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Delineating Gastrointestinal Dysfunction Variants in Severe Burn Injury Cases: A Retrospective Case Series with Literature Review

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Abstract

Background: Severe burns can significantly impact various organ systems, including the gastrointestinal (GI) system. GI complications are frequently observed in patients with over 20% total body surface area (TBSA) burn.
Objectives: This case series delves into the intricate phenomenology of post-burn GI dysfunction, challenging conventional cause-and-effect paradigms. Our aim is to discern, comprehend, and explore variables influencing positive and negative outcomes, laying the foundation for further research given the current heterogeneity in the literature.
Methods: Severe burn patients with GI dysfunction identified between April 1, 2022, and July 31, 2022, from the institutional database are included in this retrospective case-series, and comparisons were made across baseline and treatment conditions across participants. Data were collected on demographics, burn characteristics, complications, and treatment outcomes.
Results: We analysed 12 patients with severe burns and GI dysfunction and categorized them into two patterns: Pattern A, characterised by early onset symptoms, gastric and small bowel dilatation, and a relatively benign course with high recovery rates was observed in 6 patients; and Pattern B, characterised by late-onset symptoms, colonic dilatation, shock, and a high mortality rate due to megacolon was seen in 6 patients.
Conclusion: The post-burn GI dysfunction observed in our study is a complex interplay of multiple factors. Adequate fluid resuscitation, timely excision of necrotic tissue, staged food ingestion, specific nutrient administration, and appropriate use of antibiotics and judicious use of selective digestive decontamination (SDD) are essential strategies to prevent and treat this syndrome.

Introduction

Severe burns can have significant physiological impacts on the body, posing a risk to a patient's life that may be exacerbated by complications throughout the stages of treatment (1,2). Gastrointestinal (GI) complications are common in partial and full-thickness burns involving more than 20% TBSA and can include constipation, delayed gastric emptying, bacterial translocation, and sepsis, among others (2,3). While animal models suggest that burns delay gastric emptying and affect gut motility, the exact mechanism in humans is unknown (4,5). Probable causes could include large-volume fluid resuscitation, immobility, increased sympathetic drive secondary to pain, and dietary association with glutamine, opioids, and drugs such as tramadol and tapentadol. This study aims to describe two distinct patterns of bowel dysfunction observed in patients admitted with severe burns and discuss the impact of thermal injuries on gut motility and associated outcomes.

Methodology

Our study includes adult and paediatric patients with severe burns (>20% TBSA) and post-burn GI dysfunction, identified between April 1, 2022, and July 31, 2022. Data collection from discharge codes and chart reviews was conducted independently by two qualified, trained personnel for every participant from the medical records of eligible patients, employing anonymization protocols to uphold patient confidentiality during the entirety of the process. Data, including demographics, burn characteristics, complications, and response to treatment, were collected for the entire course of clinical care and subsequently compiled and reported. The burn unit at the hospital is staffed with highly skilled clinical staff members who have specialized training in treating severe burns. The assessment of treatments and data was supervised by an expert analyst at the faculty level.

Case Descriptions

The long-term outcome of a burn injury dramatically depends on the quality of care received during the initial hours. However, the majority of initial burn care is administered outside of specialized burn centres. It is essential to comprehend the intricacies of Advanced Burn Life Support (ABLS) to ensure the patient's optimal outcome. The medical team provided comprehensive intensive care to manage the patients' GI dysfunction and a description of the management, and treatment approach is summarised below.

1. Symptoms: Patients with severe burns presented with symptoms such as diarrhoea, constipation, feed intolerance, abdominal distension, and hypoactive or diminished bowel sounds.
2. Workup for diarrhoea: Patients underwent a workup that included testing for *C. difficile* toxin and stool culture and sensitivity, which both came back negative.
3. Treatment for diarrhoea: Patients were treated with oral rehydration solution (ORS), probiotics, and racecadotril capsule (1.5mg/kg). Osmotic diarrhoea mostly resolved with reducing feed volume and protein content. In non-responders with suspected *C. difficile* infection presenting with fever, leucocytosis and pain abdomen, stool sample for toxin detection or culture was sent and oral metronidazole and, or oral vancomycin therapy was initiated. In patients who progressed to paralytic ileus, IV metronidazole along with oral vancomycin and vancomycin enema were administered.
4. Treatment for constipation: Patients received syrup lactulose or syrup sodium picosulfate, liquid paraffin and milk of magnesia. Additionally, prokinetic agents were administered, and if necessary, enemas were used.

