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Digestive tract neoplasms in young individuals: Demographics, staging and risk factors

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Abstract

Background: Digestive tract neoplasms (DTN) have become increasingly common worldwide among young individuals (YIs) over the last few decades.

Aim: Aim of this research was to study the types, demographics, stage at presentation and risk factors of digestive tract neoplasms in young individuals.

Methods and results: In this cross-sectional study, YI (ie, ≤40 years) presenting with any DTN including gastrointestinal neoplasms (GIN), hepatobiliary neoplasms (HBN), periampullary neoplasms (PAN) and others from June 2016 to May 2020 were included. Baseline laboratory tests, tissue diagnosis and staging were performed while risk factors were documented. A total of 163 patients were included in the study, of whom 82 (50.3%) were males. Mean age was 29.9 (±9.57) (range: 8 months-40 years). Most DTN (93.3%; n = 152) were malignant. The commonest neoplasms were lower GIN (LGIN) 52 (31.9%), followed by HBN 46 (28.2%), upper GIN (UGIN) 44 (27%) and PAN 18 (11%). Commonest among LGIN were rectal 37; among HBN: hepatocellular cancer (HCC) 9, cholangiocarcinoma (CC) 9; and among UGIN: esophageal 25 and stomach 14. Rectal cancers were mostly sporadic (82.7%) with frequent signet ring cell histology (40.5%), and affected relatively younger ages compared to upper GIN and PAN. GIN were mostly locally advanced with higher resectability (LGIN 90.4%; UGIN 79.5%) while HBN were more advanced with lower resectability (HCC [44.4%]; CC [33.3%]). Poor dietary habits and poor socioeconomic status were common with UGIN (63.6%, 50%) and HBN (56.5%, 54.3%), respectively.

Conclusion: The commonest DTN among YI were LGIN followed by HBN, UGIN and PAN. Rectal cancers affected relatively younger ages and were mostly sporadic. HBN were more advanced in stage and unresectable compared to GIN. Poor dietary habits and poor socioeconomic status may be important contributors in carcinogenesis.

KEYWORDS

digestive tract neoplasms, gastrointestinal neoplasms, hepatobiliary neoplasms, young individuals

1 | INTRODUCTION

Cancer trends in young adults over the last few decades demonstrate significantly increased incidence of digestive tract neoplasm (DTN) including the upper gastrointestinal (UGI), lower gastrointestinal (LGI), hepatobiliary (HB) and pancreatic neoplasms.[1] Traditionally, malignant neoplasms have particularly been thought to be a disease of the elderly individuals; however, it is surprising to observe the rising incidence of such neoplasms in young individuals (YI). According to a European study, the incidence of colorectal cancer (CRC) is increasing in Europe among subjects aged 20 to 49 years and the fastest rise is in the youngest age group.[2] Rising frequency of DTN has also been observed in other countries of the world including United States, Canada, Australia and New Zealand.[3-7] Research shows that esophageal and gastric cancers are also becoming increasingly common in the young.[8,9] Apart from the neoplasms of gastrointestinal origin, recent studies also reveal rising incidences of hepatobiliary neoplasms including hepatocellular cancer (HCC) and biliary tract cancers like gall bladder cancer and cholangiocarcinoma (CC) in young individuals.[10,11]

Various diseases predispose to development of gastrointestinal (GI) and hepatobiliary (HB) neoplasms in young patients. For example, familial adenomatous polyposis (FAP) and Lynch syndrome are not only associated with CRC malignancies in young individuals but also with gastric and ampullary tumors.[12] Family history of hereditary diffuse gastric cancer (HDGC) predisposes to development of gastric cancer in young people.[13] Among the non-familial causes, obesity related GI cancers (colorectal, pancreatic and gall bladder) have also shown steeper rises in successively younger generations.[1] Other possible predispositions include environmental risk factors like poor dietary habits (presence of unidentified carcinogens in the diet, unhealthy cooking and food packaging practices, lack of healthy nutrients with anti-oxidative properties), use of addictive substances with carcinogenic potential, alteration of GI microbiome due to use of antibiotics or certain dietary preferences, and sedentary lifestyle.[14] Besides, failure to administer vaccination against hepatitis B can predispose to development of hepatitis B associated hepatocellular cancer (HCC) among young non-cirrhotic individuals. The apparent rise in the number of GI neoplasms in YI in recent years can also be attributed to the relatively greater health consciousness and earlier medical advice seeking behavior of the patients. This finding not only demands studying of the underlying pathological phenomena but also reconsideration of screening guidelines for various GI and HB cancers.

