

Early enteral feeding within 48 hours of admission reduces length of hospital stay in acute pancreatitis patients: A prospective observational study

Md Fahim Ahmad¹, Eram Nahid², M Amanullah Khan¹, Shehtaj Khan^{3*}

¹ Department of General Surgery, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, India

² Department of Endocrinology, All India Institute of Medical Sciences Jodhpur, Rajasthan, India

³ Department of Emergency Medicine, L.N Medical College, Kolar Road, Bhopal, India

Abstract

Background: Acute pancreatitis (AP) is a severe inflammatory condition with substantial morbidity and mortality, accounting for a notable proportion of hospital admissions and causes significant burden on healthcare systems globally. Timely nutritional support is vital in managing AP, with early enteral feeding (EEF) showing promise in reducing complications and mortality. The objective of this study was to evaluate the clinical outcomes of EEF compared to conventional feeding (CF) in patients with mild to moderate AP.

Material and methods: This prospective observational study was carried out at tertiary care hospital in Northern India from November 2015 to October 2017. Patients aged 18 to 60 years with mild to moderate AP were randomly assigned to Group A(CF) and Group B(EEF). Clinical parameters such as time to initiate feeding, feeding intolerance, infections, length of hospital stay and mortality were evaluated and compared between the groups.

Results: A total of 50 patients were enrolled and randomized equally in each group with similar baseline characteristics. No significant differences were observed between the groups in the incidence of infections, necrotizing pancreatitis, and mortality. However, the duration of hospital stay was significantly shorter in the EEF group (6.58 ± 1.74 days) compared to the CF group (11.21 ± 2.96 days) ($p < 0.0001$).

Conclusions: EEF can be safely given in mild to moderate AP patients and has been associated with decreased length of hospital stay, reduced hospital care costs with comparable mortality rates compared to CF. This approach proves to be cost-effective and also offers convenience for both patients and healthcare resources.

Keywords: Acute pancreatitis; conventional feeding; delayed feeding; early enteral feeding; nutritional support.

Introduction

Acute pancreatitis (AP) is a prevalent inflammatory condition of the pancreas, which can be potentially life-threatening, particularly in severe cases, with significant morbidity and mortality. It ranks among the leading causes of hospital or intensive care unit (ICU) admissions for gastrointestinal disorders [1, 2]. Gallstones and alcohol abuse are the leading causes of AP, together accounting for over 80% of cases [3, 4]. The pathophysiological mechanisms of AP encompass microcirculatory injury, leukocyte chemoattractant, release of cytokines, oxidative stress, leakage of pancreatic enzymes and

bacterial translocation [5]. In the early phase of AP, damage to the gut barrier plays a pivotal role in initiating systemic inflammatory response syndrome (SIRS), sepsis, and infected pancreatic necrosis [6].

Given the absence of a currently viable therapy to interrupt the activation of inflammatory and proteolytic cascades, treatment predominantly revolves around managing symptoms. The traditional approach to managing AP typically includes initiating a nil per os (NPO) regimen, along with administering analgesics and ample intravenous fluids to facilitate "pancreatic rest" [1, 7]. The concept of pancreatic rest is contentious and intensely debated regarding its validity [8,

*Corresponding author: Prof. Dr. Shehtaj Khan
E-mail: shehtaj@gmail.com

9]. Patients in such cases are nutritionally depleted due to the associated inflammatory response, toxic products, and infection. Given the energy-consuming nature of these processes, nutritional support becomes essential [8].

Extensive research has been conducted on two nutritional support methods for AP: enteral and parenteral [10]. Compared to total parenteral nutrition (TPN), enteral nutrition (EN) is considered safe and may contribute to a faster resolution of toxicity in patients with AP [11]. EN has been recognized for its beneficial effects in preserving gut barrier integrity and reducing bacterial translocation [12]. Additionally, the initiation of Early Enteral Feeding (EEF) within 24-48 hours of admission improves the clinical outcomes of AP by mitigating the risks of infections, organ failure, prolonged hospitalization, and mortality [13-15]. But, in the practical world, EEF has not found many takers and clinicians still have a mental barrier in initiating EEF. Consequently, this study aimed to assess the impact and significance of EEF in AP patients within the confines of a resource-constrained developing country.

Material and methods

This prospective observational study was conducted at a tertiary care hospital in Northern India from November 2015 to October 2017 with approval from the institutional ethics committee. The study enrolled all suspected AP patients admitted to the Department of General Surgery, who provided written informed consent and underwent routine blood investigations- complete blood count, renal and liver function tests, electrolyte levels, blood glucose, serum amylase and lipase. Additional assessments include arterial blood gas, electrocardiogram, chest X-ray, ultrasonography (USG) abdomen and contrast-enhanced computed tomography (CECT) abdomen.

AP diagnosis was determined based on the fulfillment of a minimum of two of the following criteria: (1) presence of typical abdominal pain, (2) serum lipase or amylase levels elevated to three times the upper limit of normal, and (3) distinctive imaging findings [16]. Inclusion criteria comprised patients with mild to moderate AP (based on the modified Glasgow score) and age between 18 to 60 years. Table 1 provides an illustration of the modified Glasgow score. Exclusion

criteria were patients with severe AP; comorbidities such as chronic lung disease, chronic kidney disease, congestive heart failure, cirrhosis; pregnant or lactating females; and those at the extremes of age (<18 or >60).