5. Management of abdominal distension: In cases of abdominal distension, bowel decompression was performed by inserting a nasogastric tube with an intermittent suction system. This procedure aimed to reduce or resolve gastric dilatation, prevent vomiting and decrease the risk of aspiration associated with paralytic ileus.
6. Intra-abdominal pressure (IAP) monitoring: Patients with abdominal distension underwent regular IAP monitoring, typically every 4 hours using indirect measurement via the bladder. If IAP exceeded 12 mmHg and was accompanied by hypotension, decreased urine output, or a tense abdomen, more frequent measurements (every 2 hours) were performed. Foley's catheter was also checked for blockage in case of increased IAP values. Monitoring continued until IAP levels dropped below 10 mmHg for several hours, along with clinical improvement.
7. Stress ulcer prophylaxis and thromboprophylaxis: Patients above the age of 3 received pantoprazole for stress ulcer prophylaxis. Additionally, adult patients received injection Enoxaparin (1mg/kg) for thromboprophylaxis and mechanical prophylaxis. These measures were continued until patients achieved full ambulation.
8. Antibiotics: Antibiotics were initiated only when signs of infection were observed, based on clinical assessment and monitoring of laboratory trends. Once definitive evidence of microbial growth from blood, urine, and wound cultures was obtained, culture-based antibiotics were started.
9. Source control: Whenever necessary, the surgical team performed source control procedures to address and manage the underlying cause.

Patient Characteristics

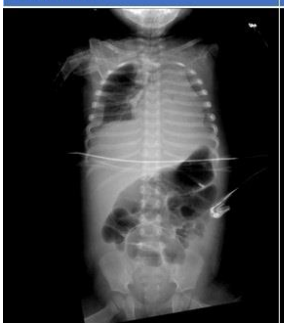
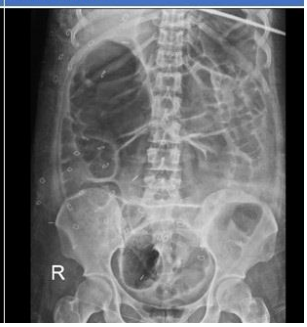
Patients were separated into two patterns based on their clinical characteristics and outcomes (Table 1) and abdominal X-rays (Table 2).

Table 1. Comparison of the Two Patterns of Presentation (to view Table 1 in a new and separate window click here)

	Pattern A (6 patients)	Pattern B (6 patients)
Time of presentation	Early (D3-4 ICU)	Late (>D7 ICU)
Antibiotics at the time of symptoms	No	Yes
Receiving tramadol/tapentadol/ pregaba at the time of symptoms	No	Yes
Bowel involvement	Gastric and small bowel (2 had only gastroparesis)	Gastric, small bowel and large bowel
SOFA score at the onset of abdominal distension	Lower (median <1)	Higher (median – 2)
Complications (ileus partial/complete, toxic megacolon, AKI, bowel perforation, bowel obstruction	Ileus – 1 Megacolon - 1	Ileus – 3 Megacolon - 3
Outcome	Better (5 were discharged, 1 expired)	Worse (3 expired, 3 discharged)

AKI=acute kidney injury

Table 2. Abdominal X-ray Patterns (to view Table 2 in a new and separate window click here)

Pattern A	Pattern B
	

Additional patient characteristics of pattern A and B are shown tables 3 and 4.

