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Childhood Gastric Carcinoma: Epidemiology and Clinical Features Based on Population and Clinical Cancer Registry Data

T. Schmid[1*], E. Wagner[1], H. Gruber[1]

[1]Department of Oncology, School of Medicine, University of Vienna, Vienna, Austria.

***E-mail** ✉ vienna.onc.25@gmail.com

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ABSTRACT

Gastric carcinoma is an extremely uncommon malignancy in children, and knowledge regarding its causes, epidemiology, and clinical presentation in the pediatric population remains limited. This study aimed to expand the understanding of the occurrence and characteristics of childhood gastric carcinoma. Cases of gastric carcinoma diagnosed between 2000 and 2017/2018 were obtained from the Surveillance, Epidemiology, and End Results (SEER) database and the German Center for Cancer Registry Data. Patients under 20 years of age were examined for demographic and tumor-specific characteristics. Additionally, clinical information from pediatric gastric carcinoma patients registered in the German Registry for Rare Pediatric Tumors (STEP) was analyzed regarding diagnostic procedures, treatment approaches, and outcomes.

A total of 91 cases were identified in the population-based registries, predominantly affecting adolescents. Among patients with documented tumor staging, advanced stages were frequent (66.7%). During the reported follow-up, 63.7% of patients with clinical follow-up data died. Within the STEP registry, eight pediatric patients were included; two had hereditary CDH1 mutations and one had Peutz–Jeghers syndrome. Three patients exhibited notably low immunoglobulin levels. Complete surgical resection was achieved in four patients, all of whom remained in remission, whereas three of the four remaining patients succumbed despite receiving multimodal therapy. The development of gastric carcinoma in children appears to be influenced by a combination of Helicobacter pylori infection along with genetic predisposition and/or immunodeficiency. Complete surgical removal offers a strong chance of long-term remission for localized tumors, whereas stage IV disease is associated with a poor prognosis, underscoring the urgent need for innovative approaches such as mutation-targeted therapies.

Keywords: Epidemiology, Gastric cancer, Pediatric oncology, Rare tumors

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Introduction

In adults, gastric cancer is a common malignancy, accounting for 5.6% of all cancers and 7.7% of cancer-related deaths worldwide [1]. Its development is influenced by multiple factors, including Helicobacter pylori infection, lifestyle-related exposures such as diet, tobacco use, and high salt intake, as well as inherited genetic susceptibility [2–4]. Histologically, the majority are adenocarcinomas [2], and they are often classified by anatomical location, as tumors of the cardia differ in causation and clinical progression from those in the distal stomach [5]. Early stages usually produce minimal or no symptoms, which often leads to late diagnosis and poor outcomes, with a 5-year survival rate of roughly 40% [6].

By contrast, gastric carcinoma in children is extraordinarily rare, with an annual incidence under 2 per million, representing only about 0.1% of pediatric cancers [7]. Only a small number of pediatric cases have been described in the literature [8–14], leaving significant gaps in understanding of their epidemiology, underlying causes, clinical behavior, and optimal management compared to adults [8, 14]. The infrequency of these tumors complicates diagnosis and treatment for clinicians. This study aims to expand knowledge on the epidemiology of

pediatric gastric carcinoma and to provide a detailed characterization of affected patients, including clinical presentation, treatment, and outcomes.

Materials and Methods

Data were collected from the German Center for Cancer Registry Data (ZfKD), which consolidates information from all population-based cancer registries in Germany in compliance with federal regulations [15]. To enable international comparison, additional data were obtained from the SEER program of the US National Cancer Institute, covering nearly half of the US population (SEER Research Plus Data, 18 Registries, Nov 2020 Submission) [16].

Eligible cases were defined as individuals diagnosed with a malignancy coded C16.0–C16.9 (ICD) before the age of 20, between 2000 and 2017 for ZfKD and 2000–2018 for SEER. Gastric carcinoma cases were identified through histology codes (ICD-O). Notably, due to reporting variations, complete German federal registry data were available only for 2009–2015.

The collected datasets included pseudonymized information on age at diagnosis, tumor site, histology, TNM stage, grading, treatment, and outcomes. Approximately 50% of ZfKD records lacked TNM staging, so analyses using TNM information were restricted to available data. Crude incidence rates for patients under 20 were calculated per person-years using population data from the Federal Statistical Office of Germany [17].

