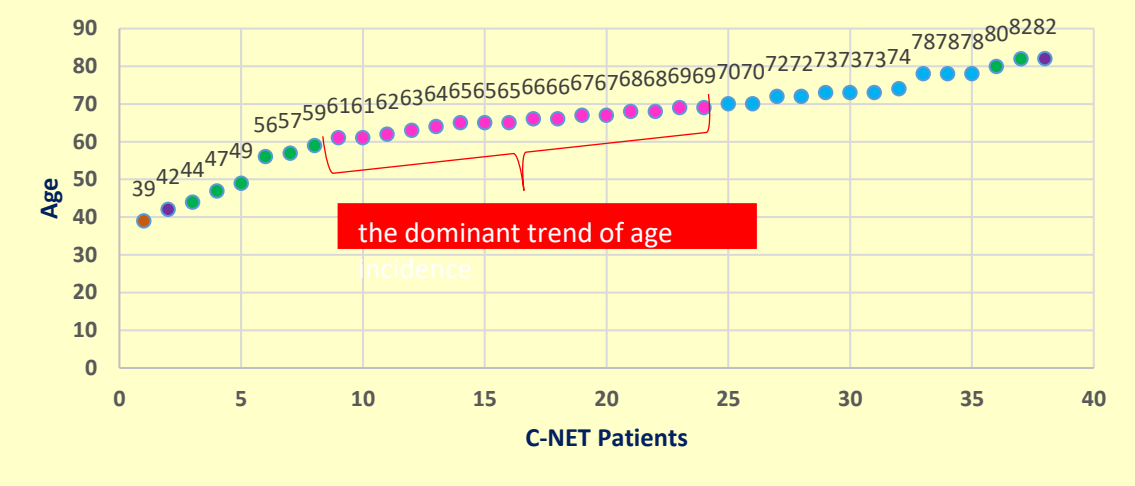

Figure 7. The ordered and phased over C-NET group.

For observing the period of life-age for diagnosis, we ordered these 38 patients by individual age (Figure 7).

In the C-NET graphic trend of incidence, we observe two possible picks of incidence by age in the sixth and seventh decades of life, in a possible enlarge group. Furthermore, we observe two possible picks of incidence by age, referring to the 60-69 age decade and the 70-79 age decade, the dominant being the development of C-NET in the sixth decade of life (statistically significant differences, $p<0.05$), in a rapport of 1.45:1 for our cohort of patients.

As we could see, from 38 patients, 16 patients were in the 60-69 age decade, 11 patients were in the 70-79 age decade and 9 patients were out of the decades of the peak of incidence (4 patients in the 40-49 age decade, 3 patients in the 30-39 age decade and other three between 80-82 years old).

The youngest patients were 39 years old, underling the trend to start in detecting C-NET to the fourth decade of life. The oldest patients new diagnosed with C-NET were 82 years old.

Also, it is interesting to observe how we can observe if we superpose the information about age and sex of our patients to reveal the real, much more exact epidemiological peak for incidence and prevalence for C-NETs.

So, we realized a graphic for evidencing the statistical trend (Figure 8).