Since, DTN among YI are not uncommon, it is important to recognize which neoplasms are most common among our population including their demographics, histology and stage of presentation. Besides, it is imperative upon us to analyze the risk factors of these neoplasms. This will not only help in making screening programs to identify the cancers early in the course of illness but also to adopt preventative measures against them. The aim of this study was, therefore, to identify the types of digestive tract neoplasms (gastrointestinal anatomical location, histology etc.) occurring in young patients (≤40 years), to determine their clinical characteristics (demographics, stage of disease, resectability etc.) and the various risk factors (family history, environmental and socioeconomic factors etc.) contributing to the development of such neoplasms.

2 | METHODS

This cross-sectional study was performed in the department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation (SIUT). All young patients (age ≤ 40 years) diagnosed with any kind of digestive tract neoplasm (gastrointestinal neoplasms [GIN], hepatobiliary neoplasms [HBN], periampullary neoplasms [PAN] etc.) were included in the study. Those patients, whose neoplastic origin was later found to be extra-gastrointestinal during the course of evaluation, were excluded. The study was performed in accordance with the declaration of Helsinki and approval was obtained from the institutional ethical review committee (ERC). Informed consent was taken from all patients who were included in the study. The study was performed over a period of 4 years, from June 2016 to May 2020. Detailed history was taken and the demographic details of such patients were recorded. Relevant questions concerning possible risk factors of the neoplasm were asked and the responses recorded.

In this study the upper GI neoplasms (UGIN) included those arising from the esophagus, stomach and small intestine up to mid jejunum; while the lower GI neoplasms (LGIN) included those from distal jejunum to anal canal. The hepatobiliary tumors included those arising from the liver, gall bladder or biliary tree; while the periampullary neoplasms were those arising from the ampulla of Vater, head of pancreas, distal common bile duct and periampullary duodenum. All relevant investigations for the diagnosis and staging of the disease were performed.

For histologic diagnosis of the disease, tumor tissue was obtained with percutaneous or endoscopic techniques. Tissue was obtained percutaneously through guidance of ultrasound, computed axial tomography (CAT) scan or magnetic resonance imaging (MRI); or endoscopically with gastroscope, duodenoscope or colonoscope for luminal growths; or with endoscopic ultrasound (EUS) guided fine needle aspiration or biopsy (FNA/FNB) for any growth or mass within or beyond the wall of the gut (eg, pancreatic mass or abdominal lymph nodes). The tumor tissue sample was examined by expert consultant histopathologists.

The staging of the disease was performed according to TNM staging with help of full body CAT scan or MRI. Endoscopic ultrasound was employed for staging of esophageal, gastric, rectal and pancreatic cancers whenever required. In some cases, as deemed necessary, diagnostic laparoscopy was performed to ascertain the stage of the cancers. Other techniques (eg, positron emission tomography (PET) scan or 68-Ga-DOTATATE [gallium-68 DOTA-DPhe1, Tyr3-octreotate] PET scan for neuroendocrine tumors) were also employed after consultation with oncologist. The patients were finally referred to the surgeon, oncologist or radiation oncologist for further management according to the stage of disease.

All data were analyzed using Statistical Package for the Social Sciences (SPSS) version 24. Continuous variables were expressed as

mean and SD, while categorical variables were expressed as frequencies and percentages. Bar chart was used to demonstrate the frequencies of different types of digestive tract neoplasms.

