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CLINICAL CHARACTERIZATION OF NEUROENDOCRINE TUMORS SYSTEMATIC REVIEW

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Abstract: Neuroendocrine tumors are neoplasms that represent a global problem due to their incidence, progression in the metastatic phase, and impact on the survival rate. Therefore, the present study aimed to "characterize clinically and epidemiologically neuroendocrine tumors." The methodology used was through a systematic review of a narrative and descriptive nature with a total of 58 studies from Pubmed, Cochrane Library, Scielo and Medline. Among the results: the prevalence of NET has an incidence of 7.5 per 100,000 inhabitants. In relation to the type of NET, pNETs had a great impact in the study, followed by GI-NET and pulmonary-NET where the Female gender was the most affected at ages between 50 and 80 years. Metastasis was reported mainly in the lymph nodes also in the liver, lung and others. Additional approaches need to be developed to better understand the biological behavior of this disease, with a focus on molecular genetics and better experimental models. In clinical practice, it is necessary to have a greater number of tumor markers to improve the diagnosis and detection of neoplasms with greater precision and at earlier stages.
Keywords: Neuroendocrine tumors, pancreas, gastrointestinal, prevalence, survival**.**

INTRODUCTION

Neuroendocrine neoplasms originate in the neuroendocrine cell system and can present benign or malignant characteristics. These are divided into 2 groups: neuroendocrine tumors (NET) and neuroendocrine carcinomas (NEC) (1). Neuroendocrine tumors are defined as well-differentiated NENs with low proliferation, while NECs are defined as NENs with low degrees and high proliferation (2).

NETs can occur in various tissues of the body. One of the initial classifications of NETs considers the embryological origin of the affected structure, which is then associated with neoplasms of the foregut: lung, bronchi, stomach, mid-intestine (small intestine, cecum and proximal colon) and rectum (distal colon). and straight) (3).

However, due to the emergence of different presentation systems and to avoid possible confusion, in 2010 the use of the World Health Organization (WHO) classification of neuroendocrine tumors (4) was established as an international standard with three groups: well-differentiated tumor or Degree I tumor, moderately differentiated or Degree II tumor, and poorly differentiated or Degree III tumor, according to the Degree of cell proliferation (measured by the Ki-67 index) and the number of mitoses in the test sample.

NETs are a growing global problem (5), they can occur in almost any organ, but the most common are the gastrointestinal tract and pancreas (6,7). Among gastroenteropancreatic NETs, the most common site is the small intestine (30.8%), followed by the rectum (26.3%), large intestine (17.6%), pancreas (12.1%), and cecum (5.7%) (8).

In Latin America there is little data on the epidemiology of this pathology, a national statistical study in argentina showed that endocrine tumors of gastroenteropancreatic origin NET-GEP represented 26% of the cases, of which 29.5% were Degree I, 35.9% Degree II and 9% in Degree III (9).

In Ecuador there are no studies that verify the incidence of neuroendocrine tumors and there are few specialized centers that allow a multidisciplinary study (10). However, there are reports of neuroendocrine tumors that are diagnosed in the metastatic phase, including: stomach, small intestine 4%, large intestine 1%, rectum 1%, pancreas 1%, bronchi and lungs < 1%, thymus < 1%, heart, mediastinum and pleura 2%, skin < 1%, among others., (11) whose problem persists due to the lack of a timely diagnosis.

Based on the existing problems, the purpose of this study is to clinically and epidemiologically characterize neuroendocrine tumors through a systematic review. The research has social relevance since it is a topic whose scientific evidence is scarce specifically in Ecuador and its impact. in health is significant if it is not diagnosed in a timely manner.

To this end, healthcare providers will have access to adequate information to understand the magnitude of the problem, prioritize a timely approach, and improve clinical practice in order to minimize the incidence of metastatic stages in affected patients.

GOALS

General goal

To characterize neuroendocrine tumors clinically and epidemiologically through a systematic review.

