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Clinical Profile, Epidemiology & Outcome in Patients with Neuroendocrine Tumour in a Tertiary Care Centre in South India

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Abstract: ***Neuroendocrine tumors (NET) arise from neuroendocrine cells in our body. Any organ in our body might be impacted by NETs. Depending on where they are located, neuroendocrine tumors (NETs) are a group of cancers with various and frequently indolent clinical features. It frequently exhibits vague symptoms, which delays diagnosis. In India, the prevalence of NETs is rising. Objectives: To analyze the epidemiology, clinical profiles, and post - treatment survival outcomes of patients with NET in a tertiary care center in South India. Methods: We analyzed data of 13 patients diagnosed with NET who presented to dept. of Medical Oncology, Govt. Royapettah Hospital and Department of Digestive Diseases and Health, Anna Nagar, Chennai between 2020 and 2022. The clinicopathological profile, treatment, and follow - up data were analyzed. The variables linked to NET - related mortality were discovered using univariate analysis. Results: Men constitute 46.15 % of the population, while women make up 53.85 %. The median age at diagnosis of NET in our study was approximately 58.15 years. A higher proportion of patients with NET were fromrural areas (61.5%) compared with those living in urban areas (38.46%). The most common primary tumor site was the duodenum (46.15%), gastric (15.38%), pancreas (15.38%), rectum (15.38%), and ileum (7.69%) in descending order. Histological grading was done according to mitotic index and Ki - 67 index showing G1 constitutes 69.23%, G2 (15.38%), and G3 (15.38%).2 patients (15.38%) had metastatic lesions. Tumor characteristics and treatment characteristics were assessed. In our study, the overall survival rate at 2 years was found to be 69.23%, and the disease - free survival rate was found to be 53.84%. Conclusion: The factors significantly associated with NET - related mortality were age, primary tumor site, surgical resection status, tumor grade, and clinical stage of the patient.***

Keywords: Neuroendocrine tumor, Chennai, duodenum, mitotic index

1. Introduction

Neuroendocrine tumors (NETs) are a diverse category of malignancies with variable therapeutic responses depending on the initial tumor site and functional hormonal activity and frequently indolent clinical - biological features [1]. Almost any organ can be impacted by these tumors because neuroendocrine cells are found throughout the body, including the lungs, small intestine, rectum, colon, appendix, and stomach [2, 3]. This leads to various nonspecific symptoms and delays in diagnosis. Even though some NETs have the potential to spread quickly and affect other organs, the majority of NETs are indolent in nature. Thought to make up just around 2% of all malignant neoplasms, NETs are becoming more widespread, as evidenced by the several registries that are currently accessible [4]. A revised classification of NETs based on clinical, pathological, pharmacological, and prognostic criteria was recommended by the World Health Organization (WHO) in 2010; an update was published in 2017 [6]. Although the incidence of NETs appears to be increasing in India, the data on the characteristics of NETs among the Indian population are sparse. Owing to the rarity and difficulty in diagnosis, the clinical, behavioral, and survival outcomes of patients with NETs in this demographic region remain ill - defined.

Objectives

To analyze the epidemiology, clinical profiles, and post - treatment survival outcomes of patients with NET in a tertiary care center in South India.

Study Design: Retrospective Observational Study.