3 | RESULTS

A total of 163 young patients with digestive tract neoplasms were included in the study. Of these, about half, that is, 82 (50.3%) were males. Most of the neoplasms (95.1%; n = 155) were malignant. The various groups of DTN in descending order of frequency are shown in Figure 1. The frequency of the subtypes of various DTN in the descending order and the precise anatomical location of the affected organ is shown in Table 1. The overall mean age of the patients was 29.9 (±9.57) years (range: 8 months-40 years). The mean ages of the various types and subtypes of DTN and gender predominance are shown in Table 2. The youngest patient in this study was a baby boy of age 8 months who was diagnosed as a case of hepatoblastoma. Patients with LGIN were relatively younger than those with UGI and PA neoplasms. The histopathology of the various types of digestive tract neoplasms are shown in Table 3. Signet ring cell cancers were common among the rectal (15/37, 40.5%) and gastric cancers (8/14, 57.1%). Among the nine cholangiocarcinoma cases, 7 (77.8%) were hilar in location while 2 (22.2%) involved the mid CBD. Although adenocarcinoma was the commonest tumor affecting the pancreas, neuroendocrine and solid pseudopapillary tumors (SPT) were not uncommon. Eleven patients had benign neoplasms which included neuroendocrine tumors 4 (hepatic 2, pancreatic 2), solid pseudopapillary tumors of pancreas 3, fibronodular hyperplasia of liver 1, perivascular epithelioid cell oma (PEComa) 1, hepatic mucinous cystic neoplasm 1 and gastric gastrointestinal stromal tumor (GIST) 1. Neuroendocrine tumors (NET) were diagnosed in nine (5.52%) patients of which four originated from pancreas, three from liver and one from small intestine and esophagus each. The Ki-67 index (indicator of the grade of tumor) was >20% in five cases, while <20% in remaining four. Lymphomas were diagnosed in five (3.06%) cases, of which four were hepatobiliary lymphomas with associated gastroduodenal involvement while one case affected the stomach alone. All these were non-Hodgkin lymphomas: four of them were diffuse large B cell lymphoma and one Burkitt lymphoma.

The stage of disease and the likelihood of resectability at first presentation or after neoadjuvant chemotherapy are shown in Table 4. Majority of the patients with LGIN, UGIN and PAN presented with locally advanced stage, although presence of metastatic disease was higher with UGIN (gastric and esophageal) as compared to those with LGIN. Among the HBN, patients with cholangiocarcinoma and gall bladder cancer had a greater tendency to present with advanced or metastatic stage of the disease. However, most of the cases with hepatoblastomas presented at a relatively early stage of disease. Also, the chances that the patient would undergo upfront curative surgical resection or after receiving neoadjuvant chemotherapy was higher for the UGIN, LGIN and PAN; whereas, this was relatively lower for those with the HBN particularly the gall bladder cancer and cholangiocarcinoma (Table 4).

The percentage of patients exposed to various possible risk factors for development of neoplasms is shown in Table 5. A family history of GI or non-GI malignancy in first and second degree relatives was highest with UGIN. Among those with LGIN who had a positive family history, three had Lynch syndrome (determined on the basis of Amsterdam criteria for hereditary nonpolyposis colorectal cancer [HNPCC]), two had familial adenomatous polyposis (FAP), two had first degree family members with colorectal cancer and the remaining two had first or second degree family members with extra-colonic GI and non-GI related cancers. Chronic viral hepatitis was particularly common among patients with HBN: 32.6% of all HBN, 100% of hepatocellular cancers (HCC) and more than half the patients (55.5%) with cholangiocarcinoma having either hepatitis B or C virus infection (Table 5). Among the nine patients with HCC, six had hepatitis B while three had hepatitis C; while among the nine patients with cholangiocarcinoma, five had chronic viral hepatitis: hepatitis C in three and hepatitis B in two.

