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## Ulcerated benign jejunal gastrointestinal stromal tumor causing gastrointestinal bleeding: A case report

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### Abstract

#### BACKGROUND

Gastrointestinal stromal tumors (GISTs) are rare mesenchymal tumors that rarely present with gastrointestinal (GI) bleeding due to tumor erosion. GISTs com-

monly arise in the stomach, followed by the small bowel. They are typically diagnosed through histopathology and immunohistochemistry. The presence of mucosal ulceration and tumor locations outside the stomach are linked with a greater risk of tumor progression to malignancy. This case highlights a benign ulcerated jejunal GIST presenting as GI bleeding.

### CASE SUMMARY

A 42-year-old male presented with dark stools and light-headedness over five days. On examination, he was hypotensive, tachycardic, tachypneic, and had pallor. Laboratory tests revealed normocytic normochromic anemia, with a significant one-day drop in hemoglobin (from 7.2 g/dL to 6.4 g/dL). Upper GI endoscopy and colonoscopy were normal, but double-balloon enteroscopy revealed a subepithelial lesion distal to the duodenojejunal flexure, and an overlying ulcer. These findings were suggestive of GIST and were corroborated by a contrast-enhanced computed tomography abdomen scan, which revealed a well-defined, homogeneously-enhancing solid exophytic lesion (30 mm × 22 mm × 26 mm) arising from the proximal jejunal loops. He underwent resection anastomosis with complete *en-bloc* surgical removal of the lesion. Histopathological analysis of the resected specimen confirmed a GIST with presence of spindle cells and positive CD117 staining. His hemoglobin levels were stable on regular follow-ups, and there was no documented recurrence six months later.

### CONCLUSION

GISTs should be suspected in cases of unexplained GI bleeding. Early diagnosis and complete surgical resection are key to favorable outcomes.

**Key Words:** Gastrointestinal stromal tumor; Gastrointestinal bleeding; Jejunal tumor; Small bowel; Double-balloon enteroscopy; Endoscopy; Case report

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**Core Tip:** Gastrointestinal stromal tumors (GISTs) are rare mesenchymal tumors that rarely cause gastrointestinal (GI) bleeding. Mucosal ulceration and unfavorable tumor locations are risk factors for tumor progression and malignancy. We present a case of GI bleeding in a 42-year-old man complaining of melena over five days, which was diagnosed as a benign, ulcerated, jejunal GIST on histopathology and immunohistochemistry. Prompt evaluation using specialized diagnostic tools to locate obscure bleeding sources and complete surgical resection are key to favorable outcomes. GI bleeding in GIST is associated with a poor prognosis. Hence, detailed follow-ups are essential to detect and prevent tumor recurrence.

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## INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are generally recognized as spindle cell, epithelioid, or occasionally pleomorphic tumors that usually develop in the gastrointestinal (GI) tract. Originating from mesenchymal cells of the GI tract, GISTs make up 1%-3% of all GI malignancies and progress to malignancy in approximately 10% to 30% of cases[1,2]. A greater risk of tumor progression is linked to GISTs associated with mucosal ulceration and those that develop outside of the stomach[1,3]. Many GISTs carry mutations in the genes encoding type III receptor tyrosine kinases, particularly *KIT* or *PDGFRA*, which is the case in up to 85% of instances. A significant majority, about 95%, of these tumors are positive for the KIT protein when tested with immunohistochemistry[4]. The most common places where GIST arises are the stomach, followed by the small bowel[2]. In 19% of cases, GISTs manifest asymptotically, particularly in cases of smaller tumors of the intestinal tract. Studies show that around 10% of these cases were caught at autopsy and 20% during abdominal surgery for other conditions, making them a common incidental finding rather than a clinical suspicion[5,6]. Patients who are symptomatic may exhibit non-specific symptoms such as nausea, vomiting, abdominal distension, early satiety, abdominal pain, and, in rare cases, a palpable abdominal mass. Obstruction of the GI lumen by endophytic growth or compression of the GI tract by exophytic growth may result in dysphagia, obstructive jaundice, or constipation in larger tumors, contingent upon the mass's specific location[1]. Very rarely do these tumors present as an acute, severe, life-threatening GI bleeding[7]. Herein, we describe a case report of a rather unusual presentation of GIST, *i.e.*, symptomatic GI bleeding caused by an ulcerated jejunal GIST, which was found to be benign in nature. This case report emphasizes the importance of maintaining a high suspicion of this disease when all routine workups for GI bleeding show no obvious findings.