All patients who obtained the diagnosis of NET (carcinoid, atypical carcinoid, and well - differentiated NET) between 2020 and 2022 were included in the retrospective data collection from the Hospital Cancer Clinical Registry. The pathological diagnosis and grading of hematoxylin and eosin - stained slides that were accessible at our institution were evaluated in accordance with the 2010 WHO classification and grading system as well as the updated guidelines in the 2017 WHO classification of endocrine organs. Data were acquired from laboratory and clinical information systems for slides that couldn't be reviewed. Gastroenteropancreatic (GEP) NETs were graded into 3 tiers (G1, G2, and G3) according to the following definitions of mitotic count and Ki - 67 index: G1—mitotic count <2 per 10 high - power fields (HPFs) and/or <3% Ki - 67 index, G2—mitotic count 2 to 20 per HPF and/or 3% to 20% Ki - 67 index, and G3—mitotic count >20 per HPF and/or >20% Ki - 67 index. Details on the patient, tumor, treatment, and aftercare were examined in accordance with a predetermined standard procedure. Age at diagnosis, sex, and illness status at the most recent follow - up were all features of the patient. By matching the patient's residential postcode, we were also able to record each patient's degree of isolation. Tumor characteristics included primary location (lung/gastrointestinal tract/pancreas/hepatobiliary system), size (<20 mm vs ≥20 mm), clinical stage (localized and regional vs distant and metastatic), grade, functional activity, and histology. Treatment characteristics included surgical procedures, somatostatin analogue therapy, or chemoradiation.

Inclusion Criteria: All patients who received the diagnosis of NET (carcinoid, atypical carcinoid, and well - differentiated NET) between 2020 and 2022

Exclusion Criteria: Small - cell and large - cell neuroendocrine carcinomas of the lung were excluded because of their vastly different biological and survival profile.

Study Period: January 2020 to December 2022.

Study Methods: Data was collected from hospital records of patients from the Hospital Cancer Clinical Registry

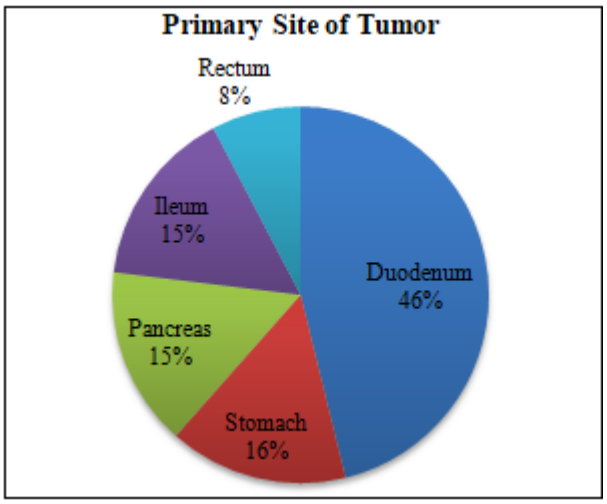
2. Results

The study revealed that men constitute 6/13 patients (46.15%) and women 7/13 (53.85%) patients. The male: female ratio revealed in our analysis is 1: 1.2, showing a slight female preponderance. The mean age at diagnosis of NET is 58.15 years. The females presented at a mean age of 59.7 years and the males at a mean age of 56.33 years. The age of presentation for females and males was similar with a comparatively early presentation for males.

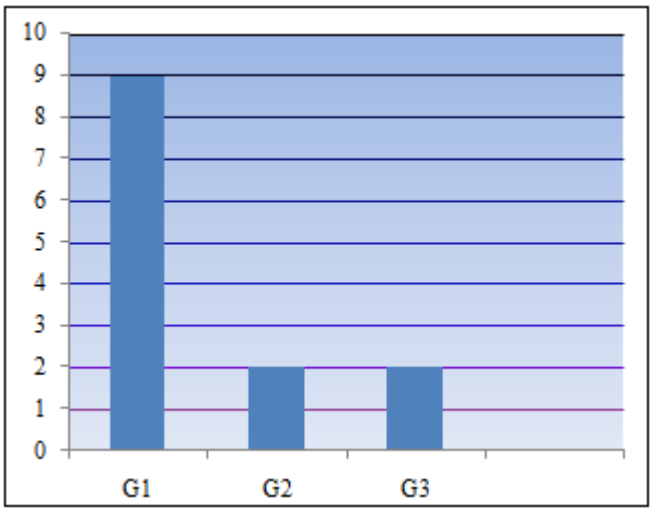
	Total number (%)	The mean age of presentation (years of age)
Females	7 (53.85%)	59.7
Males	6 (46.15 %)	56.33