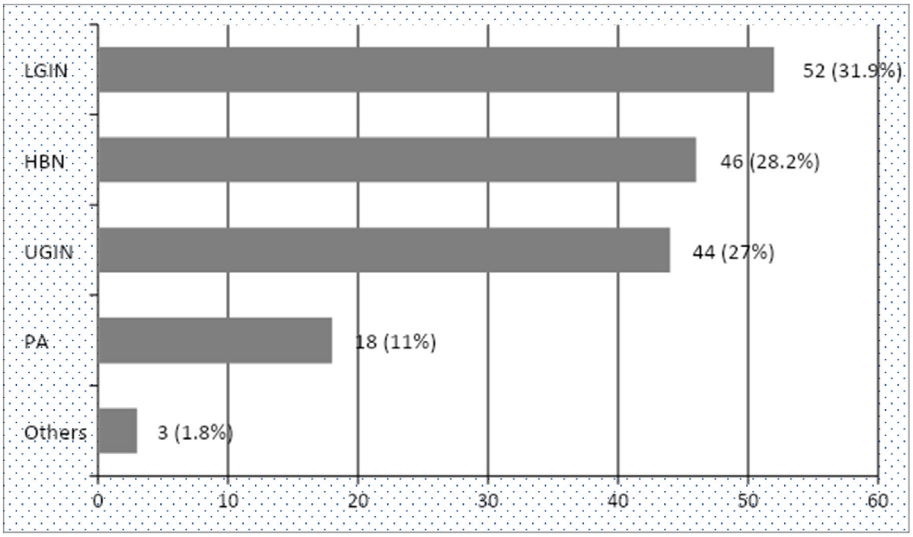

FIGURE 1 Frequency of digestive tract neoplasms (DTN) among young individuals (YI). HBN, hepatobiliary neoplasms; LGIN, lower GI neoplasms; PA, peri-ampullary neoplasms; UGIN, upper GI neoplasms

TABLE 1 Frequency of sub-types of various digestive tract neoplasms (DTN) in young individuals (YI)

	Region	No.	Region	No.
Lower GI tract neoplasms (n = 52)	Rectum	37	Descending colon	2
	Anal canal	4	Transverse colon	1
	Ascending colon	4	Hepatic flexure of colon	1
	Sigmoid	3		
Hepatobiliary neoplasms (n = 46)	Hepatocellular cancer	9	Hepatic metastasis of unknown primary	2
	Cholangiocarcinoma	9	PEComa	1
	Gall bladder cancer	7	Biliary cystadenoma	1
	Hepatoblastoma	7	FNH	1
	HB lymphoma	4	Hepatic MCN	1
	Hepatic NET	3	RBCT	1
Upper GI tract neoplasms (n = 44)	Esophagus[a]	25	GE junction	1
	Stomach[b]	14	Proximal jejunum	1
	Duodenum[c]	3		
Peri-ampullary neoplasms (n = 18)	Head of pancreas	9	Duodenum[d]	3
	Ampulla of Vater	6		
Others (n = 3)	Pancreatic NET[e]	2	Body of pancreas	1

Abbreviations: BOP, body of pancreas; FNH, fibronodular hyperplasia; HB, hepatobiliary; MCN, mucinous cystic neoplasm; NET, neuroendocrine tumor; PEComa, perivascular epitheliod cell oma; RBCT, round blue cell tumor of Liver; TOP, tail of pancreas.
[a]Esophagus cancers: mid and lower esophagus 22, upper esophagus 3.
[b]Gastric cancers: antrum and body 8, body only 3, fundus 3, muscularis propria 1.
[c]Third or fourth part of duodenum.
[d]Periampullary duodenum.
[e]Pancreatic NET: body of pancreas 1, tail of pancreas 1.

TABLE 2 Age and gender distribution among young individuals (YI) with digestive tract neoplasms (DTN)