Table 3. Clinical Characteristics, Laboratory, and Imaging Findings of Patients with Pattern A GI Dysfunction (to view Table 3 in a new and separate window click here)

Pattern A	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age/Sex	2y/F	2y/F	22months/F	28y/M	2y/M	40y/M
Comorbidity						T2 DM
% TBSA	15	35	15	50	35	55
Day on onset of symptoms	D3	D3	D3	D4	D2	D3
SOFA at onset	0	2	1	2	0	0
Part of bowel involved (As evident on imaging)	Gastric	Gastric + Small Bowel	Gastric + Small Bowel	Gastric + Small Bowel	Gastric	Gastric + Small Bowel
Diarrhoea/Constipation	Constipation	Diarrhoea	Diarrhoea	Diarrhoea	Diarrhoea	Diarrhoea
Concurrent Antibiotic Use	N/A	N/A	N/A	Cefoperazone and Sulbactam D2	N/A	N/A
Response to prokinetics	Yes	N/A	N/A	N/A	N/A	N/A
Serum Potassium on the day of onset of symptoms	4.7	4.3	3.4	3.6	3.9	3.8
Is patient on Ventilator at onset	No	No	No	No	No	No
Complications	Ileus	Shock	Ileus/Megacolon	None	None	None

TBSA=total burn surface area
SOFA=Sequential Organ Failure Assessment Score

Table 4. Clinical Characteristics, Laboratory, and Imaging Findings of Patients with Pattern B GI Dysfunction (to view Table 4 in a new and separate window click here)

Pattern B	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Patient 12
Age/Sex	4y/M	11y/M	25y/F	25y/M	28y/M	36y/M
Comorbidity						T2 DM
% TBSA	45	30	50	55	40	30
Day on onset of symptoms	D9	D13	D25	D8	D10	D10
SOFA at onset	1	2	2	2	2	2
Part of bowel involved (As evident on imaging)	Gastric + Small Bowel + Large Bowel	Gastric + Small Bowel + Large Bowel	Large Bowel	Gastric + Small Bowel + Large Bowel	Gastric + Small Bowel + Large Bowel	Gastric + Small Bowel + Large Bowel
Diarrhoea/Constipation	Diarrhoea	Constipation	Diarrhoea	Diarrhoea	Constipation	Diarrhoea
Concurrent Antibiotic Use and days of usage	Piperacillin and Tazobactam D5	N/A	Ceftazidime, Avibactam and Aztreonam D14	Cefoperazone and Sulbactam D2	Cefoperazone and Sulbactam D6	Meropenem and Polymyxin D8
Response to prokinetics	N/A	Yes	N/A	N/A	Yes	N/A
Serum Potassium on the day of onset of symptoms	3.4	4.2	4.2	4.4	3.8	3.6
Is patient on Ventilator at onset	No	No	No	No	No	No
Complications	Shock/Ileus	Shock/Ileus	Shock/Megacolon	Megacolon	Shock/Ileus/ Megacolon	None
Outcome	Death	Discharged	Death	Discharged	Death	Discharged

The two groups differed in baseline characteristics. The first group had a smaller median TBSA compared to the second group (32.5% vs 42.5%). Additionally, the first group comprised primarily paediatric patients, and their GI dysfunction developed earlier (median day 3 vs day 10), with a lower median SOFA score (0 vs 1). The second group had colonic dilatation in addition to gastric and small bowel dilatation, and all patients had signs and, or evidence of infection and were on antibiotics by the time they developed GI dysfunction. The median serum potassium levels were also slightly different between the two groups (3.8 vs 4.2). Notably, there were more deaths in the second group (50%) compared to the first group, where most patients recovered and were shifted to a step-down unit.

Discussion

The stress response, metabolic changes, and nutritional deficiencies primarily cause most gastrointestinal (GI) issues associated with burn injuries. If not promptly recognized and appropriately treated, these complications can lead to severe consequences, including fatal haemorrhage or perforation. Implementing early prophylactic measures during the post-burn period is crucial to prevent these outcomes. One common complication of thermal injuries is gastric distention and dysfunction.