## CASE PRESENTATION

### Chief complaints

A 42-year-old male with no comorbidities presented with several episodes of black, tarry stools for five days.

### History of present illness

The melena was sudden in onset, occurring two to three times per day, and associated with light-headedness. It was not accompanied by abdominal pain, jaundice, altered mentation, altered bowel habits, blood in vomitus, any other bleeding manifestations, early satiety, or weight loss.

### History of past illness

The patient denied any history of similar or related complaints in the past. There was no history of any malignancies.

### Personal and family history

The patient denied any family history of malignant tumors or bleeding disorders. He had no history of recent travel, smoking, or alcohol intake and was not on any regular medications.

### Physical examination

On physical examination, he was conscious and oriented to time, place, and person. He was tachycardic with a pulse rate of 132 beats/minute, hypotensive (supine and erect blood pressures 94/60 mmHg and 80/54 mmHg, respectively), and tachypneic with a respiratory rate of 26/minute. Additionally, he showed signs of pallor. There were no signs of icterus or chronic liver disease. The systemic examination was unremarkable. Considering the patient's history and presentation, the differentials were between peptic ulcer disease and vascular malformations of the gut, like Dieulafoy lesions or angiodysplasia.

### Laboratory examinations

Laboratory investigation revealed normocytic normochromic anemia [hemoglobin (Hb) 7.2 g/dL], with a significant drop in Hb over a day (from 7.2 g/dL to 6.4 g/dL). The liver function test, kidney function test, electrolyte levels, and clotting profile were unremarkable. All his laboratory tests have been summarized in [Table 1](#).

### Imaging examinations

After initial fluid resuscitation and two units of packed red cell transfusion, he underwent an upper GI endoscopy, which was unremarkable. A colonoscopy showed fresh and altered blood clots all along the entire length of mucosa, which was normal and did not reveal any source of bleeding. He underwent a double-balloon enteroscopy (DBE), which revealed a subepithelial lesion (2 cm × 1.5 cm) approximately 150 cm distal to the duodenojejunal flexure and an overlying ulcer that was not actively bleeding ([Figure 1A](#)). A contrast-enhanced computed tomography (CT) scan of the whole abdomen corroborated the above findings, revealing a well-defined, round-shaped, homogeneously enhancing solid exophytic lesion (30 mm × 22 mm × 26 mm) arising from the proximal jejunal loops, without any obvious adjacent organ involvement, internal necrotic foci or calcification ([Figure 1B](#)). These imaging findings were suggestive of a GIST originating from the proximal jejunum.

## FINAL DIAGNOSIS

Combined with the endoscopic and postoperative histopathological findings, the final diagnosis was a benign jejunal GIST, which was confirmed by histopathological examination of the postoperative specimen.

## TREATMENT

He underwent resection anastomosis with complete *en-bloc* surgical removal of the suspicious lesion with a reasonable tumor-free margin. The post-operative recovery period was uneventful. Histopathology identified a submucosal tumor with spindle cells, mild hyperchromasia with a low mitotic index, and no necrosis or epithelioid cells ([Figure 2](#)). The cells were diffusely immunopositive for CD117 and DOG1, which confirmed GIST ([Figure 3](#)).