Specific goals

1. Describe the type of NET with the highest incidence in the population.
2. Identify the prevalence of NET stage in the study population.
3. Determine the vulnerable population in the incidence of NET according to age and sex.
4. Know the survival of patients after 5 years in relation to the severity of the disease.

Neuroendocrine Tumors

Neuroendocrine tumors (NET) are heterogeneous neoplasms that arise in the secretory cells of the diffuse neuroendocrine system (12,13), they are characterized by a relatively slow growth rate and the ability to secrete various hormones, cells with properties both nervous and endocrine cells (14).

Classification

Historically, neuroendocrine tumors have been classified according to their embryonic origin: foregut (lung, stomach, duodenum, upper jejunum, and pancreas), midgut (lower jejunum, ileum, caecum, and cecum), and hindgut (colon and rectum). The World Health Organization (WHO) (15) classifies NEN to reflect tumor biology and better predict the disease based on tumor characteristics.

Index Ki-67 (%).	Miotic index-67
Well differentiated NEN	
NET G1	<2/10 HPF
NET G2	2-20/10 HPF
Poorly differentiated NEN	
NEC G3	>20/10 HPF
NMEN/MENEM	

Table 1: World Health Organization classification of neuroendocrine tumors.

Source: World Health Organization, Classification of neuroendocrine tumors (15).

Abbreviations: HPF, high power field; MINEN/MENEN, mixed endocrine non-endocrine neoplasms; NEC, neuroendocrine carcinoma; NEN, neuroendocrine neoplasia; NET, neuroendocrine tumor.

ETIOLOGY

About 20% of NETs are associated with genetic causes, including multiple endocrine neoplasia type 1 (MEN1) and neurofibromatosis type 1 (NF-1) (2). It is estimated that the majority of cases occur sporadically, although they may be part of familial endocrine cancer syndromes such as multiple endocrine neoplasia type 1 (MEN1), multiple endocrine neoplasia type 2 (MEN2), neurofibromatosis type 1 (NF1), von Hippel-Lindau disease and the Carney complex (16).

PATHOPHYSIOLOGY

Many neuroendocrine cells contain membrane-bound neurosecretory granules that contain biogenic hormones and amines such as serotonin, corticotropin, histamine, dopamine, substance P, neurotensin, prostaglandins, and kallikrein. The release of these substances into the systemic circulation can cause various secretory syndromes, which can manifest as hot flashes, diarrhea, wheezing, skin rashes, or even multiple organ failure. (2).

Somatostatin receptors and their downstream signaling pathways have been found to be key regulators of neuroendocrine cell proliferation, protein synthesis, and hormone secretion (17).

NET cells secrete several proangiogenic factors. These include vascular endothelial growth factor, FGF, PDGF, semaphorins, and angiopoietins. This leads to the recruitment, proliferation and neovascularization of endothelial cells, making the tumor highly vascularized (the microvascular density becomes 10 times greater than that of epithelial tumors). (12).

CLINICAL MANIFESTATIONS

NETs can be found accidentally, the symptoms of which are manifested by an increase in mass or progression of the disease and overproduction of hormones. CS is present in 19% of NET cases, which is associated with a significant increase in the levels of serotonin, bradycin, histamine, kallikrein, etc. In case of Metastasis, the substances produced can escape destruction in the liver and enter the systemic circulation, causing the characteristic symptoms of CS: hot flashes, diarrhea, abdominal pain, bronchial obstruction, damage to the heart valves. If CS is clinically suspected, evaluation must include echocardiography to evaluate cardiac involvement. (18).

TREATMENT

Treatment involves both a surgical approach, for both primary and metastatic lesions, as well as medical management to manage symptoms and disease progression (2). For NET 1 or 2, curative surgery may be considered even if there are metastasis to the liver or lymph nodes (1).