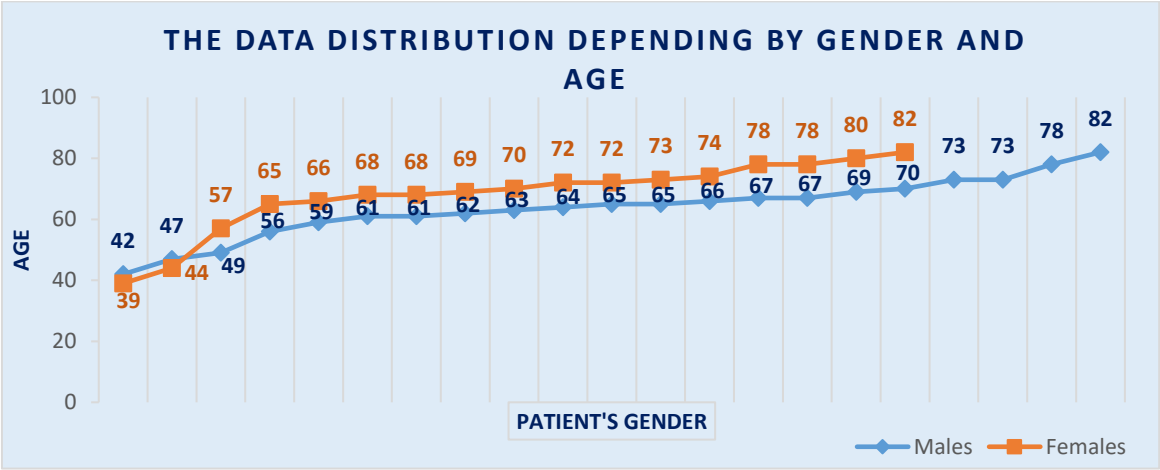

Figure 8. Statistical trend for C-NETs.

Assuming the associations between GEP-NETs and exposures, we tried to identify if there were some associations between residence, alcohol consumption, smoking, family (Table 1), and personal medical history (Table 2).

We obtained significant associations in males between alcohol consumption and smoking with all three locations, G-NET, SB-NET, and C-NET ($p<0.05$). Our analysis also highlighted a significant association between C-NET and the rural area of residence ($p<0.05$). These results can be explained by the poor accessibility of patients to the hospital, as well as by specific lifestyles, occupations, and environmental factors. On the other hand, it is known that rural residents have less access to adequate and quality health services.

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Table 1. Associations between residence, smoking, alcohol consumption, family and GEP-NETs.

Parameters	***G-NET***	*p*-value (Fisher's test)	***SB-NET***	*p*-value (Fisher's test)	***C-NET***	*p*-value (Fisher's test)
Area of residence						
rural	**3**	$p \geq 0.05$	**4**	$p \geq 0.05$	**23**	$p < 0.05$*
urban	**6**		**4**		**15**	
Alcohol Consumption						
males	**7**	$p < 0.05$*	**5**	$p < 0.05$*	**16**	$p < 0.05$*
females	**2**		**1**		**7**	
Smoking						
males	**7**	$p < 0.05$*	**5**	$p < 0.05$*	**21**	$p < 0.05$*
females	**2**		**1**		**11**	
Family history						
gastric cancer						
males	**2**	$p \geq 0.05$	**1**	$p \geq 0.05$	**1**	$p \geq 0.05$
females	**1**		**0**		**2**	
colorectal cancer						
males	**1**	$p \geq 0.05$	**2**	$p \geq 0.05$	**8**	$p < 0.05$*
females	**0**		**0**		**3**	
cardiovascular diseases						
males	**4**	$p \geq 0.05$	**3**	$p \geq 0.05$	**11**	$p < 0.05$*
females	**1**		**0**		**6**	
diabetes mellitus						
males	**3**	$p \geq 0.05$	**2**	$p \geq 0.05$	**4**	$p < 0.05$*
females	**1**		**1**		**7**	

We identified the following diseases and disorders in our GEP-NETs group: gastric and colonic cancers, peptic ulcers, gastritis, arterial hypertension, diabetes mellitus, lithiasic and alithiasic chronic cholecystitis (some with cholecystectomy), chronic viral hepatitis B, alcohol cirrhosis, and one case of kidney lithiasis, scleroderma, and psoriasis in association with GEP-NETs.

We only found significant associations in males between arterial hypertension, diabetes mellitus, and alcoholic cirrhosis with C-NET location ($p < 0.05$), (Table 2).

Table 2. Associations between personal medical history and GEP-NETs.