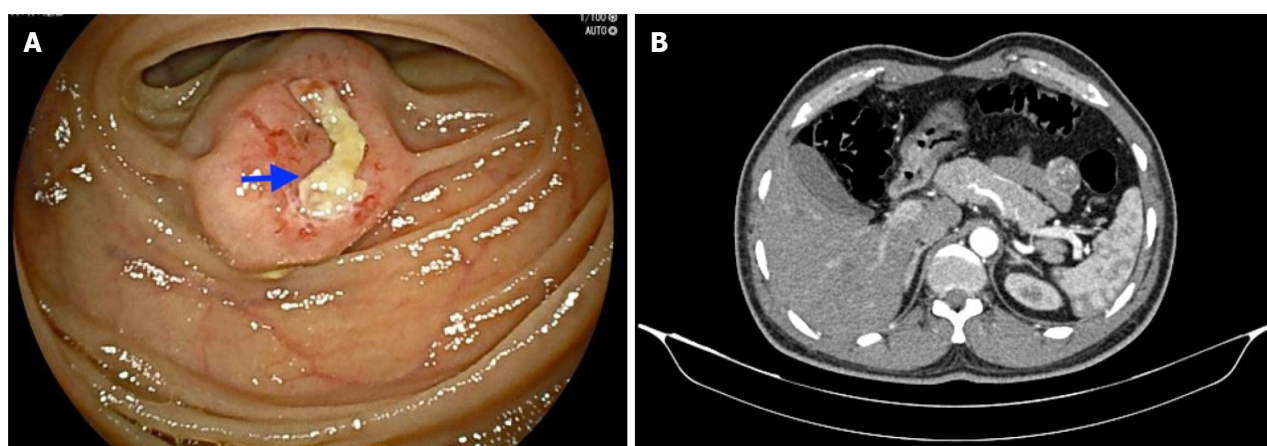
## OUTCOME AND FOLLOW-UP

Our patient was postoperatively well and followed up for six months thereafter. His Hb level was stable on regular follow-ups, and there was no documented recurrence six months later.

**Table 1** Laboratory investigations following admission

Parameter (units)	Day 1	Day 2	Day 3	Day 4
Hemoglobin (g/dL)	7.2→6.4	7.9	8.4	8.6
Total leukocyte count (cells/cu mm)	5.1	6.6	5.1	-
Differential count (neutrophil/lymphocyte)	77/12	80/16	82/11	-
Platelet count (cells/cu mm)	3.3	2.7	2.2	-
Bilirubin total/Direct (mg/dL)	0.8	0.9/0.1	-	-
SGPT (IU/L)/SGOT (IU/L)	31	28/33	-	-
ALP (IU/L)	-	118	-	-
Total protein (g/dL)	-	6.2	-	-
Serum albumin (g/dL)/globulin (g/dL)	3.8	4.0/2.2	-	-
PT (seconds)/INR	0.98	1.11	-	-
Serum urea (mg/dL)/creatinine (mg/dL)	31/0.9	27/0.7	20/0.8	-
Na <sup>+</sup> (mEq/L)/K <sup>+</sup> (mEq/L)	141/3.7	139/4.1	139/3.9	-

SGPT: Serum glutamic pyruvic transaminase; SGOT: Serum glutamic-oxaloacetic transaminase; ALP: Alkaline phosphatase; PT: Prothrombin time; INR: International normalized ratio; Na<sup>+</sup>: Sodium; K<sup>+</sup>: Potassium.