In patients with advanced disease, tumor debulking strategies such as hepatic artery embolization (HAE), selective internal radiation therapy (SIRT), radiofrequency ablation (RFA), and palliative cytoreductive liver surgery can significantly reduce tumor burden. or result in symptomatic improvement to hormonal excess (1).

Treatment of G3 tumors is based on limited evidence and includes surgical resection and chemotherapy or PRRT for well-differentiated tumors. Furthermore, recently published case series report promising immunotherapy results, while several ongoing phase II studies are investigating the activity of immune checkpoint inhibitors in NETs (19).

NETS CAN DIVERSIFY IN DIFFERENT PARTS OF THE BODY SUCH AS:

a. Gastrointestinal net: Neuroendocrine tumors of the gastrointestinal tract are rare, slow growing, with diverse histological, biological and clinical characteristics, whose incidence and prevalence have increased in recent decades (14).

GI-NETs constitute 7% to 8% of all NETs. The incidence is increasing (more than 10 times in the last 30 years). According to records, G-NET coverage increased from 0.31 per 1,000,000 inhabitants in 1975 to 4.85 per 1,000,000 inhabitants in 2014 (20).

Type I and type II gastric NETs can present with symptoms such as gastric ulcers, bleeding gastric polyps, or gastric carcinoma. Type III and IV gastric NETs are more aggressive and have similar characteristics to gastric adenocarcinoma (2).

GASTROINTESTINAL NETS ARE SUBDIVIDED INTO:

- **Small intestine tumors (SI-NET):** It is the most common primary malignant neoplasm of the small intestine, representing 25% of all GI-NETs, they are indolent, often multifocal, have a distal disposition and develop Metastasis more frequently than other NETs. (21).

- **Duodenal tumors (d-NET):** They make up 2% to 3% of all GI-NETs. They are small, solitary lesions confined to the duodenal mucosa and submucosa. At diagnosis, 40-60% of d-NETs metastasize to regional lymph nodes and 10% to the liver. (21–23).

- **Jejuno-ileal tumors (JI-NET):** CThey make up 23% to 28% of all GI-NETs. Most jejunoiliac NETs (JI-NETs) do not work. Clinically, patients may be completely asymptomatic or present with abdominal pain, ileus, gastrointestinal bleeding, and decreased urination. (24).

- **Appendiceal tumors (a-NET):** It is the third most common NET in the gastrointestinal tract. In most patients, the disease is asymptomatic, and appendectomy is diagnosed incidentally in 0.3-0.9% of cases. Histologically, appendiceal NETs are EC (serotonin-producing) cell NETs, L-type NETs, and MiNENs (goblet and adenocarcinoma).) (14).

- **Colonic tumors:** It is the second most common advanced gastrointestinal cancer after colorectal cancer. Colonic NETs are sometimes seen as a large lesion during screening colonoscopy. Treatment is segmental colectomy with extensive regional lymphadenectomy. Imaging studies must be performed to determine the NET stage of the colon (25).

-**Rectal tumors:** The incidence of NET of the rectum is approximately 1 case per 100,000 inhabitants per year (26). Most rectal NETs remain asymptomatic and are diagnosed incidentally during screening colonoscopy or during lower endoscopy for another reason. (14).

b. Pancreatic NET: They are a rare and heterogeneous group of pancreatic neoplasms with a wide spectrum of malignant potential. They can present as slow-growing, non-infiltrating tumors, locally invasive masses, or even rapidly metastatic cancers. (27).

PNETs are considered rare, with an annual incidence of less than 1 in 100,000 people, however, these tumors are becoming increasingly common worldwide (6), (28). The World Health Organization pNET classification is based on Ki-67 expression and number of mitoses. Degree 1 and 2 tumors are considered well-differentiated (Ki-67 < 20%) and Degree 3 tumors are classified as well-differentiated NET or neuroendocrine carcinoma. (NEC) (29).