Patients meeting the inclusion criteria were randomized into two groups using the plain chit box method in 1:1. Group A, referred to as the Conventional Feeding (CF) group, involved patients in whom feeding initiation occurred only after the restoration of bowel functions. Group B, designated as EEF group, comprised individuals in whom oral feeding commenced within 48 hours of admission and started with oral sips of water (25 ml) given every 2 hours for the initial 24 hours. Over the subsequent 24 hours, fluid intake increased (100 ml) hourly, accompanied by the introduction of semi-solid to solid foods like biscuits, cake, or small pieces of bread. If a patient experienced more than two episodes of vomiting or abdominal distension, oral intake was discontinued and a nasogastric (NG) tube was inserted. Such patients were categorized as not tolerating EEF. Parameters such as time of initiating feeding, intolerance to the EEF (nausea, vomiting and/or abdominal distension), infections, necrotizing pancreatitis, organ dysfunction, length of hospital stay and mortality were assessed and compared between the two groups.

Statistical analysis

Continuous data are shown as mean \pm standard deviation, and categorical data are presented as numbers (percentages). An independent t-test was used to analyze continuous variables, while the Chi-square test was employed for categorical variables. Statistical significance was set at $p < 0.05$. The data analysis was performed using SPSS (Statistical Package for Social Sciences) version 23.

Results

A. Baseline characteristics

During the study period 72 patients with AP were screened, 22 were excluded; 10 had severe AP, 6 had comorbidities, 2 below 18 years and 4 above 60 years of age. Consequently, the study included 50 patients who were admitted and randomized into two groups, each comprising 25 participants (group A: CF, group B: EEF) (Figure 1).

Baseline characteristics, as depicted in Table 2, were evenly distributed between both groups. The mean age of the studied population was 35.98 ± 10.53 years, with comparable ages observed in both groups: 36.6 ± 11.39 years in group A and 35.36 ± 9.67 years in group B ($p = 0.406$). The sex ratio (male : female) of the study population was 1 : 1.38 overall, with a ratio of 1 : 1.77 in group A (9 males, 16 females) and 1 : 1.08 in group B (12 males, 13 females). The observed disparity between the groups was not significant ($p = 0.390$). Regarding etiology, gallstones were the implicating factor in majority of the patients (62%, $n = 31$) followed by alcohol abuse (24%, $n = 12$), post-traumatic (4%, $n = 2$), drug induced (2%, $n = 1$), while no cause was found in (8%, $n = 4$) (Figure 2).

Table 1. Modified Glasgow Score

Parameters	Score- 0	Score- 1
Age (Years)	≤ 55	> 55
PaO ₂ (mmHg)	≥ 60	< 60
WBC count (per cu mm)	$\leq 15,000$	$> 15,000$
Serum Calcium (mmol/l)	≥ 2	< 2
Serum Urea (mmol/l)	≤ 16	> 16
Serum Albumin (g/l)	≥ 32	< 32
Enzymes (IU/L)	LDH ≤ 600 or AST/ALT ≤ 200	LDH > 600 or AST/ALT > 200
Blood glucose (mmol/l)	≤ 10	> 10

Severe pancreatitis – score ≥ 3

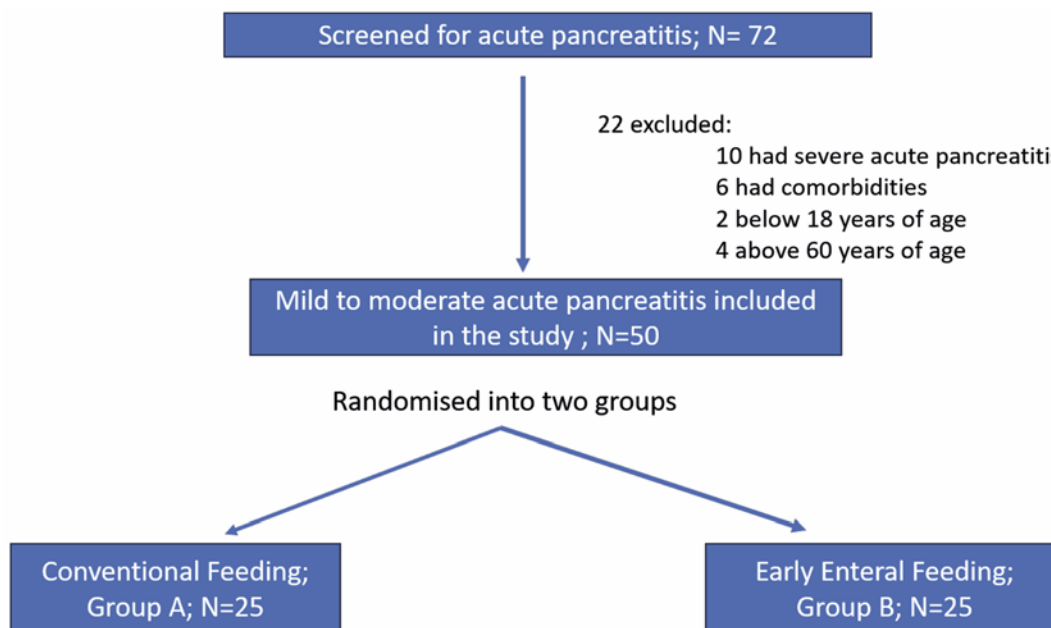


Figure 1. Study flow diagram.