Further clinical evaluation was conducted using the STEP registry, a prospective database of the German Society for Pediatric Oncology and Hematology (GPOH) for rare pediatric tumors. Patients younger than 18 diagnosed with gastric carcinoma were included. Standardized case report forms were used to collect pseudonymized data on patient characteristics, tumor features, and treatments. Tumor staging followed the AJCC TNM classification [18]. All patients or their legal guardians provided informed consent, and the registry was approved by institutional review boards.

Results and Discussion

In total, 91 pediatric and adolescent gastric carcinoma cases were identified (ZfKD: 31; SEER: 60). Most diagnoses occurred during adolescence, with 80.2% aged 15–19. The median age among ZfKD patients was 17.6 years (range: 0–19). Females slightly outnumbered males (57.1%). Almost all tumors were adenocarcinomas, with poorly cohesive types, including signet ring cell carcinoma, being most prevalent (38.5%). Based on the Laurén classification, diffuse-type tumors dominated, followed by intestinal and indeterminate types [19]. Nearly half of the cases (47.5%) were coded as adenocarcinoma not otherwise specified, preventing precise histologic classification. No Epstein-Barr virus–associated lymphoepithelioma-like carcinomas were reported. Tumors were mainly located in the cardia (n = 19), body (n = 12), and antrum (n = 13), rarely appearing in the curvature.

TNM T stages were fairly evenly distributed from T1 to T4. Lymph node involvement occurred in 51.2% of cases, while distant metastases were present in 61.1%, resulting in frequent advanced-stage disease (stage IV: 66.7%). Most tumors were poorly differentiated, with 86.9% classified as high-grade. While patterns were generally similar across ZfKD and SEER, SEER cases had more overlapping lesions and a higher proportion of distant metastases and stage IV tumors (ZfKD: 56.3%; SEER: 71.4%). ZfKD also included a slightly larger share of patients younger than 15 years (ZfKD: 25.8%; SEER: 16.7%).

Table 1. Patient characteristics and clinical features of gastric carcinoma in patients aged 0–19 years registered at the German Center for Cancer Registry Data 2000–2017 and in the Surveillance, Epidemiology, and End Results Program 2000–2018. Proportions are calculated based on cases with recorded data. Abbreviation: n.a., not applicable.

Characteristics	German Center for Cancer Registry Data (ZfKD) 2000–2017 (n = 31)		Surveillance, Epidemiology, and End Results Program (SEER) 2000–2018 (n = 60)	
	Count	Proportion	Count	Proportion
Sex				
Male	13	41.9%	26	43.3%
Female	18	58.1%	34	56.7%

Age at diagnosis				
<10	5	16.1%	0	0%
10–14	3	9.7%	10	16.7%
15–19	23	74.2%	50	83.3%
Histology				
Adenocarcinoma	30	96.8%	60	100.0%
Signet cell carcinoma thereof	10	32.3%	25	41.7%
Squamous cell carcinoma	1	3.2%	0	0%
Localization				
Cardia (C16.0)	9	29.0%	10	16.7%
Fundus (C16.1)	0	0%	3	5.0%
Stomach body (C16.2)	8	25.8%	4	6.7%
Antrum (C16.3)	4	12.9%	9	15.0%
Pylorus (C16.4)	1	3.2%	4	6.7%
Lesser curvature (C16.5)	0	0%	1	1.7%
Greater curvature (C16.6)	0	0%	3	5.0%
Overlapping lesion (C16.8)	0	0%	6	10.0%
Not specified (C16.9)	9	29.0%	20	33.3%
T stage				
1	4	30.8%	11	44.0%
2	2	15.4%	7	28.0%
3	3	23.1%	3	12.0%
4	4	30.8%	4	16.0%
X/no data	18	n.a.	35	n.a.
N stage				
0	5	41.7%	16	51.6%
1	4	33.3%	10	32.3%
2	2	16.7%	2	6.5%
3	1	8.3%	3	9.7%
X/no data	19	n.a.	29	n.a.
M stage				
0	7	43.8%	14	36.8%
1	9	56.3%	24	63.2%
X/no data	15	n.a.	22	n.a.
Disease stage				
I	5	31.3%	8	22.9%
II	2	12.5%	1	2.9%
III	0	0%	1	2.9%
IV	9	56.3%	25	71.4%
Unknown/no data	15	n.a.	25	n.a.
Grading				
Low-grade (I/II)	4	20.0%	4	9.8%

High-grade (III)	16	80.0%	37	90.2%
Unknown/no data	11	n.a.	19	n.a.