The clinical picture may be associated with the excessive secretion of tumor hormones, such as excess insulin (insulinoma), gastrin (gastrinoma), glucagon (glucagonoma), vasoactive intestinal peptide (VIPoma), somatostatin (somatostatinoma) or pancreatic insufficiency. (30).

c. Pulmonary NET: they are rare neoplasms that show significant heterogeneity from well-differentiated tumors to poorly differentiated small cell lung cancers. (31).

The World Health Organization classification of bronchial NEN (32) is based on a combination of the mitotic index and the presence of necrosis. The most common clinical features are cough, hemoptysis, recurrent respiratory infections and dyspnea, but rarely pulmonary NEI can be associated with carcinoid or Cushing's syndrome. (1).

The only radical treatment for bronchial NET is surgical resection (33). The prognosis varies greatly between typical and atypical pulmonary NEN. TCs are associated with a

10-year survival rate of around 82-100% and ACs with 18-74%. For small cells, large cells and mines, the patient's prognosis is very poor and combined therapeutic strategies can be used, including chemotherapy and radiotherapy. (34).

d. Pituitary NET: It is the third most common intracranial neoplasia (15%) and the most common tumor (85%) in the sellar-suprasellar region. Timely diagnosis and effective treatment to control hormonal hypersecretion and alleviate mass effects along with replacement of deficient hormones are crucial to reduce these associated health risks. (35).

Hypersecretion of ACTH causes Cushing's disease, with features of hypercortisolism, hypersecretion of GH leads to acral overgrowth and metabolic dysfunction associated with acromegaly, and hypersecretion of PRL leads to gonadal insufficiency, secondary infertility, and galactorrhea. (36) although they are most commonly found in the gastrointestinal tract and respiratory system. The skull base and sellar region are extremely rare sites for neuroendocrine carcinoma. Consequently, in this case, both diagnosis and definition of surgical goals, as well as further treatment strategies were challenging. CASE DESCRIPTION: A 65-year-old woman was admitted to our Neurosurgery Department with a rapidly progressive visus reduction, drowsiness, polyuria, and polydipsia. Neuroimaging showed a sellar/suprasellar mass (diameter of 2 cm.

More rarely, hypersecretion of TSH causes hyperthyroxinemia and goiter, and hypersecreted gonadotropins (or their respective subunits) cause gonadal dysfunction. In contrast, tumors that arise from gonadotroph cells do not efficiently secrete their gene products and are usually clinically silent. (37).

e. Gallbladder NET: They are considered extremely rare and represent only 0.5% of all tumors. As a consequence, gallbladder NETs are extremely difficult to diagnose with traditional imaging methods and are often discovered incidentally at a later stage. (38)887 single cells was obtained and characterized as 10 cellular clusters, including epithelial, neuroendocrine tumor cells, T&NK cells, B cells, RGS5+ fibroblasts, POSTN+ fibroblasts, PDGFRA+ fibroblasts, endothelial, myeloid cells, and mast cells. Different types of GC harbored distinct epithelial tumor subpopulations, and squamous cell carcinoma could be differentiated from adenocarcinoma cells. Abundant immune cells infiltrated into adenocarcinoma and squamous cell carcinoma, rather than neuroendocrine neoplasms, which showed significant enrichment of stromal cells. CD4+/FOXP3+ T-reg and CD4+/CXCL13+ T helper cells with higher exhausting biomarkers, as well as a dynamic lineage transition of tumor-associated macrophages from CCL20(hi.

The difficulty in diagnosing these tumors is due in part to the poor correlation with specific symptoms. As with most cancers, a biopsy is considered essential for definitive diagnosis. Currently, the mainstay of therapy for these tumors is mainly surgery with adjuvant chemotherapy if appropriate. (39).