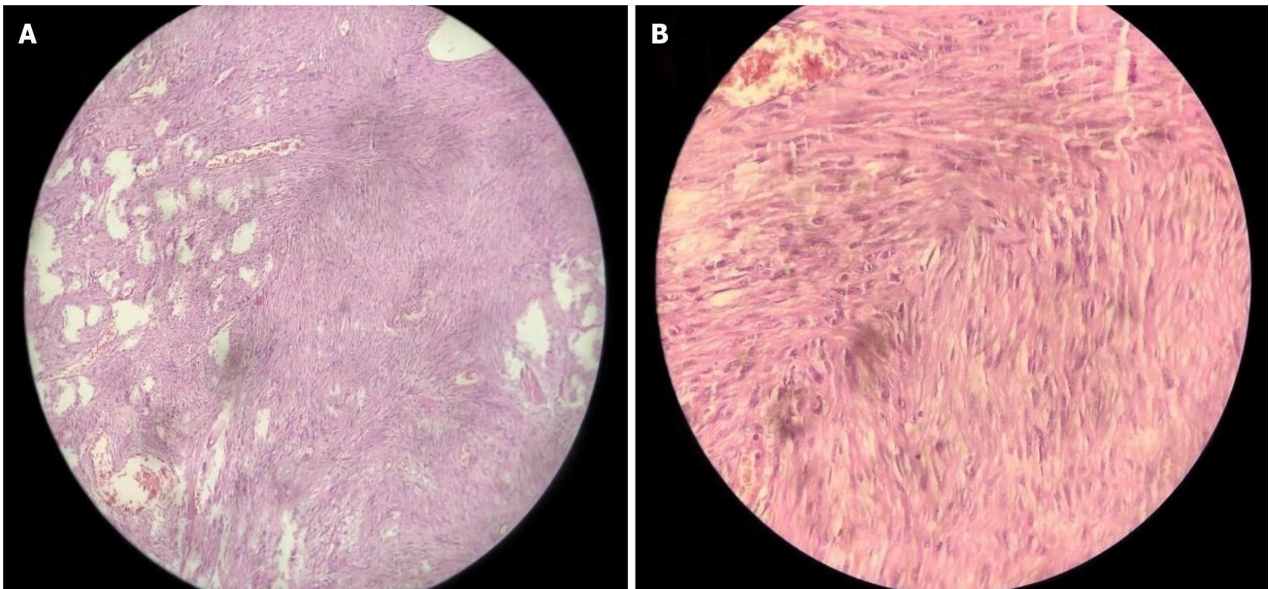


**Figure 1** Imaging examinations. A: Double-balloon enteroscopy image showing a subepithelial lesion (2 cm × 1.5 cm) approximately 150 cm distal to the duodenojejunal flexure and an overlying ulcer without any active bleeding; B: A contrast-enhanced computed tomography abdomen scan revealing a well-defined, round-shaped, homogeneously enhancing solid exophytic lesion (30 mm × 22 mm × 26 mm) arising from the proximal jejunal loops without any obvious adjacent organ involvement, internal necrotic foci or calcification.

