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Prevalence of Neuroendocrine tumours among patients at a tertiary centre in India

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Abstract:

Neuroendocrine tumours (NETs) are uncommon neoplasms with heterogeneous anatomical distribution; grading and clinical behaviour and large institutional series from India remain limited. We retrospectively analysed prospectively maintained data for 117 patients diagnosed and treated for NETs at a tertiary-care centre from January 2010 to December 2022, assessing anatomical site, WHO grade, immunohistochemistry and early follow-up. Most tumours involved the gastrointestinal tract (65.8%), followed by the hepatopancreatobiliary region (33.3%); grade 1 tumours were most frequent (51.3%), while grade 3 disease remained common (29.1%) and Ki-67 index correlated strongly with mitotic count ($r = 0.82$, $p < 0.001$). Indian NETs in this cohort showed an upper-gastrointestinal and periampullary/pancreatic clustering with a substantial high-grade burden at presentation, supporting earlier endoscopic evaluation, wider functional imaging access and multidisciplinary care.

Keywords: Neuroendocrine tumours (NETs), gastrointestinal neuroendocrine tumours, hepatopancreatobiliary neuroendocrine tumours, Ki-67 index

Background:

Neuroendocrine tumours (NETs) are epithelial neoplasms with neuroendocrine differentiation. They arise in several organs, most commonly the gastrointestinal tract and pancreas and bronchopulmonary system [1, 2]. Diagnosis relies on morphology supported by immunohistochemistry, particularly synaptophysin and chromogranin A [2, 3]. Ki-67 index and mitotic count guide grading and prognostication [2-5]. The World Health Organization classification separates well-differentiated NETs from poorly differentiated neuroendocrine carcinomas [4, 5]. Population-based studies have reported a sustained rise in NET incidence. This rise is partly related to improved endoscopy, imaging, pathological classification and clinical awareness [6, 7]. Indian data remain relatively limited, but available series suggest differences in anatomical distribution and stage at presentation [8-10]. Therefore, it is of interest to evaluate the clinic pathological distribution, grading and early follow-up outcomes of NETs at a tertiary gastrointestinal and hepatopancreatobiliary unit in India.

Methodology:**Study design:**

This retrospective observational study used prospectively maintained departmental and hospital records to evaluate patients diagnosed and treated for NETs between January 2010 and December 2022. The institutional review board approved the study and the work was conducted in accordance with ethical guidelines for human research.

Study population:

Patients with histologically confirmed NETs of all grades were eligible. Tumours were categorized by anatomical site and graded using WHO criteria based on mitotic count and Ki-67 index when available. A total of 117 patients met the inclusion criteria.

Data collection:

Demographic data, clinical presentation, date of diagnosis, tumour location, operative details, and histological grade,

staging information, immunohistochemistry findings and follow-up outcomes were extracted from electronic medical records.

Statistical analysis:

Continuous variables were summarised using means and standard deviations and categorical variables were summarised using frequencies and percentages. Survival and early mortality outcomes were compared descriptively; $p < 0.05$ was considered statistically significant.

Ethical considerations:

Patient confidentiality was maintained by anonymizing data and storing records securely. Written informed consent was waived because of the retrospective nature of the analysis.

Results:

During the study period, 117 NET cases were diagnosed. Patient age ranged from 33 to 78 years, with a mean age of 55.6 years; 78 patients were male and 39 were female. Most patients (108, 91.5%) were older than 40 years. Diagnosis was established using endoscopic biopsies in 42 cases and surgical specimens were available for histopathological examination in 105 patients. Gastrointestinal NETs were more often diagnosed by biopsy, whereas pancreatic and periampullary lesions were commonly identified in resected specimens. Based on available grading data, 60 tumours were grade 1, 17 were grade 2 and 34 were grade 3 (Table 1). Six cases were not graded because Ki-67 and mitotic-index data were unavailable. Four gastric mixed adenoneuroendocrine carcinomas were identified and 40 patients had metastasis at diagnosis. The most common presenting symptoms were abdominal pain, weight loss or anorexia, gastrointestinal bleeding, jaundice/pruritus, nausea and vomiting. Four patients had symptoms suggestive of functional NETs, including headache, sweating, palpitations or hypoglycaemia (Table 2, Figure 1). NETs were located in the gastrointestinal tract in 77 patients (65.8%) and in the hepatopancreatobiliary region in 39 patients (33.3%) (Table 3,