The incidence of NEC of the gallbladder is very low. Although gallbladder cancer is the sixth most common cancer in the digestive system, gallbladder NECs account for only about 2% of all gallbladder cancers and about 0.5% of all NECs. (40).

f. NET Thymus: They are neoplasms extremely rare, accounting for approximately 0.4% of all carcinoid tumors and less than 5% of all anterior mediastinal neoplasms. Furthermore, these neoplasms have been found to be malignant in more than

80% of cases, unlike lung carcinoids, which are considered malignant in only approximately 25% of cases. (41)large cell neuroendocrine carcinoma (LCNEC.

METHODOLOGY

STUDY TYPE AND DESIGN

It is a systematic review of a narrative and descriptive nature.

SEARCH STRATEGY

Keywords: incidence; neuroendocrine tumor; prevalence; survival; Neuroendocrine neoplasia, Carcinoid, Epidemiology, Survival, Predictors of survival/incidence; neuroendocrine tumor; predominance; survival; Neuroendocrine neoplasia, Carcinoid, Epidemiology, Survival, Survival predictors.

Database: Scielo, Medigraphic, Pubmed, Elsevier and Scholar.

Boolean operators: Neuroendocrine Tumors AND Incidence, Neuroendocrine Tumors OR neuroendocrine neoplasia.

MeSH Terms: It is the linguistic tool par excellence to carry out high-quality bibliographic searches in Pubmed (42). The search terms used were: NET, Gastrointestinal Neoplasms / epidemiology, Gastrointestinal Neoplasms / pathology, Neuroendocrine Tumors / epidemiology, Neuroendocrine Tumors / pathology, Pancreatic Neoplasms / epidemiology, Pancreatic Neoplasms / pathology, Prevalence.

Critical analysis: A comparative analysis will be carried out by different authors on the prevalence of neuroendocrine tumors, types and other relevant clinical characteristics. Selection criteria

Inclusion:

- Studies from the last 7 years.
- Articles in Spanish-English.
- Use of databases in health sciences.

Exclusion:

- Articles without scientific relevance.
- Research without scientific contribution.
- Information from blogs, letters to the author and monographs.

SELECTION OF EVIDENCE

From the selection of studies, 160 articles were collected, of which 75 were discarded due to exclusion criteria, giving a total of 90 publications.

In the processing of each scientific article, the title, summary, methods, results, conclusions and recommendations were analyzed, verifying the presence of some documents that do not meet the selection criteria and their topics not related to the study, resulting in 23 copies being eliminated. 58 publications thus met the required search criteria (fig. 1).

DISCUSSION

In recent years, the incidence of neuroendocrine tumors has increased, probably due to an increase in the sensitivity of diagnostic tests. However, despite the diagnostic methods, timely identification is relatively low, which leads to a high rate of patients in the metastatic phase.

A total of 18 studies showed the prevalence of NET, of which the authors Yan (58) reported an incidence of 7 per 100,000 inhabitants, for their part, Shah et al., (50) demonstrated a decrease of 1.7 in incidence (5.3 per 100,000). Unlike the previously reported values, the authors Chauhan et al., (44) expressed that the number of cases is variable and can be considered between 3.1 to 10.3 per 100,000.