Although treatment information in the ZfKD dataset was limited, the SEER registry provided more comprehensive details regarding therapeutic approaches **(Table 2)**. Overall, chemotherapy was the most commonly administered treatment, used in 71.6% of cases, while a majority of SEER-registered patients (62.1%) did not undergo surgical removal of the primary tumor. By comparison, 52.9% of patients recorded in the ZfKD underwent surgery. Radiotherapy was relatively uncommon, applied in only 13.7% of patients, typically as an adjuvant measure. During the documented follow-up period, 63.7% of pediatric gastric carcinoma patients died **(Table 3)**. In the ZfKD cohort, 48.4% of patients were reported as deceased, including 77.8% of those with stage IV disease, whereas the corresponding mortality in the SEER dataset was 71.7%. SEER data indicated a median follow-up duration of 8 months (mean: 26.7 months, range 0–168 months). Similarly, the ZfKD data showed a median interval from diagnosis to death of 10.2 months (range 0–28 months), with a median age at death of 18.8 years (range 13.5–20.9 years).

Table 2. Treatment characteristics of gastric carcinoma in patients aged 0–19 years registered in the Surveillance, Epidemiology, and End Results Program 2000–2018.

Treatment Modalities	Count	Proportion
Surgery of primary tumor		
Local excision	1	1.7%
Partial gastrectomy	8	13.3%
Near total/total gastrectomy	12	20.0%
Surgery not otherwise specified	1	1.7%
No resection of primary tumor	36	60.0%
Unknown	2	3.3%
Lymph node surgery		
Resection of ≥4 regional lymph nodes	17	28.3%
No lymph node resection	31	51.7%
Unknown	12	20.0%
Radiation		
Yes	8	13.3%
neoadjuvant	2	3.3%
adjuvant	6	10.0%
No	52	86.7%
Chemotherapy		
Yes	45	75.0%
No/unknown	15	25.0%

Table 3. Outcome of/last reported follow-up for gastric carcinoma in patients aged 0–19 years registered at the German Center for Cancer Registry Data 2000–2017 and in the Surveillance, Epidemiology, and End Results Program 2000–2018.

Status	German Center for Cancer Registry Data (ZfKD) 2000–2017 (n = 31)		Surveillance, Epidemiology, and End Results Program (SEER) 2000–2018 (n = 60)	
	Count	Proportion	Count	Proportion
Alive	16	51.6%	17	28.3%
Deceased	15	48.4%	43	71.7%

Using data from the ZfKD between 2009 and 2015, the crude incidence of gastric carcinoma among children and adolescents in Germany was calculated at 0.16 cases per million during this period. Eight pediatric patients were included in the STEP registry, with a median age at diagnosis of 16.1 years (range 12.7–17.4). Patient characteristics are summarized in **Table 4**. The most frequent presenting symptoms prompting diagnostic evaluation were abdominal pain (n = 4), altered bowel habits (n = 2), and anemia (n = 2), typically appearing one to three months prior to diagnosis. Initial diagnosis was achieved via gastroscopy in seven patients and imaging in one patient, with all cases confirmed by histopathology.

All tumors were adenocarcinomas, with signet ring cell carcinoma representing the most common subtype (n = 3). According to the Laurén classification, three tumors were diffuse type, two were intestinal type, and three were mixed type, all of which included signet ring cell components [19]. Precancerous changes included intestinal metaplasia in the context of chronic gastritis (n = 2) and hyperplastic polyps with intestinal metaplasia (n = 1). One patient with hereditary diffuse gastric cancer (HDGC) also showed moderate foveolar hyperplasia consistent with in situ carcinoma. No Epstein-Barr virus was detected in any tissue sample, and analysis for HER2/neu overexpression and microsatellite instability was negative in all examined cases (n = 6 and n = 4, respectively).

During subsequent investigations, one patient was diagnosed with Peutz–Jeghers syndrome. Two patients were identified with germline CDH1 mutations associated with HDGC, one of whom had the carcinoma detected at an early stage during a screening gastroscopy. Immunoglobulin levels were markedly reduced in three patients, two of whom had type A gastritis, and one had a pre-existing diagnosis of autosomal recessive agammaglobulinemia. Histopathology revealed chronic gastritis in seven patients, and Helicobacter pylori infection was present in six.