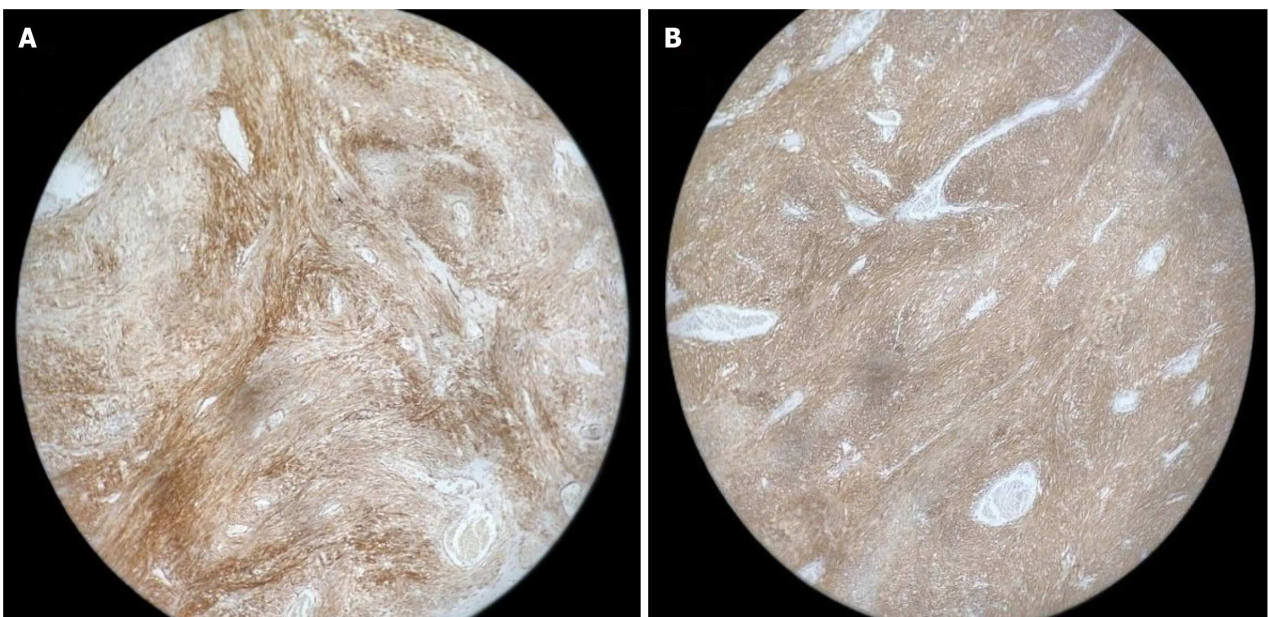
## DISCUSSION

GISTs usually occur as solitary lesions and are thought to originate from the interstitial cells of Cajal, a complex cellular network that regulates peristalsis[1]. These are rare tumors, having a reported incidence ranging from 0.4 cases to 2 cases per 100000 annually. Males have a slightly higher incidence of GIST, and the median age of presentation is approximately 60 years to 65 years[8]. GISTs can originate anywhere in the GI tract; however, the most common locations are the stomach, followed by the small bowel[6]. Less than 3% of all GI tumors are jejunal GISTs[9]. GISTs can rarely occur even outside the GI tract in the retroperitoneum or mesentery[2]. The presentation of GIST varies, ranging from non-specific symptoms including nausea, vomiting, and abdominal distension to a palpable abdominal mass. While symptoms due to large tumors are usually attributed to mass effect, perforated neoplasms may present with peritonitis or GI bleeding[1]. Ongoing active acute blood loss, as in the above patient with no comorbidities, warrants a complete visualization of the GI tract to look for any bleeders, which includes visualization of the small intestine. Most GIST cases are attributed to oncogenic mutations in *KIT* or *PDGFRA* that result in gain-of-function of tyrosine kinases; these mutations are found in approximately 85% of GISTs. A subset of cases is associated with alternative mechanisms, including the inactivation of *NF14* or genes that encode subunits of succinate dehydrogenase (SDH). SDH-deficient GISTs have a slower clinical progression than *KIT*/*PDGFRA*-mutant GISTs. Although most cases occur sporadically among adults, a few of them may occur in children and young adults as part of the non-hereditary Carney triad syndrome (comprising multifocal gastric





**Figure 2** Histopathological image of postoperative jejunal specimen. A: A 10× view of a submucosal tumor comprising spindle cells arranged in a long, fascicular pattern; B: A 40× view of spindle cells showing minimal pleomorphism mild hyperchromasia, low mitotic index, without any necrosis or epithelioid cells.



**Figure 3** Immunohistochemical profile of postoperative jejunal specimen showing diffuse immunopositivity. A: CD117; B: DOG1 markers.

GISTs, paraganglioma, and pulmonary chondroma) or autosomal-dominant Carney-Stratakis syndrome (comprising multifocal gastric GIST and paragangliomas)[4]. GISTs can be detected using abdominal ultrasound, CT, magnetic resonance imaging, and positron emission tomography. CT enterography is the most effective modality for identifying the location of tumors, assessing any perforation, evaluating invasion into adjacent structures, and detecting metastasis. Small tumors display homogenous densities on radiological investigations, but large tumors reveal heterogeneous enhancement, mucosal ulceration, central and coagulative necrosis, and irregular lobulated borders[1]. Histologically, GISTs are of three types: Spindle cell, epithelioid, and mixed type. Since they are often misdiagnosed as leiomyoma or leiomyosarcoma, immunohistochemical analysis is essential. 95% of GISTs are positive for CD117, while DOG1 is expressed in 98% of cases. Additionally, PDGFRA and CD34 are expressed in 80% and 70%-80% tumors, respectively. The diagnosis is confirmed when CD117 and/or DOG1 are present. Furthermore, there is loss of SDH-B expression in SDH-deficient tumors, making it an important diagnostic test in SDH-deficient GIST[4]. Schwannoma, along with leiomyoma and leiomyosarcoma, are some notable differentials of GIST. While almost all GISTs are negative for desmin (marker for mature smooth muscle cells) and S100 protein (Schwann cell marker), they are positive in the above-mentioned differentials, *i.e.*, smooth muscle tumors (leiomyoma and leiomyosarcoma), and Schwannomas express desmin and S100 protein positivity, respectively[10]. The most important and life-threatening complication of GIST is GI hemorrhage[11, 12]. Tumor growth may cause digestive tract mucosa to become restricted, altering the local mucosal blood supply.