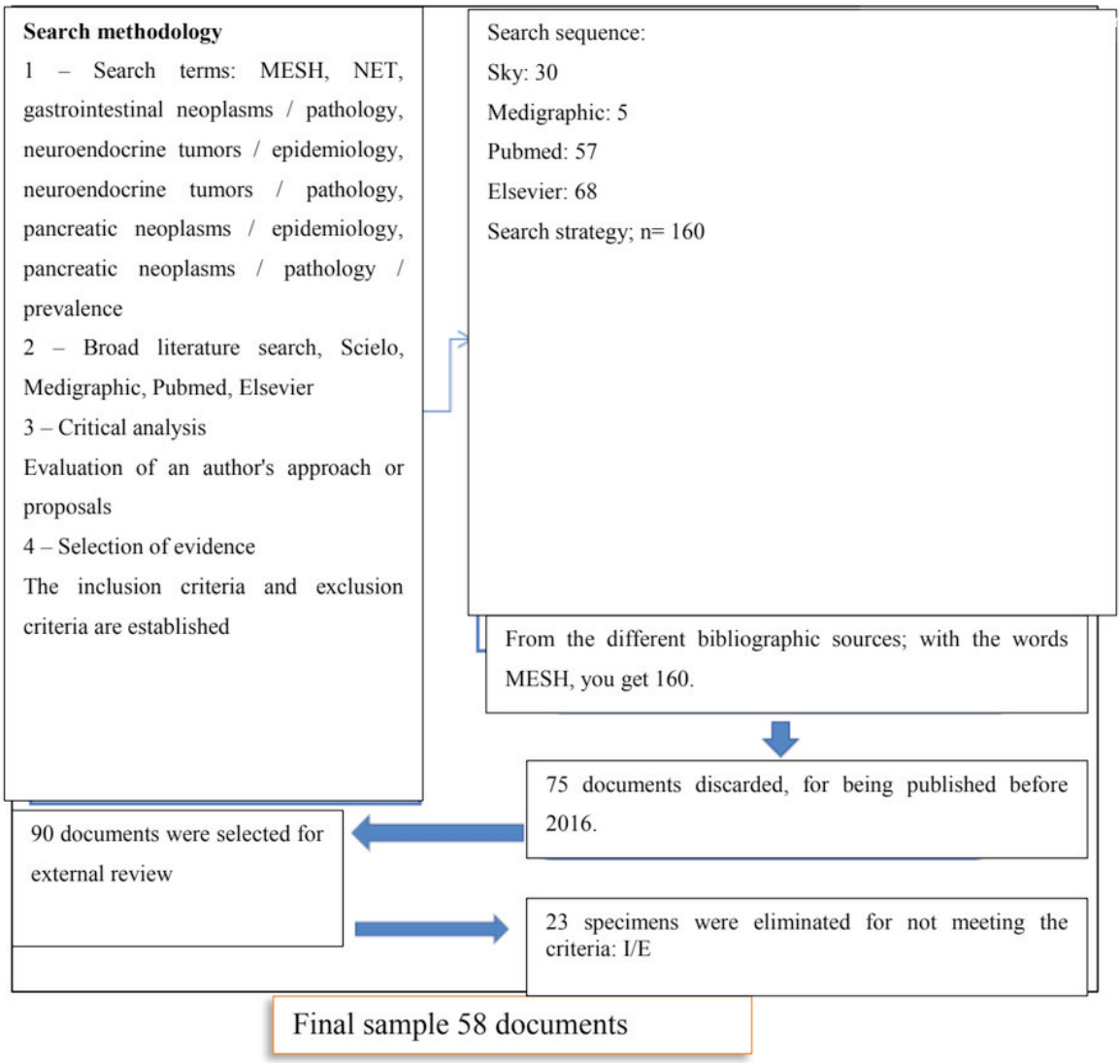

Figure 1: Document selection flowchart.

Own elaboration.