Parameters	***G-NET***	*p*-value	***SB-NET***	*p*-value	***C-NET***	*p*-value
Arterial Hypertension						
males	3	$p \geq 0.05$	1	$p \geq 0.05$	14	$p < 0.05$
females	1		0		8	
Diabetes Mellitus						
males	3	$p \geq 0.05$	2	$p < 0.05$	7	$p < 0.05$
females	1		0		2	
Gastric Ulcers						
males	2	$p \geq 0.05$	1	$p \geq 0.05$	2	$p \geq 0.05$
females	0		0		1	
Gastritis						
males	2	$p \geq 0.05$	2	$p \geq 0.05$	2	$p \geq 0.05$
females	0		1		3	
Gastric cancer						
males	4	$p \geq 0.05$	0	-	2	$p \geq 0.05$
females	2		0		0	
Alithiasic Chronic Cholecystitis						
males	2	$p \geq 0.05$	0	-	2	$p \geq 0.05$
females	1		0		0	
Lithiasic Chronic Cholecystitis						
males	2	$p \geq 0.05$	2	$p \geq 0.05$	4	$p \geq 0.05$
females	1		0		4	
Alcoholic Cirrhosis						
males	2	$p \geq 0.05$	0	-	6	$p < 0.05$
females	1		0		2	

Also, we tried to identify the possible associations between demographic and most relevant clinical characteristics between the GEP-NETs and majoritarian C-NETs groups of patients, (Table 3).

Although it is a group of 55 patients, as a rare disease, we could obtain some data about the main clinical outcomes, like incidences of pain/discomfort, weight loss, pallor, malaise, and fatigability, which form the biggest group of diseases in the C-NETs group.

Obtaining much relevant information, probably by the dimensions of this one, is important for a rare disease. The incidence of the alternation between constipation and diarrhea, slowing in bowel movement, absence of intestinal transit (for both-stool and flatulence), and hematochezia is much fewer, respectively, from 2.63% to 5.26% in the C-NETs group of patients. The probability that a patient who has C-NET will present all four physical signs and symptoms is 59.63% and 28,84% for presenting all the clinical elements that we presented.

Table 3. Clinical presentation about GEP-NETs patients' group.

Parameters	***G-NET***	***SB-NET***	***C-NET***	*p*-value
Pain/Discomfort				
males	3	4	16	$p < 0.05$
females	2	3	12	
Weight Loss				
males	3	0	11	$p < 0.05$
females	0	0	13	
Pallor				
males	2	0	11	$p \geq 0.05$
females	1	1	9	
Nausea				
males	0	3	0	-
females	0	0	0	
Vomiting				
males	0	3	0	-
females	0	0	0	
Malaise/Fatigability				
males	4	0	8	$p \geq 0.05$
females	2	0	11	
Loss of Appetite				
males	2	0	1	-
females	0	0	0	
Alternation between Constipation and Diarrhea				
males	0	0	0	$p < 0.05$
females	0	0	2	
Slowing in Bowel Movement				
males	0	0	1	-
females	0	0	1	
Absence of Intestinal Transit (for both - stool and flatulence)				
males	1	0	0	-
females	0	0	1	
Hematochezia				
males	0	0	0	$p < 0.05$
females	0	0	2	

Regarding the G-NETs patient group, just 1 patient (male) presented a NET overlap by a gastric resection.

Also, the stool test for Helicobacter pylori was proven for 8 of 9 of all G-NET group patients, and no one presented a positive result.

Important to mention, at the moment of diagnosis, there were just 17 (30.90%) patients presenting metastases, 2 from the G-NETs group, 1 from the SB-NETs group, and 13 from the C-NETs group (within 5 cases of loco-regional metastatic dissemination), and from the last cohort, 5 were females (1 female with local, 2 females with loco-regional, 1 female with hepatic, and 1 female with peritoneal metastases).

For males, 2 patients in G-NETs group with local metastases, 1 patient in SB-NET with lymph-node metastases, and 8 patients from the C-NETs group (2 with distant metastases, 5 with loco-regional metastases, and 1 with local invasion).

From our group of GEP-NETs, 2 patients from the C-NETs presented symptoms that corresponded to the carcinoid syndrome.