Advanced disease was common at presentation, with five patients classified as stage IV; the peritoneum was the most frequent site of metastasis. Complete surgical resection (CR) via gastrectomy was achieved in four patients, all of whom remained in remission at last follow-up. The remaining four patients had tumors that were unresectable due to extensive metastatic spread; three of these patients died shortly after diagnosis, and the fourth exhibited disease progression despite therapy. First-line chemotherapy regimens included 5-fluorouracil, cisplatin or oxaliplatin, and docetaxel (n = 5). Additional treatments administered included immunotherapy and regional deep hyperthermia.

Table 4. Characteristics of pediatric patients with gastric carcinoma registered with the German Registry for Rare Pediatric Tumors (STEP). Abbreviations: H.p., Helicobacter pylori; 5-FU, Fluorouracil; FU, Follow-up. * Chemotherapy: Carboplatin, Ifosfamide, Etoposide/Adriamycin.

Gender	Age at Diagnosis (Years)	TNM	Stage/Grading	Site of Metastases	Pre-Existing Diseases	Surgery of Primary Tumor	Therapy of Metastases	Medical Therapy	Status at Last FU	Time Since Diagnosis (Years)
f	14.3	T1aN0M0	IA/G3	-	Chronic gastritis (H.p. pos.), CDH1 mutation	Gastrectomy	-	-	Alive off therapy	2.8
f	16.1	T1aN0M0	IA/G3	-	Chronic type A gastritis (H.p. neg.), IgG/IgA low	Resection (endoscopic)	-	-	Alive off therapy	0.7
f	16.1	T3N0M0	IIA/G3	-	Chronic gastritis (H.p. pos.)	Gastrectomy	-	5-FU, Leucovorin, Oxaliplatin, Docetaxel (FLOT, 6 cycles, 4 thereof neoadjuvant)	Alive off therapy	1.8

f	16.0	TxN + M1	IV/G3	Ovaries, Peritoneal carcinomatosis, lymph nodes	Chronic gastritis (H.p. pos.), IgG/IgA low, CDH1 mutation	-	Resection of an ovarian metastasis	5-FU, Leucovorin, Oxaliplatin, Docetaxel (FLOT, 5 cycles)	Dead of disease	1.2
m	15.4	T3N0M1	IV/G2	Singular peritoneal metastasis	Autosomal recessive agammaglobulinemia, Chronic type A gastritis (H.p. pos.)	Gastrectomy	Resection	-	Alive off therapy	6.5
f	12.7	T4N1M1	IV/G2/3	Peritoneal carcinomatosis	Dysembryoplastic neuroepithelial tumor (WHO I°), Peutz–Jeghers syndrome	-	-	5-FU, Cisplatin, Docetaxel/Epirubicin (6 cycles), 5-FU, Leucovorin, Irinotecan, Oxaliplatin (FOLFOXIRI, 3 cycles), regional deep hyperthermia + chemotherapy (2×) *	Dead of disease	0.8
f	16.7	TxN3M1	IV/G3	Lung, liver, lymph nodes, bones, bone marrow	Chronic gastritis (H.p. pos.)	-	-	5-FU, Leucovorin, Oxaliplatin, Docetaxel (FLOT, 6 cycles), 5-FU, Leucovorin, Irinotecan (FOLFIRI, 13 cycles), Ramucirumab/Paclitaxel, Nivolumab	Dead of disease	1.0
f	17.4	T4N2M1	IV/G3	Peritoneal carcinomatosis	Chronic gastritis (H.p. pos.)	-	-	5-FU, Cisplatin, Docetaxel (6 cycles)	Alive on therapy	0.3

Gastric carcinoma predominantly affects older adults, with fewer than 10% of cases occurring in individuals under 45 years of age, although recent trends indicate a rising incidence among younger adults [20, 21]. In children, these tumors are extremely rare, representing less than 0.1% of all gastric cancers [22]. Our analysis of cases from the ZfKD, SEER, and STEP registries revealed that gastric carcinoma tends to emerge more frequently during adolescence, a pattern also noted in other studies [8, 14], though younger children can also be affected. Interestingly, whereas adult gastric cancer shows a male predominance, we observed a higher incidence among females in pediatric cases, the reasons for which remain unclear [23].

Similar to adults, adenocarcinomas comprised nearly all pediatric gastric carcinomas [2]. Although multiple histopathologic classifications exist (e.g., WHO, Laurén, Japanese Gastric Cancer Association), these distinctions

have little impact on therapeutic decisions in adult treatment guidelines [19, 23, 24]. Signet ring cell carcinoma, a subtype with debated prognostic implications [10, 25, 26], was identified in 38.5% of pediatric cases—significantly higher than the 20% reported in adults [22].