Studies have shown that gastric emptying is significantly reduced by approximately 37-42% at 6 hours after a burn (4-6). In our study, we observed early gastric dilation upon admission. Burn injuries also affect the standard slow wave frequency in the stomach, increasing the occurrence of bradygastria (7). However, patients who arrived at the emergency department within 2 hours of the burn injury and received timely resuscitation mostly remained asymptomatic. Radiological evidence revealed gastric dilation, which eventually resolved during their hospital stay.

Animal studies have demonstrated that small intestinal transit time is significantly decreased in burn injury models compared to control groups at 2 hours (8,9) and 6 hours post-burn (5,6,9,10). In our study, we observed early small bowel dilation and ileus during the ICU stay. Chen et al conducted a study with rat models, revealing that the gastrointestinal motility in burn-injured rats treated with saline is notably higher compared to untreated burn-injured rats (11). This finding aligns with our observations, as most patients who arrived early and received timely resuscitation showed resolution of bowel dilation.

Colonic transit time was delayed compared to the control group in burn injury patients (5,12). We could not find any literature on this topic in human subjects, highlighting the need for prospective studies. We noticed colonic involvement in symptomatic patients approximately one week after the burn injury. In cases of severe abdominal distension, dilated bowel loops, and feed intolerance, supplemental parenteral nutrition/TPN was administered. Early fluid resuscitation within 2 hours of a thermal injury is crucial in preventing multiple organ failure and mortality (18).

As described above, "Pattern A" patients experienced early symptoms during their ICU stay, showed minimal signs of infection, and had a relatively milder course with a lower mortality rate compared to "Pattern B" patients. Pattern B patients presented later, experienced more complications, and had higher morbidity and mortality rates. Dysmotility in these patients could be attributed to sepsis, opioids, or antibiotics. We tested for C. difficile toxin and culture, which came back negative. Immobility, opioid use, pain, and dietary glutamine are common causes of GI dysfunction in both patient groups. Incremental fentanyl infusion was administered to all patients within 24-48 hours of the injury. Breakthrough and procedural pain were managed with sub-anaesthetic doses of IV ketamine and IV fentanyl. Patients presenting with Pattern B symptoms were often prescribed slow-release oral tramadol/oral tapentadol/ pregabalin formulations to supplement or replace opioids due to concerns about constipation, tolerance, and addiction. Opioids could exacerbate GI symptoms like vomiting and constipation (14). Tramadol was found to delay colonic transit but did not affect upper gastrointestinal transit.[15] Tapentadol, on the other hand, provided analgesia with a more tolerable side effect profile and resulted in less deterioration of gastrointestinal function and symptoms compared to standard opioids (16,17). However, results from different studies on tapentadol' s effects on gastric emptying and bowel function are inconsistent, making its routine use in severe burns unclear (18,19). NSAIDs are effective for mild to moderate burns, but opioids are preferred in severe cases due to acute kidney injury (AKI) concerns. AKI is common in severe burns and an independent mortality risk factor. While opioids and NSAIDs may have contributed to large bowel dysmotility in Pattern B patients, a causal relationship cannot be established.

Burn-injured patients often experience acute and chronic neuropathic pain. Pregabalin has shown efficacy in reducing neuropathic pain and improving sleep but may cause constipation (20,21). Stress ulcer prophylaxis with pantoprazole was administered to patients above three years of age. Short-term treatment with proton pump inhibitors (PPIs) has been reported to delay gastric emptying of solid meals in healthy individuals (22). The effects of PPIs on liquid emptying are inconsistent (23). Prolonged gastric residence of PPIs due to delayed emptying may impact their pharmacological effectiveness, which can be clinically relevant in managing conditions such as GERD, functional dyspepsia, and diabetes (24). However, routine administration of PPIs in severe burn patients is not recommended. Although a systematic review and meta-analysis suggested a potential correlation between the usage of proton pump inhibitors (PPIs) and a heightened likelihood of contracting Clostridium difficile infection (CDI), we did not find any substantiating evidence of CDI (25). Further high-quality and prospective studies are needed to establish a causal relationship.