	Mean age ± Std. deviation	Gender distribution M:F	Remarks
Lower GIN	29.2 ± 6.9	26:26	Equal gender distribution
Rectal/anal	28.3 ± 5.9	21:20	–
Remaining colon	32.6 ± 9.6	5:6	–
HBN	28.4 ± 13.7	26:20	Overall male predominance
HCC	30.6 ± 14.5	5: 4	–
Cholangiocarcinoma	35.3 ± 4.6	7:2	M > F
Gall bladder cancer	36.1 ± 3.5	0:7	F > M
Hepatoblastoma	3.8 ± 1.9	7:0	M > F
Upper GIN	31.5 ± 6.8	17:27	Overall female predominance
Esophagus	30.2 ± 7.5	8:17	F > M
Stomach	34.6 ± 4.9	6:8	F > M
Duodenum	31.0 ± 3.6	2:1	–
Periampullary	31.36 ± 9.3	12:6	Overall male predominance
Pancreatic Head	28.6 ± 11.3	3:6	F > M
SPT	15.8 ± 4.9	0:3	F > M
Ampullary	37.0 ± 2.8	6:0	M > F
PA duodenum	28.3 ± 8.5	3:0	M > F
Others	35.6 ± 4.0	1:2	–

Abbreviations: GIN, gastrointestinal neoplasms; HBN, hepatobiliary neoplasms; HCC, hepatocellular cancer; PA, periampullary; SPT, solid pseudopapillary tumor.

TABLE 3 Histopathology of the various digestive tract neoplasms in young individuals

	Affected region	Histology types	
LGIN (52)	Rectum (37)	AC	WD 8, MD 18, PD 11 (SRCH 15)
	Remaining colon (11)	AC	MD 8, PD 3
	Anal canal[a] (4)	SCC	3
		AC	1
UGIN (44)	Esophagus (25)	SCC	20
		AC	3
		NET	1
		Sarcomatoid cancer	1
	Stomach (14)	AC[b]	12 (SRCH: 8)
		GIST	1
		Lymphoma	1
	Small intestine (4)	AC	3
		NET	1
	GEJ (1)	AC	1
HBN (46)	Liver (25)	HCC	9
		Hepatoblastoma	7
		Hepatic NET	3
		Hepatic metastasis	2
		PEComa	1
		Hepatic MCN	1
		FNH	1
		RBCT	1
	Biliary tract (21)	Cholangiocarcinoma	9
		Gall bladder AC	7
		Lymphoma	4
		Biliary cystadenoma	1
PA (18)	Pancreas head (9)	AC	WD 1, MD 2, PD 1
		NET	2
		SPT	3
	Ampulla of Vater (6)	AC	WD 3, MD 3
	PA duodenum (3)	AC	WD 1, MD 1, PD 1
Others (3)	Pancreas body/tail (3)	NET	BOP 1, TOP 1
		AC	BOP 1

Abbreviations: AC, adenocarcinoma; GEJ, gastroesophageal junction; MD, moderately differentiated; NET, neuroendocrine tumor; PD, poorly differentiated; PEComa, perivascular epithelioid cell oma; SCC, squamous cell cancer; SPT, solid pseudopapillary tumor; SRCH, signet ring cell histology; WD, well differentiated.

[a]Of total 4 anal canal cancers: MD SCC 3 and AC 1.

[b]Of total 12 gastric AC: PD 7, MD 4, WD 1.

A history of addiction was not uncommon among patients with DTN, with nicotine being the most commonly abused agent either in the following forms: cigarette smoking (including "hukka"), tobacco mixed betel nuts ("gutka"), tobacco powder with betel leaves ("paan"), and powdered tobacco snuff ("niswar"). Other addictions included alcohol, cannabis ("charas") and opiate agents, for example, heroin. Dietary habits were consistently poor among patients with all kinds of DTNs and included use of unpacked cooking oil, spices and milk; use of unboiled water; and, use of betel nuts ("chhalia") (Table 5). Among the patients with UGIN, 72% patients with esophageal cancer had a history of frequent betel nut chewing, most of whom consumed more than 8 to 10 packets per day for more than 5 years. Poor dietary habits were present in more than half of the patients with HBN (56.5%), particularly those with cholangiocarcinoma (66.7%) (Table 5). Poor socioeconomic status, in general, was commonly found among patients with DTN, but in particular, in patients with HBN (54.3%) and UGI neoplasms (50%).