Globally, non-cardia gastric cancers, often associated with H. pylori infection, high salt intake, and alcohol consumption, constitute roughly 80% of cases, whereas proximal gastric cancers are more frequent in North America and Western Europe and are linked to obesity and gastroesophageal reflux [23, 27]. In our pediatric cohort, the cardia was a common site, but most tumors occurred elsewhere in the stomach. Notably, H. pylori infection was detected in six of the eight STEP patients. While this information is not captured in large epidemiologic registries, prior reports indicate frequent H. pylori positivity in pediatric gastric cancers [8, 14]. Given its established role in adult carcinogenesis, involving a progression from chronic inflammation to atrophy and intestinal metaplasia [3, 11, 23, 28, 29], H. pylori likely contributes to pediatric gastric cancer as well.

Childhood H. pylori infection is common, with prevalence ranging from 10% in the US and Western Europe to up to 80% in parts of India, Africa, and Latin America [30]. Interestingly, the frequency observed in our cohort was higher than expected in the German pediatric population. In a Turkish study of 750 children undergoing upper endoscopy, 52% were H. pylori positive; of these, 74% had chronic gastritis, and 6.2% and 2.8% had progressed to atrophy and intestinal metaplasia, respectively, but none developed cancer [30]. This suggests that infection alone may be insufficient to drive carcinogenesis in childhood. Unlike adults, where prolonged gastritis, lifestyle, and dietary factors increase cancer risk [2, 31], genetic predisposition appears to play a more central role in pediatric gastric carcinoma [32].

Several hereditary cancer syndromes are associated with gastric carcinoma in adults, including HDGC, GAPPS, and familial intestinal gastric cancer (FIGC) [4], as well as syndromes not specific to gastric cancer but linked with it, such as Li-Fraumeni, Lynch, familial adenomatous polyposis, juvenile polyposis, and Peutz–Jeghers syndrome [4, 33–36]. In adults, purely hereditary cases account for about 3% of gastric cancers, though up to 10% show familial clustering [4]. HDGC, caused by germline CDH1 or CTNNA1 mutations, is the most common hereditary predisposition, inherited in an autosomal dominant manner with high penetrance, conferring a lifetime gastric cancer risk of ~80% and a 60% lifetime risk of breast cancer in women [10, 37].

In the STEP cohort, two of eight patients had HDGC and one had Peutz–Jeghers syndrome, indicating a higher prevalence of cancer predisposition than typically seen in adults. Additionally, immunodeficiencies were present: one patient had autosomal recessive agammaglobulinemia, and two others had markedly reduced IgA and IgG at diagnosis. Various immunodeficiency disorders, including X-linked and autosomal recessive agammaglobulinemia, common variable immunodeficiency, and IPEX syndrome, have been linked to increased gastric cancer risk in adults and sporadically in children [38–43]. Our findings suggest that immunodeficiency may similarly contribute to pediatric gastric carcinogenesis.

Overall, these observations indicate that pediatric gastric carcinoma likely arises from a combination of H. pylori infection along with genetic predisposition and/or immunodeficiency, underscoring the multifactorial nature of the disease in children.

Because the clinical manifestations of gastric carcinoma in children are often vague, diagnosis is frequently delayed by several months, a pattern also noted in prior studies [10, 14]. This diagnostic delay, combined with the generally poor differentiation of tumors, contributes to the frequent presentation of advanced-stage disease. In our cohort, stage IV tumors were notably more common (66.7% vs. 41%) and high-grade differentiation was observed in 86.9% of cases compared with 65% in adults [22]. While stage IV disease carries a poor prognosis, complete surgical removal of localized tumors offers a substantial chance of long-term remission, as seen in adult patients [23]. This trend appears consistent in pediatric cases: all STEP patients who underwent complete resection remained in remission, whereas children with stage IV cancer in the ZfKD cohort had a survival rate of only 22% (compared with 5–15% in adults) [44, 45].