Major burns trigger an inflammatory response and catabolism, which can lead to severe nutrition deficiencies when combined

with burn wound nutrient losses. These deficiencies can impair immune function and wound healing and increase the risk of organ injury and mortality (26). Sepsis causes dysbiosis and bacterial translocation (27). Severe burn patients frequently experience sepsis-induced ileus (28). Early and staged enteral nutrition has been shown to reduce gram-negative bacteraemia in burn patients and promote a healthy intestinal microenvironment (29-32). Caloric requirements were calculated using the Curreri formula for adults and Curreri junior formula for paediatric patients. However, as the formula often overestimates caloric needs, a target of 70-80% of the calculated requirement was set. Using continuous feeding bags, oral and/or nasogastric feeding was initiated from day 1 in the ICU. Post-pyloric feeding was administered to patients with feed intolerance or high gastric residual volume. Micronutrients and trace elements were supplemented, and glutamine and fibre were added to the diet for adult patients. Glutamine stimulates the release of glucagon-like peptide-1, which increases postprandial insulin secretion and slows gastric emptying (33). Current recommendations support using glutamine in severe burn patients due to promising evidence and minimal adverse effects. The RE-ENERGIZE trial showed mortality at 6 months was 17.2% in the glutamine group and 16.2% in the placebo group (hazard ratio for death, 1.06; 95% CI, 0.80 to 1.41) and no substantial between-group differences in serious adverse events (26).

We hypothesize that prudent utilization of selective digestive decontamination (SDD) may reduce infections and improve survival in severe burn patients (34). In a randomized trial, SDD demonstrated improved survival. However, according to a meta-analysis, enteral antibiotic use did not reduce mortality in severe burn patients, which aligns with our findings (35).

Managing wounds in the early stages and providing postoperative care after skin grafting pose challenges in patients with extensive burns. Effective use of negative pressure wound therapy (NPWT) can facilitate better wound healing and reduce infections. Patients with burns involving the perineum and genitalia present particular challenges due to increased wound infections, graft loss, and sepsis caused by dressing soiling (36-38). We hypothesize that faecal management systems might reduce infections by diverting faeces and improving personal hygiene in severe burn patients. A retrospective study found a survival benefit with no significant complications associated with faecal management systems (39).

Limitations

Our study is a retrospective case series that has inherent constraints. Our study lacked a control group. Selection bias and treatment assignment bias cannot be ruled out. These unregulated and unidentified factors of variation have the potential to influence the general applicability of the study's outcomes. Further prospective studies are needed to establish causal associations.

Conclusions

The first pattern of patients, primarily children without underlying health conditions, appeared to have experienced bowel dysfunction as a stress response amplified using PPIs. Diarrhoea in these cases was not due to an infection, and excessive sympathetic activity could be the contributing factor. On the other hand, the second pattern of patients, primarily adults with comorbidities, were seriously ill and received a combination of antibiotics, opioids, and gabapentin. These patients were also experiencing sepsis and sepsis-induced ileus, which is common in individuals with severe burns. In this group, diarrhoea could be caused by an infectious or non-infectious agent, and while testing for C. difficile was negative, there may have been delays in the

transportation and analysis of stool samples that resulted in false negative results. It is important to note that repeating the tests is unlikely to improve the sensitivity of the results (40).

Learning Points

1. Post-burn gastrointestinal issues are caused by a combination of factors that disrupt the balance of gut microbes leading to sepsis and multiple organ dysfunction syndrome (MODS).
2. Further prospective studies are needed to establish the effect of tramadol, tapentadol and pregabalin on GI system in severe burns.
3. The regular use of PPIs may worsen the impact of severe burns on the gut.
4. Managing serious burns necessitates a collaborative strategy encompassing prompt and effective fluid replacement, timely removal of deceased tissue, cautious initiation of nutrition, targeted use of antibiotics, and thoughtful application of selective digestive decontamination (SDD) to prevent gastrointestinal complications and reduce mortality.
5. Faecal management systems and negative pressure wound therapy (NPWT) can help to improve wound care and hygiene in patients with perineal burns.

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