RESULTS

Author	Year	Population	Prevalence	Type	Age/ average	Gender	Stadium	Metastasis	Survival to 5 years
Yang et al., (20)	2018	3740	4,85 per each 1.000 000	GI-NET	60 years	Female 59,9%	G1: 91,7%	6.32-fold increase in GI-NET mortality	86,7 % ± 0,7 %
Zhang et al., (25)	2019	1248	NET: 25,1% NEC: 74,9%	Colonics	60 years	Male 59,9%	Degree 1: 19,2% Degree 2: 4,8% Degree 3: 76%	Lymph node metastasis 59.7%	Degree 1: 100 % Degree 2: 90,0 % Degree 3: 82,8 % Degree 4: 53,9 %
Du et al., (43)	2016	832	0,8 per each 1.000. 000	SI-NET 35,2% pNET 18,7% NET-Bronquial 15,3% Other 30,6%	55 years	Female 53%	Differentiated 95,3% little differentiated 4,6%	Metastasis 47,9%	-
Chauhan et al., (44)	2018	6179	The incidence rate is 3.1 to 10.3 per 100,000	Pulmonary NET 30.6% SI-NET 16.82% rectal NET 11.35% Colonic NETS 9.71%	50 a 64 years 38%	Female 54,74%	G1: 52% G2: 3% G3: 22% Unknown: 23%.	Metastasis 22%	G1: 67,5 % G2: 28,6 % G3: 3,9 %,
Qingquan et al., (45)	2022	237	NET: 48,9% 1,16 per each 10.000 NEC: 51,1%	GB-NET GB-NEC	68 years	Female 67,5%	G1 y 2: 14,8% G3 y 4: 27,0% Unknown: 58,2%	Lymph node metastasis 30.4%	10 months
Kasajima et al., (46)	2022	1513	NET: 71% 11,3 per each 10.000 NEC: 17% MiNEN: 10%	pNET: 28% GI-NET: 44% pulmonary NET: 11%	59 ± 16 years	Both genders 50:50 %	G1 y 2: 68% G3: 32%	Metastasis 69% -Liver: 74% -Lymph nodes 11% -Other 14%	-
Alkhayyat et al., (47)	2021	30.324.050	aNET: 7 por 100.000	aNET: 0,2%	65 years	Female 64%	G1: 90.56%	Carcinoid syndrome 8.2%	-
Blažević et al., (48)	2022	559	SI-NET: 3,4 per each 10.000	SI-NET	52-68 years	Female 47%	I y II: 2% III: 20% IV: 78%	Liver metastasis: 72% Mesenteric metastasis: 71%	-
Dasary et al.,(49)	2018	9319	1.49 per 100,000 lung 3.56 per 100,000 gas-troenteropancreatic infections	NET colon: 12.43% NET Lung: 30.77% pNET: 7.43% GI-NET: 24.54%	>80 years 27,69%	Female 55,80%	Degree I: 52,70% Degree II: 6,65% Degree III/IV: 15,35% Unknown: 22,61% Mixta: 2,68%	Metastasis: 5,26%	Months: Colon: 14 Pancreas: 60 Lung: 24 Small intestine: 103
Shah et al.,(50)	2021	124.969	5,3 per each 100.000	Pulmonary NET	60 years	Female 67%	G1: 6.5% G 2 y 3: 93%	Metastasis 84 %	64%

Xu et al., (51)	2021	12.428	1,05 per 100000	GEP-NET	58 years	Female 51,2%	Degree 1: 71,13 % Degree 2: 17,44 % Degree 3: 8,74 % Degree 4: 2,69 %	Metastasis 2.6%	Degree 1: 91,4 % Degree 2: 80,8 % Degree 3 :28,8 % Degree: 4 :23,0 %
Loosen et al., (52)	2020	662	6.62 per 10000	pNET	62 years	Male 53.9%	Degree 1: 1,5 % Degree 2: 8,5 % Degree 3: 5,0 % Degree 4: 85,0 %	Liver 89.0% Peritoneum 8.0% Lung 11.0% Bones 6.0% lymph nodes 28,2 %	-
Titan et al., (53)	2020	249	0,3 per each 100000	pNET	57 years	Male 57%	Degree 1: 53 % Degree 2: 47%	Metastasis: 1%	91%
Şincu et al., (54)	2021	91	0,6 per each 10000	NET	61 years	Male 66%	G1: 46,6 % G2: 13,3 % G3: 40%	12,08% metastatic	-
Sada et al.,(55)	2020	121	0,0-0,27 cases per million	pNET	56 years	57 % Male	Degree I: (2,2% Degree II: (6,6%) Degree IV: (0,8%) Undetermined or undeclared cell type:(60,3%)	16% metastatic	84 % survival
Pang y Guo et al., (56)	2021	431	0,3 per each 10000	NET ovary	63 years	Female 100%	I 92.7% II 2% III 2.4% IV 3.3%	Metastasis 58,9%	I: 83,3 % II: 30,0 % III: 20,3 % IV 9,8 %
Wang et al., (57)	2022	206	4% per each 10000	pNET	64 years	58 % men	Degree 1 :46.6% Degree 2/3: 53.4%	8% of the patients	92% of survival
Yan (58)	2022	11	7,0 % each 100.000	pNET	53 years	63,6% Female	G1: 18% G 2: 82%	Metastasis: 72%	G1: 35,0 G2: 26,0 months