The observed differences in mortality between the ZfKD and SEER registries likely reflect this disparity, as SEER recorded a higher proportion of stage IV cases and fewer patients who underwent primary tumor resection. Treatment regimens, including first-line chemotherapy, were largely adapted from adult protocols **(Table 5)** [23]. However, current guidelines advise against taxane-based triplet therapy in advanced disease due to a lack of survival benefit over doublet regimens and increased toxicity [23]. While trastuzumab is recommended in adults with HER2-positive advanced gastric cancer (10–20% prevalence), none of the STEP tumors tested (n = 6) exhibited HER2/neu overexpression [23, 46]. PD-L1 status was infrequently assessed at diagnosis, and only one STEP patient received PD-L1 blockade, and then as fourth-line therapy. In adults, nivolumab is indicated for

advanced cancers with a combined positive score ≥5 regardless of H. pylori infection, though HP-positive tumors may be less responsive [23, 47, 48]. Given the high rate of HP positivity in pediatric gastric carcinoma, this could limit the efficacy of PD-L1–directed therapy.

Currently, management of pediatric gastric carcinoma should be guided primarily by adult evidence-based protocols and involve collaboration with adult oncologists, especially for microsatellite unstable tumors, which show excellent long-term outcomes with PD-L1 inhibition [23, 36]. Initial evaluation should include genetic testing for cancer predisposition **(Table 6)**, as well as assessment of HP infection, HER2/neu, and PD-L1 status. Children with a family history of gastric cancer or known predisposition syndromes or immunodeficiencies should undergo regular endoscopic surveillance to enable detection at localized stages, as demonstrated in one patient from our cohort, which can markedly improve survival. In addition, eradication of HP should be considered in patients with chronic gastritis and confirmed infection to reduce cancer risk [49]. Finally, consistent documentation of these rare pediatric cases in registries like STEP is critical to refining diagnostic and therapeutic strategies over time, ensuring improved management of childhood gastric carcinoma.

Table 5. Simplified treatment strategy for gastric carcinoma based on European Society for Medical Oncology guidelines [23]

Stage	Surgical Approach	Additional / Systemic Therapy
IA	Endoscopic resection or limited surgical removal	None required
IB–III	Radical gastrectomy with D2 lymph node dissection	• Perioperative chemotherapy using a triplet regimen (fluoropyrimidine, platinum agent, docetaxel; standard FLOT: 5-fluorouracil, leucovorin, oxaliplatin, docetaxel) • Adjuvant chemotherapy if preoperative therapy was not given • Consider radiotherapy if microscopic residual disease (R1) remains • For microsatellite instability: skip adjuvant chemotherapy; neoadjuvant FLOT may be applied for downstaging
IV / Locally advanced unresectable	Surgery only in highly selected cases	• First-line doublet chemotherapy (fluoropyrimidine + platinum) • Add trastuzumab for HER2-positive tumors • Add PD-1/PD-L1 inhibitors if PD-L1 CPS ≥ 5 (nivolumab) or ≥ 10 (pembrolizumab) • Second-line: ramucirumab (VEGFR inhibitor) combined with paclitaxel

Table 6. Overview of cancer predisposition syndromes associated with gastric carcinoma and the respective underlying genetic alterations [20, 23, 50].

Genetic Alteration	Associated Cancer Predisposition Syndrome
CDH1, CTNNA1	Hereditary Diffuse Gastric Cancer (HDGC)
APC promotor 1B	Gastric Adenocarcinoma and Proximal Polyposis of the Stomach (GAPPS)
APC	Familial Adenomatous Polyposis (FAP)
BMPR1A, SMAD4	Juvenile polyposis syndrome
TP53	Li-Fraumeni syndrome
MLH1, MSH2, MSH6, PMS2	Lynch syndrome
STK11 (LKB1)	Peutz–Jeghers syndrome

Conclusion

This study offers a comprehensive overview of pediatric gastric carcinoma, highlighting its distinct clinical features. Children with localized tumors who undergo complete surgical resection have a favorable chance of achieving long-term remission, whereas those presenting with stage IV disease generally have poor outcomes. Unlike adult gastric carcinogenesis, genetic cancer predisposition syndromes and immunodeficiencies are more prevalent in childhood and, along with H. pylori infection, appear to accelerate early tumor development. Optimal management requires close collaboration with adult oncology specialists to account for these unique pediatric characteristics and to minimize long-term treatment-related morbidity [51]. Consequently, an interdisciplinary

network of pediatric cancer experts, such as the European Cooperative Study Group for Pediatric Rare Tumors (EXPeRT), is crucial to deliver care aligned with the latest evidence and clinical experience for these rare childhood tumors [52].

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