Consequently, cell necrosis damages the barrier, which when combined with digestive fluids, can lead to ulcerative bleeding[11]. Tumors larger than 4 cm are likely to cause life-threatening GI bleed due to overlying mucosal and sub-mucosal destruction by the growing tumor along with the invasion of vessels leading to rupture[12]. Conventional endoscopy's inaccessibility of the small intestine sometimes makes it challenging to identify bleeding. The modalities involve capsule endoscopy, CT angiography (CTA), conventional CT scan with intravenous and/or oral contrast, DBE, and magnetic resonance enterography when conventional endoscopy fails[13-15]. A single-center study identified that DBE identified the tumor in approximately 88% of the cases, whereas CTA was at 71%[16]. Similar cases of jejunal GISTs presenting with GI bleeding have been reported in the literature, highlighting the challenges of diagnosing these rare tumors. Wadhwa *et al*[17] described a patient with hemorrhagic shock due to a bleeding jejunal GIST, which was successfully managed with imaging and surgical resection. Similarly, another report documented a patient with a large submucosal jejunal mass identified during upper GI endoscopy and initially managed with epinephrine injection before surgical intervention as a definitive treatment[18]. These cases underscore the importance of prompt evaluation using specialized diagnostic tools like DBE and CTA to locate obscure bleeding sources, followed by surgical resection to achieve definitive management. According to the current guidelines, the standard treatment of localized GISTs is complete surgical excision of the lesion, with no dissection of clinically negative lymph nodes in order to achieve R0 resection [8]. Imatinib, a tyrosine kinase inhibitor, is the standard first-line treatment for locally advanced, inoperable, and metastatic GISTs. It is also recommended as an adjuvant therapy in localized GISTs with a significant risk of relapse following surgery. However, it is avoided in NF1-related and SDH-negative GISTs as they are resistant to imatinib. For imatinib-resistant GISTs, sunitinib, regorafenib, and ripretinib are the standard second-, third-, and fourth-line treatments, respectively[8]. Newer therapies such as nivolumab and ipilimumab hold promise in tyrosine kinase inhibitor-resistant and unresectable cases, showing beneficial effects in a phase II randomized controlled trial[19]. GISTs have varied malignant potentials: Approximately 20%-25% of gastric GISTs and 40%-50% of small intestine GISTs exhibit malignant tendencies[20]. Therefore, we must consider the risk of recurrence in the patient. We used the consensus approach by Fletcher *et al*[21] and estimated the risk of recurrence to be very low. Thus, the patient did not require any further adjuvant imatinib therapy. The currently known prognostic factors of primary GISTs are the size and location of the tumor, mitotic count, and mutational status. In addition to the above, a retrospective analysis identified mucosal ulceration as a prognostic factor and independent risk factor for disease progression in GISTs[3]. Despite the unfavorable location and presence of a risk factor, the GIST in our patient was found to have a low mitotic index, making it a benign tumor. This is a rare occurrence, given the fact that small intestine tumors and ulcerated GISTs are usually associated with tumor progression and malignancy. GISTs associated with GI bleeding have an increased likelihood of recurrence. Compared to patients without GI bleeding, such GISTs also have an increased risk of malignancy[11]. Furthermore, GI bleeding significantly affects the recurrence-free survival and overall survival in GIST, particularly in patients with gastric GIST bleeding. Thus, GI bleeding is an independent risk factor of tumor recurrence and should be considered as a significant indicator of poor prognosis during risk stratification of GIST patients[11,22]. In view of the increased recurrence risk, such patients would benefit from a thorough follow-up and a reduced threshold for postoperative therapy[11].

## CONCLUSION

GISTs can present with GI hemorrhage due to erosion of the epithelial layers. It is important to recognize this and evaluate the possible causes of GI hemorrhage, one of which is likely a GIST. The surgical resection in cases of small tumors with tumor-free margins and histopathological analysis for molecular subtyping and confirmation of GIST should be mainstream. Physicians should be aware of the increased risk of GIST recurrence following GI bleeding and should carry out a close follow-up of such patients. Assessment of further need for adjuvant imatinib based on molecular studies and risk assessment criteria for recurrence is also essential.

## FOOTNOTES

**Author contributions:** Maity R, Rathna RB, and Fernandes N conducted literature review and wrote the primary manuscript; Maity R and Rathna RB contributed equally to this article, they are the co-first authors of this manuscript; Dhali A conceptualized the article and wrote the primary manuscript; Biswas J and Kapoor GS wrote the primary manuscript; Dhali GK supervised the work and wrote the revised manuscript; Dhali A and Kapoor GS contributed equally to this article, they are the co-corresponding authors of this manuscript; and all authors have read and approved the final manuscript.

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