Table 2: Clinical characterization of neuroendocrine tumors.

GEP- NET: gastroenteropancreatic neuroendocrine tumors, pNET: pancreatic neuroendocrine tumors, GI-NET: gastrointestinal neuroendocrine tumors, TNET: thymus neuroendocrine tumors, pulmonary NET: lung neuroendocrine tumors. SI-NET: small intestine neuroendocrine tumors. aNET: appendix neuroendocrine tumors.

In relation to the type of NET, it has been shown that pNETs have had a great impact in the study, whose incidence according to the authors Loosen et al., (52), Titan et al., (53) and Sada et al.,(55) is estimated at 0.3 per 100,000 inhabitants, followed by GI-NET with a significant increase of 1.16 per 10,000 inhabitants (44) and pulmonary-NET with a prevalence of 1.49 per 100,000 (49).

Based on the incidence of sex, it was observed that the female gender is the most affected (20) (43) (44) (45) (47) (48) (50) (51) (56) (57) (58), whose age was included by the adult and older adult population within the range of 50 to 80 years. The studies showed that the most frequent stage is grade 1, as indicated by Yang et al., (20) in 91.7%, Alkhayyat et al., (47) 90.56%; Unlike the authors Kasajima et al., (46) and Chauhan et al., (44) the values decrease considerably by 68% and 52% respectively.

However, although primary tumors have a greater impact in the study, a high incidence of metastasis is reported. The authors Shah et al., (50) showed metastasis in 84% with a survival of 64%. Unlike Zhang et al., (25) demonstrated a prevalence of 59.7% in lymph nodes with a relatively low survival of 53.9%. For their part, Qingquan et al., (45) agree that lymph node metastasis is common but with an incidence of less than 30.4%, whose survival is 10 months to 5 years.

The authors Kasajima et al., (46) reported 69% metastasis, of which the liver was 74%, lymph nodes 11% and others 14%. Similar data were demonstrated by Loosen et al., (52) with 89% in the liver, 28.2% lymph nodes and 11% lung.

CONCLUSIONS

Neuroendocrine tumors are neoplasms that, although they were identified a century ago, are considered neoplasms that do not have adequate management and timely detection and, consequently, the survival rate has not improved significantly to date.

Within the study, the prevalence of NET was characterized, where the authors demonstrated a variability in incidence with an average of 7.5 per 100,000 inhabitants. In relation to the type of NET, pNETs have had a great impact in the study, followed by GI-NETs and pulmonary-NETs.

Based on the incidence of sex, it was observed that the female gender is the most affected, whose age group was between 50 and 80 years old. A high incidence of metastasis was reported, of which the lymph nodes have the highest number of cases with a low 5-year survival; metastasis were also evident in the liver, lung and others.

Additional approaches need to be developed to better understand the biological behavior of this disease, with a focus on molecular genetics and better experimental models. In clinical practice, it is necessary to have a greater number of tumor markers to improve the diagnosis and detection of neoplasms with greater precision and at earlier stages.

There are few interinstitutional studies in this area and comparison of different therapeutic modalities is difficult. Therefore, it is necessary to create concentration centers that allow research on these neoplasms to continue developing, create databases and, most importantly, constantly evaluate them within the framework of a national and global panorama.

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