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Discussion

The purpose of this study was to examine the epidemiological and clinical characteristics of D-NET patients hospitalized between May 2016 and April 2024 using epidemiological and clinical data, so we tried to observe if we could create a profile of patients diagnosed with this type of tumor pattern in our hospital.

The incidence and prevalence of NETs are thought to be rising, but updated epidemiologic data are lacking.

GEP-NETs are rather uncommon-in Europe, Germany, and the US, there are only 1 and 3.5 new instances year, per 105 inhabitants, respectively-but during the past 40 years, their incidence rate has more than tripled [14,15,16,17].

Most likely as a result of endoscopy's increasing use, the incidence of G-NETs has grown recently (increased identification).

According to one study, the frequency of G-NETs rose from 0.31 per 106 individuals in 1975 to 4.85 in 2014 [18].

The most prevalent small bowel tumor in 2000 was SB-NETs, which replaced adenocarcinomas.

Its incidence is estimated to be 1.2 per 105 people, a six-fold rise from the 1970s [14].

The small bowel is the second most prevalent GEP main site of NETs after the rectum, accounting for about 17% of all diagnosed NETs [19].

According to a review realized by Mafficini and Scarpa, SB-NETs make up 25-30% of all GEP-NENs and are the most common NETs of the digestive tract in the West, while they are uncommon in Eastern nations and extremely rare in South Asia [17,20,21,22].

Over the 25-year period from 1990 to 2015, the incidence in the UK increased by more than double, from 1 to 2.5 cases per 10^5 persons/year.

There is currently uncertainty regarding potential correlations with dietary risk factors. Small bowel cancer has also been connected to industrial exposures [23].

The primary cause of the rising prevalence of neoplastic patients is an increase in duodenal tumors [24].

Our study revealed some specific findings that contradict the previous studies: tumors located in the colon predominated (69.10%); we did not diagnose rectal tumors, and small intestine locations were only in 14.55% of the total tumors diagnosed.

Depending on the portion of the human embryo from which most of the intestines develop, three portions are distinguished. The *foregut* is the anterior part of the alimentary canal, from the distal esophagus to the first half of the duodenum at the entrance of the bile duct. The region of the human embryo from which the majority of the intestines develop is called the *midgut*; it consists of the section of the alimentary canal from the end of the foregut at the bile duct entrance to the hindgut that passes through the transverse colon approximately two-thirds of the way. From posterior to caudal, the alimentary canal has the *hindgut* (sometimes called the epigaster); it includes the splenic flexure, the last third of the transverse colon, and the descending, sigmoid, and ano-rectal junctions.

We observed the following incidence of NET after taking this classification into account: 9 tumors in foregut localization, 30 tumors located in the midgut region, and 16 tumors in the hindgut part.

Colorectal NETs (CR-NETs) have an incidence of 0.2 and 1.2 new cases per 10^5 persons/year [3].

C-NETs represent approximately 5-7% of all well differentiated GEP-NETs, but 25% of all GEP neuroendocrine carcinomas (GEP-NECs) [25].

Over the past 35 years, there has been a 10-fold increase in R-NETs, according to the Surveillance, Epidemiology, and End Results (SEER) database. This increase is likely the result of increased incidence and better, more frequent colonoscopies brought on by the widespread use of screening endoscopies to detect colorectal cancers [14].

It's important to note that incidence varies significantly across countries. Whereas R-NETs account for as much as 60% of GEP-NETs in Korea and Japan, they make up only 5-27% of GEP-NETs in Europe and the US. This geographic variety is likely caused by variations in database compilation, classification, colonoscopy screening programs, and potential ethnic diversity [26].

The results of our retrospective clinical study could be a support or a part of an extensive study regarding the generic profile of patients with GEP-NETs.

The first discussion of our study referred to patient profiles by age category, an obviously detailed detail, that being the most significant associations in addition to the incidence, the possible types of complications, and clinical and histopathological features. The scope of creating an epidemiological and clinical anamnestic is rare today in medical literature.