TABLE 4 Stage at presentation and resectability of digestive tract neoplasms among young individuals

Gastrointestinal neoplasms				
	Localized	**Locally advanced**	**Metastatic**	**Resectability[a]**
LGIN	9 (17.3%)	36 (69.2%)	7 (13.5%)	47 (90.4%)
Rectal/anal (41)	7 (17.1%)	28 (68.3%)	6 (14.6%)	36 (87.8%)
Remaining colon (11)	2 (18.2%)	8 (72.7%)	1 (9.1%)	11 (100%)
UGIN	6 (13.6%)	25 (56.8%)	13 (29.5%)	35 (79.5%)
Esophagus	3 (12%)	16 (64%)	6 (24%)	21 (84%)
Stomach	2 (14.3%)	7 (50%)	5 (35.7%)	10 (71.4%)
Duodenum	2 (66.7%)	–	1 (33.3%)	2 (66.7%)
Periampullary	9 (50%)	6 (33.3%)	3 (16.7%)	15 (83.3%)
Pancreatic head	5 (55.6%)	2 (22.2%)	2 (22.2%)	4 (66.7%)
Ampullary	2 (33.3%)	3 (50%)	1 (16.7%)	5 (83.3%)
PA duodenum	2 (66.6%)	1 (33.3%)	–	3 (100%)
Others	–	1 (33.3%)	2 (66.6%)	1 (33.3%)
Hepatobiliary neoplasms				
	Localized/locally advanced	Advanced[b]/metastatic		Resectability
HCC	4 (44.4%)	5 (55.5%)		4 (44.4%)
Cholangiocarcinoma	3 (33.3%)	6 (66.6%)		3 (33.3%)
GB carcinoma	1 (14.3%)	6 (85.7%)		1 (14.3%)
Hepatoblastoma	5 (71.4%)	2 (28.6%)		5 (71.4%)

[a]Percentage of patients deemed resectable at first presentation (ie, candidates for upfront surgery) or after neoadjuvant chemotherapy.
[b]Presence of any of the following: vascular invasion, involvement of second or third order hepatic ducts or locoregional lymphadenopathy.

TABLE 5 Potential risk factors for various digestive tract neoplasms (DTN)

Risk factors of gastrointestinal and hepatobiliary neoplasms					
Type of neoplasm (No.)	**Family Hx[a]**	**Viral hepatitis**	**Addictions[b]**	**Poor dietary habits[c]**	**Poor SE status**
LGIN (52)	9 (17.3%)	8 (15.4%)	13 (25%)	29 (55.8%)	18 (34.6%)
UGIN (44)	12 (27.3%)	6 (13.6%)	10 (22.7%)	28 (63.6%)	22 (50%)
Esophagus (25)	8 (32%)	2 (8%)	5 (20%)	18 (72%)	15 (60%)
Stomach (14)	4 (28.6%)	3 (21.4%)	4 (28.6%)	10 (71.4%)	5 (35.7%)
Small intestine (4)	0	2 (50%)	1 (25%)	2 (50%)	2 (50%)
Periampullary (18)	0	4 (22.2%)	5 (27.7%)	10 (55.5%)	8 (42.1%)
Hepatobiliary (46)	7 (15.2%)	15 (32.6%)	11 (23.9%)	26 (56.5%)	25 (54.3%)
HCC (9)	2 (22.2%)	9 (100%)	4 (44.4%)	5 (55.5%)	6 (67%)
Cholangiocarcinoma (9)	0	5 (55.5%)	3 (33.3%)	6 (66.7%)	6 (67%)
GB carcinoma (7)	1 (14.3%)	1 (14.3%)	1 (14.3%)	3 (42.8%)	4 (57.1%)

[a]Family history of any GI or non-GI cancer among first and second degree relatives.
[b]Abuse of any of the following: nicotine [tobacco, cigarette smoking, gutka (betelnuts with tobacco), niswar]; alcohol: cannabis (charas); heroin.
[c]Use of any of the following: unpacked spices, unpacked oil, unpasteurized milk, unboiled water, betelnut chewing, Multani clay, quicklime (chuna).