Primary Site of Tumor

Site	Percentage
Stomach	15.38%
Duodenum	**46.15%**
Pancreas	15.38%
Ileum	15.38%
Rectum	**7.69%**



The most common site of primary tumor observed was seen at the duodenum (46.15%) followed by the stomach (15.65%), ileum (15.65%), pancreas (15.65%), and the least incidence was seen at the rectum (7.69%). This clearly shows that upper GI involvement (76.9%) is much more common than lower GI involvement (23%). Most of the patients with duodenal NET were asymptomatic. Most of the patients were detected with NET incidentally while performing gastroscopy for dyspepsia. Dyspepsia was the most common clinical presentation in the majority. Abdominal pain was the second most common clinical presentation in our study population.



Grades of Tumor

Most of the patients (69.2%) had G1 disease which carries a better prognosis compared to other stages. The most common site where G1 lesions were reported was the duodenum. All patients with gastric NET had G1 - grade of disease. They had the Ki - 67 index of less than 2%. G2 disease was reported in 15.4% of patients. Both of the G2 disease patients had NET in the duodenum. G3 disease was seen in 15.4% of patients, with the tumor being located in the rectum and ileum.

3. Discussion

The neuroendocrine system forms the largest endocrine organ of our body constituting around 14 different cell types and nearly 30 different peptides. All NETs arise from these cells. NETs are notorious for the discordance between the size of the tumor and the extent of metastasis. Most of the NETs are clinically silent. It can be true silent which is often detected incidentally. It can be the primary tumor being silent and metastatic lesions being symptomatic as well. It can be clinically manifesting primary tumors which are functional. NETs remain silent due to their small size and indolent nature. This study was conducted to observe the various clinical manifestations and clinical outcomes in the South Indian population. The study revealed that the females had more incidence of this tumor, with a peak incidence in the 5^{th} decade of life for both males and females. The primary site of the tumor can be seen anywhere along the GI tract. Most of the primary tumors were detected in the duodenum followed by the stomach, pancreas, ileum, and rectum in descending order. Most of the patients had well - differentiated (G1 and G2 grades) tumors having a safer clinical profile and a better prognosis. G1 grade was the most commonly observed grade among the well - differentiated tumors. The symptomatic patients were managed medically followed by curative therapies in lower - grade tumors while higher - grade tumors were managed with various chemotherapy regimens. Inj. Octreotide was given for symptomatic patients presenting with diarrhea followed by surgical options as curative procedures. Most patients underwent resection surgery. Gastrectomy,

Whipple's procedure, wedge resection, resection, and anastomosis, LAR were the other surgical procedures performed depending on the location and character of the tumor. Endoscopic resection techniques like EMR and ESD could be offered for lower grades of tumors. Higher grades of tumor were given various chemotherapy regimens like Cddp+ Etoposide[8], Capecitabine + Temozolomide[9]. At 2 years, the overall survival rate was found to be 69.2%.

4. Conclusion

NETs, due to their indolent course and the smaller size of the primary tumor, are often missed in many patients. Even though they are notorious for their aggressive metastatic lesions, the prevalence of the higher grades of the disease is lesser in our regional population. A high index of suspicion should always be kept in any patients, particularly the elderly, presenting with milder commoner symptoms like dyspepsia, abdominal pain, or diarrhea. Since most of the patients had primary tumors located inthe duodenum, we recommend biopsy and evaluation of any suspicious lesion seen while routine endoscopies in otherwise normal patients. Older age, advanced unresectable tumors, evidence of metastasis, and higher - grade tumors were associated with poor outcomes. The lower grades of tumors should be offered curative procedures to improve the survival benefit in such patients.

5. Limitations

Our study population had a smaller population cohort and it was a single - centre study.

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