In our study group, the patients' ages were between 39 and 86 years, with a mean of 66.04, except for the patient who was 39 years old, as we mentioned below.

We registered a small number of patients under the age of 40 (n=1 case, or 1.81%), which determines us to think that the incidence of GEP-NETs in young patients is low. In particular, we debated an 8-year-old patient group of study, which is included here, like a general aspect, those few cases of MiNENs that have been excluded from our study from the beginning.

Also, we noted that between 60 and 79 years old, there was the highest proportion of cases (n=40 cases, or 72.72% of total cases).

Between the same interval (60-79 years), we noted a 1.18-fold higher registration of cases from the urban area compared to the rural area (31 vs. 24 cases).

Fewer studies published in the last few years have emphasized the increasing incidence of GEP-NETs in the general population [6,27,28,29], in spite of the improvement of diagnostic methods, and somehow, by increasing the specialty medical units, especially in elderly patients, they could have a reduced 5-year survival rate [30].

In our study, we observed an important increase in the number of cases after the age of 60, as well as a large proportion of patients aged between 60 and 69 years old (43,63%), which is the statistical part with the highest aggregation of patients. The sixth and seventh groups were the most balanced in terms of patient gender (17.58% male patients and 15.38% female patients, respectively, 18.68% male and 23.08% female patients).

Furthermore, in Romania, a retrospective study conducted in Iasi revealed an incidence of 37 GEP-NETs patients from 2005 until 2019.

Patients were between 20 and 79 years old, being represented by 15 males and 22 females.

From his study, 5 NETs were with gastric localization, 10 patients presented with SB-NETs, and 17 cases were with colorectal localization (10 apendix and 7 colorectal) [31].

About 6-21% of gastric NENs are gastric neuroendocrine carcinomas (NECs), and men are more likely to be affected than women (male to female ratio of 2:1) with an average age of 65 years (range 41-76 years) [32].

According to Volante et al., the C-NETs have a mean age of 65 and a clinical appearance akin to colonic adenocarcinomas. R-NETs typically present between the ages of 55 and 60, and diagnoses are frequently made by accident during screening colonoscopies [25].

The SEER program determined age-specific incidence rates for three age groups: under 50, 50 to 64, and 65 years or older. Patients 65 years of age or older saw the largest increase in incidence, increasing by more than 8-fold to 25.3 per 105 individuals, and those 50 to 64 years old saw an increase of 14.3 per 105 individuals. Patients under 50 years old saw a more moderate 3-fold increase, reaching 1.75 per 105 individuals [14].

Men and women experience SB-NETs equally, with a mean age of 65.4 years [33].

Analyzing the area of residence, there was an almost similar proportion of patients from the urban area (n=30-54.55%) compared to those from the rural area (n=25-45.45%). This can be explained by the suitable accessibility of patients to medical services, but also probably by the upgrading of environmental factors.

In addition, regarding the immune mediation and the involvement of neurotransmitters in GEP-NETs, it is considerable for research the association between arterial hypertension (27 patients, 49.09%-probably associated with other causes, too, regarding the age and the pathological modifications that surveillance through epigenetic and risk factors; 18 males, 32.73% and 16.36% females), also through the same evidenced substrate of catecholamines and proinflammatory factors, the association with diabetes mellitus, psoriasis, and chronic liver diseases [34-45].

Also, no one patient was treated with pump inhibitors in our studies regarding the risk of NETs [43-46].

Conclusion

The results obtained in our should consist in the initial hypothesis proposed for creating a paradigm through, beginning with anamnestic information being helpful for integration in paraclinical and histopathological features, for creating a much useful template of the patients with GEP-NETs.

Our study of statistical information suggested us some particularities of male and female patients diagnosed with GEP-NETs.

Also, we wished to identify a part of a complex process for a rapid and opportune diagnosis in this type of sever disease, for creating an easy way to obtain much rapidly the suitable treatment measures, even if medicals or surgical ones.

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Conflict of interests

There is nothing to declare.

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