4 | DISCUSSION

Our study demonstrated that the most common neoplasm among YI (≤40 years) was colorectal cancer (CRC), of whom three-fourths had cancers of the rectum and sigmoid; the second most common neoplasm being hepatobiliary, with hepatocellular and bile tract cancers representing about half of them; and the third most common were upper GI neoplasms of whom more than half were esophageal cancers. Our finding that CRC is the commonest GI cancer among YIs is supported by similar results found in other parts of the world including developed countries like United States, Europe, Canada, Australia and New Zealand where a sharp rise in such cases has been demonstrated.[2-7] In Pakistan too, this trend has been noted in earlier studies and emphasis has been laid upon need for further research work and

early age of screening to detect rectal cancers.[15-17] A significant proportion of our patients with rectal cancers exhibited signet ring cell histology (SRCH). Various studies done elsewhere in the world show that SRCH is more common in young than in old patients and may represent more advanced stage at presentation and worse prognosis compared with mucinous and non-mucinous rectal adenocarcinomas.[18,19] Among our patients with CRC, a family history of hereditary conditions (HNPCC or FAP) was present in only 5 (9.61%) patients; a family history of CRC among first or second degree relatives in 17.3% patients; while the remaining appeared to be sporadic cases of CRC. This finding conforms to the general finding whereby hereditary conditions (due to highly penetrant inherited mutations) are seen in just 2% to 5% of cases, while a family history of CRC (due to alterations in the less penetrant single genes) is present in 20% to 30% cases.[20] A large proportion of our patients with CRC were sporadic cases and the etiology remained unclear. Various risk factors have been thought to contribute including poor dietary habits consisting of hidden carcinogens and nutritional deficiencies, addictive substances including passive smoking, and sedentary lifestyles. Evidence published recently, linked sedentary lifestyles with gut dysbiosis and prolonged time sitting watching television with an increased risk of developing the CRC in young Americans.[21] In our study, about 86.5% patients with CRC had localized or locally advanced disease and was deemed resectable in 90.4% cases (Table 5). These figures are again consistent with generally observed data, whereby only 20% of the cases are found to have metastatic disease of which 80% to 90% cases are found to have unresectable metastatic disease.[22]

The second most common neoplasm in our study population was of hepatobiliary origin with hepatocellular cancer (HCC) being the commonest, followed by cholangiocarcinoma, gall bladder cancer and hepatoblastoma. Our finding conforms to the update regarding hepatobiliary tumors occurring in all ages, which states that tumors of the liver and biliary tree, mainly HCC and cholangiocarcinoma (CC) are the second leading cause of cancer related deaths worldwide.[23] This indicates that while HB tumors represent a significant burden of oncological disease in all age groups, so do they occupy an important place among the young population. In our study, most of the HCC cases were associated with hepatitis B virus (HBV) related liver disease, signifying the well-established role of HBV in incorporating into and altering the host genome to initiate the carcinogenic pathway.[24] Also, more than half of CC cases were associated with chronic viral hepatitis, signifying its role in predisposing to biliary tract cancers.[25] A significant proportion of patients with HB tumors in our study had poor dietary habits: CC (66.7%) and HCC (55.5%) (Table 5) including use of unpacked spices, oils, contaminated betel nuts, unboiled water, unpasteurized milk etc. The role of environmental and dietary carcinogens is demonstrated by different studies in various parts of the world. One report from Japan described an outbreak of CC among young workers in a printing company who were exposed to the chemical dichloro methane and 1,2 dichloropropane.[26] Other studies from India suggest the role of environmental pollutants (heavy metals) and edible oil adulterants (argemone oil, adulterated mustard oil and butter yellow) in the development of gall bladder cancer in young patients.[27,28] Studies have also shown the role of vinyl chloride and use of plastic tea bags in contributing to development of liver malignancies.[29,30] Furthermore, majority of our cases with CC (77.8%) had hilar tumors (Klatskin's tumor) and only 33% of the cases were resectable. These findings are similar to the two American studies where 50% of cases of CC in the young were peri-hilar in location and 65% of the cases with hilar CC were found to be unresectable.[31,32] In our study, hepatoblastomas represented 15.2% cases of all HB tumors and occurred only in males with a mean age of 3.8 years. Similar demographics and rising incidence of this tumor have also been reported in recent years.[33] However, a high number of hepatoblastoma cases in our study can also be attributed to the fact that ours is a hepatobiliary center where most of the cases from the peripheral parts of the country are referred.