Figure 2). The common gastrointestinal sites were stomach, duodenum, ileum, rectum, jejunum, appendix, caecum, colon, oesophagus and anal region. Among pancreatic NETs, the head of pancreas was the most frequent site, followed by the body and tail. Postoperative complications were classified using the Clavien-Dindo system. Grade II complications were the most frequent followed by Grade I complications (**Figure 3**). Operative mortality occurred in four patients and 29 patients had no complications. Histopathology commonly showed tumour cells arranged in islands and lobules with granular

eosinophilic cytoplasm and monomorphic nuclei with stippled chromatin. Immunohistochemistry showed synaptophysin positivity in 73 cases, chromogranin A positivity in 16 cases, neuron-specific enolase positivity in 4 cases and cytokeratin positivity in 18 cases. At three-year follow-up, 71 of 77 patients with GI NETs and 38 of 39 patients with HPB NETs were available for analysis. Mortality within one year was recorded in six patients with GI NETs and one patient with HPB NETs ($p = 0.42$).

Table 1: WHO classification of NETs

WHO category	Ki-67 index (%)	Mitotic rate per 10 HPF
Well-differentiated NET Grade 1	<3	<2
Well-differentiated NET Grade 2	3-20	2-20
Well-differentiated NET Grade 3	>20	>20
Poorly differentiated NEC Grade 3 (small-cell or large-cell type)	>20	>20

Table 2: Clinical features of neuroendocrine tumours

Symptoms	No. of cases	Percentage (%)
Abdominal pain	43	36.8
Anorexia, wt loss	22	18.8
Nausea & vomiting	10	8.5
Jaundice, prurites	15	12.8
Abdominal mass	3	2.5
Dyspepsia	6	5.1
Dysphagia	5	4.2
GI bleed	16	13.6
Fever	8	6.8
Incidental	3	2.5
Others(cough, dyspnoea and haemoptysis hemoperitoneum, abdominal distention, retroperitoneal mass, backpain)	10	8.5
Headache, sweating, palpitations	4	3.4
Hypoglycaemia	2	1.7
Erythema	1	0.9

Table 3: Comparison between GI and HPB NETs

Type	No. of cases	Size	Operative time	Blood loss	Hospital stay
GI NETs	77	3.10 cm	303.9 min	299.2 ml	9.9 days
HPB NETs	39	3.54 cm	387.9 min	470.3 ml	8.7 days

Table 4: Comparison of GI and HPB NETs based on 3-year follow-up

Type	N	3-year follow-up	Mortality (<=1 year)
GI NETs	77	71	6
HPB NETs	39	38	1
p-value			0.42