In our study, the third most common neoplasms originated from the upper GI tract, with more than half being esophageal cancers and about one-third being gastric neoplasms. The esophageal cancer patients in our study were largely females, histology being squamous cell cancer (SCC) in 80% (20/25) of the cases, having a family history of cancer in 32% and having a strong history of frequent betel nut use (72%). This is in contrast to the case series of 109 esophageal cancer patients from western Kenya which showed slight male predominance with 79% patients having a family history of cancer.[34] However, the majority of the cases here too were SCC (98%). Furthermore, a SEER analysis that compared young and older patients with esophageal cancer showed higher frequency of males, lower esophagus involvement, adenocarcinoma histology and a stage III/IV in the younger age group.[8] In our study, among patients with gastric cancer, two-thirds of the patients had signet ring cell histology (SRCH), which is similar to the Mexican study of gastric cancer patients under 30 years of age where the predominant histology was SRCH.[35] Also, antrum was involved in more than half of gastric cancer patients in our study which may reflect the role of *Helicobacter pylori* which predisposes to non-cardia gastric cancers. The dietary habits were poor in both the esophageal and gastric cancer patients while the socioeconomic status was poor in patients with esophageal cancers which may suggest the protective role of micronutrients in a healthy balanced diet in cancer prevention.[36]

The strength of this study is that, to the best of our knowledge, it is the first one to determine the types, characteristics and risk factors of DTN among young individuals (YI) in our country; while, the limitation is that it does not study the outcome of such patients which can provide valuable information regarding the prognosis. Other limitation is that, due to lack of financial support we could not evaluate our patients for various other risk factors including role of aflatoxin and occult hepatitis B in causing HCC and CC; genetic work up for hereditary gastric and pancreatic cancers; *H. pylori* and atrophic gastritis in gastric cancers; parasitic infections and chronic typhoid carriage in gall bladder cancer etc. However, the rising number of DTN among YI strongly implicates that further studies be conducted to not only evaluate all the diverse risk factors of the individual DTN, but also determine the prognosis of these neoplasms.

5 | CONCLUSION

GI neoplasms are becoming increasingly common among young individuals just as they have been observed in other parts of the world. Lower GI tract malignancies, especially rectal cancer, are the commonest type of neoplasms in this age group and most of them present at a locally advanced and resectable stage. It is essential to formulate guidelines stressing upon beginning screening tests like sigmoidoscopy at a younger age. Hepatobiliary malignancies are rising alarmingly and rank second in young individuals with majority being unresectable at presentation. Ensuring widespread administration of vaccination against the oncogenic hepatitis B virus at birth is essential to reduce the burden of this preventable cancer. As most of our patients with esophageal cancer had history of betel nut chewing with or without tobacco ("gutka" and "chhalia"), a campaign should be launched in collaboration with electronic and print media to raise awareness regarding their potential harms. Since poor socioeconomic status was commonly observed among GI and HB malignancies, it behooves that accessibility to healthy foods that contain protective anti-oxidatives and micronutrients be made affordable for the underprivileged. Furthermore, poor dietary habits and unhealthy cooking practices which result in exposure to hidden carcinogens in various commonly used food products should be strongly discouraged. Last but not the least, it is very important to initiate research work focusing on genetic profiling of family members of patients with colorectal and gastric neoplasms to better understand their role in carcinogenesis in our part of the world.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

A.T.: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing-original draft; writing-review and editing. **N.L.:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing-original draft; writing-review and editing.

DATA ACCESSIBILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL STATEMENT

Approval was obtained from the institutional ethical review committee (ERC). Informed consent was taken from all patients who were included in the study. In the consent form, the patients have given their consent for the clinical information to be reported in the journal.

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