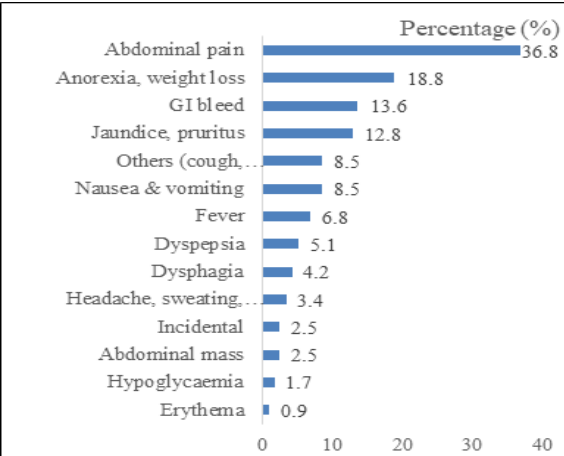


Figure 1: Clinical presentation of NETs

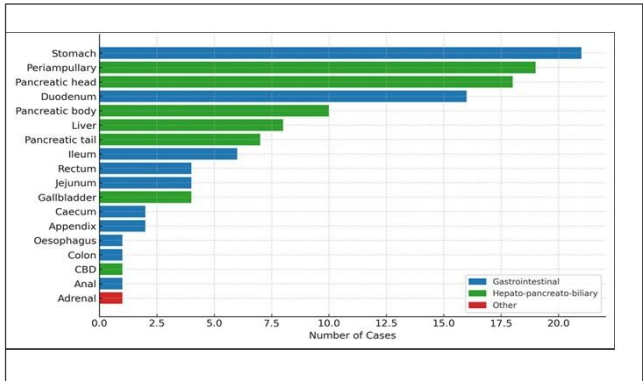


Figure 2: Anatomical distribution of NETs

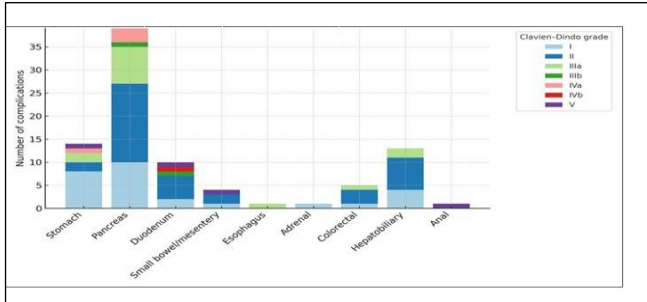


Figure 3: Clavien-Dindo postoperative complications.

Discussion:

This 13-year institutional experience supports the increasing recognition of NETs in Indian tertiary-care practice and highlights anatomical and biological features that may differ from large Western registry cohorts [6, 7]. The gastrointestinal tract was the most common primary region in this cohort, but upper-gastrointestinal, periampullary and pancreatic sites were prominent. This distribution may reflect referral patterns to a gastrointestinal and hepatopancreatobiliary unit, patterns of endoscopy use and regional differences in diagnosis [8-10]. Grade 1 disease was the largest group; however, nearly one-third of tumours were grade 3, indicating a clinically important burden of high-grade disease at presentation. This finding reinforces the need for earlier evaluation of persistent abdominal symptoms and better access to cross-sectional and functional imaging. The expected relationship between Ki-67 index, mitotic count and tumour grade was observed, supporting Ki-67 as a practical grading tool in routine pathology workflows [3, 4]. Standardized reporting of Ki-67 and mitotic count should therefore remain central to NET evaluation. Most patients presented with non-specific symptoms such as abdominal pain and weight loss rather than classic hormonal syndromes. This pattern is consistent with the diagnostic challenge of NETs and may contribute to delayed diagnosis in resource-variable settings [1, 8]. The early mortality difference between GI and HPB NETs was not statistically significant in this cohort. The high follow-up rate strengthens the reliability of early outcome assessment, although longer follow-up and disease-specific survival analysis are needed. The study is limited by its retrospective design, single-centre setting and incomplete Ki-67/mitotic data in a small number of cases. Nevertheless, the cohort provides useful regional data from a long study period and underscores the value of multidisciplinary care for NETs. Grade 1 disease was the largest group; however, nearly one-third of tumours were grade 3, indicating a clinically important burden of high-grade disease at presentation. Recent studies continue to emphasise the marked heterogeneity of gastroenteropancreatic neuroendocrine neoplasms with respect to primary site, grade, metastatic behaviour and outcome, supporting the prognostic importance of accurate tumour classification and staging [11, 12]. The substantial proportion of metastatic and high-grade disease in our cohort is therefore clinically relevant and may reflect delayed presentation and referral to a tertiary gastrointestinal and hepatopancreatobiliary centre. This finding reinforces the need for earlier evaluation of persistent abdominal symptoms and better access to cross-sectional and functional imaging. Contemporary reviews also highlight the increasing role of somatisation-receptor-based imaging and multidisciplinary management in the diagnostic and therapeutic pathway of GEP-NETs [12, 13]. The expected relationship between Ki-67 index, mitotic count and tumour grade was observed, supporting Ki-67 as a practical grading tool in routine pathology workflows [3, 4 and 14].

Conclusion:

NETs predominantly involved the gastrointestinal and hepatopancreatobiliary regions, especially pancreatic, gastric, periampullary and duodenal sites. Grade 1 tumours were most common, though a substantial proportion presented with grade 3 disease or metastasis. Ki-67 correlated with mitotic count, supporting its role in grading and prognostication; earlier diagnosis and multidisciplinary care may improve outcomes.

Advancement to knowledge:

This study provides a relatively large, long-term Indian tertiary-care experience of neuroendocrine tumours, showing a predominance of gastrointestinal and hepatopancreatobiliary NETs, a substantial proportion of grade 3 disease and metastasis at presentation and a strong relationship between Ki-67 index and mitotic count. It also highlights an upper-GI, periampullary and pancreatic clustering that may differ from patterns reported in larger Western cohorts.

Ethical Correspondence:

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- [1] Patients or the public WERE NOT involved in the study.
- [2] Reprints will not be available from the authors.

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