Parameters	Group A (CF)	Group B (EEF)	p-value
Age (years), Mean \pm SD	36.6 \pm 11.39	35.36 \pm 9.67	0.406
Sex ratio (Male : Female)	1 : 1.77	1 : 1.08	0.390
Basis for acute pancreatitis etiology			
Gall stone	15 (60%)	16 (64%)	
Alcohol	6 (24%)	6 (24%)	
Trauma	2 (8%)	0	
Drug induced	0	1 (4%)	
Idiopathic	2 (8%)	2 (8%)	

Abbreviations: CF: conventional feeding; EEF: early enteral feeding; SD: Standard Deviation.

B. Clinical outcomes

Table 3 summarizes the clinical outcomes for each group. The mean time for feeding initiation in group A (CF) was 86.84 ± 11.4 hours and in group B was 32 ± 4.88 hours. After starting enteral feeding nausea and vomiting were reported in 11 patients (44%) in Group A as compared to 9 patients (36%) in Group B ($p = 0.563$). Abdominal distension was observed in 5 patients (20%) in group A while only in 3 patients (12%) in group B ($p = 0.440$). No difference between incidence of new onset infection was found in both the groups. Necrotising pancreatitis was seen in 3 patients (12%) in group A and only 1 patient (4%) in group B ($p = 0.297$). Organ dysfunction was observed in 8 patients (32%) in group A while in 5 patients (20%) in group B ($p = 0.333$). The duration of hospitalization was notably shorter in the EEF group compared to the CF group: 11.21 ± 2.96 days in group A and 6.58 ± 1.74 days in

group B ($p < 0.05$). The mortality rates were 8% ($n = 2$) in group A and 4% ($n = 1$) in group B, but the difference was found to be statistically insignificant ($p = 0.551$).

Discussion

The present study demonstrated that EEF in AP was safe and well tolerated by the patients. Additionally, it was associated with decreased length of hospital stay and eventually decreased hospital care cost compared to delayed enteral or conventional feeding.

The early phase of AP is marked by damage to the gut barrier, which is pivotal in initiating SIRS, sepsis, and infected pancreatic necrosis. Statistics indicate that 33% of pancreatic infections occur within the first 24 hours, with 75% occurring between 48 and 96 hours [17]. Hence, the timing of nutrition

Cause of Pancreatitis

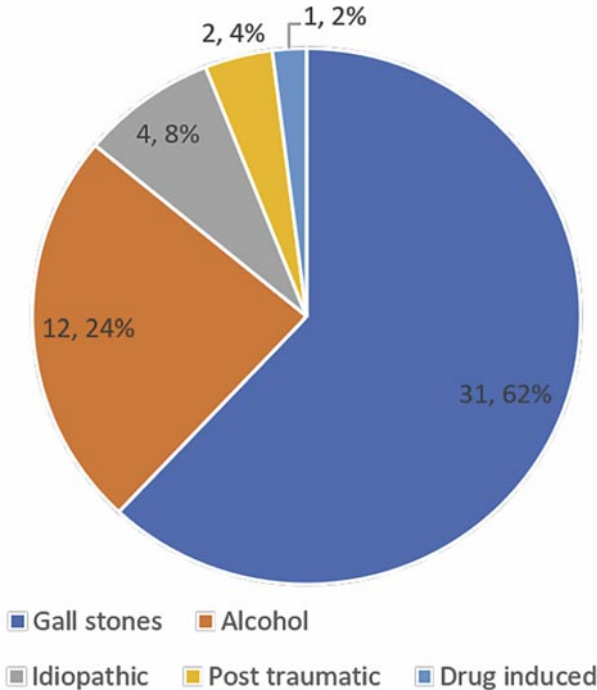


Figure 2. Etiology of acute pancreatitis in the studied population.

is crucial for patients with AP, as it not only affects the gut barrier but also impacts outcomes. Numerous trials have demonstrated that enteral nutrition is superior in preserving the gut barrier and reducing bacterial translocation [11, 12]. Clinical and experimental data support the beneficial effects of early enteral feeding in AP [13-15, 18]. Still clinicians are skeptical when asked to initiate EEF.

In our study, there were no significant differences in age ($p = 0.406$) and other clinical parameters at presentation between patients in the EEF and CF group. Thus, both groups were matched, eliminating a potential bias. There was a higher proportion of females compared to males, which may be attributed to the higher incidence of gallstones in females. This finding aligns with our study's identification of gallstones

as the major etiology of AP.

A study by Sun et al. found that the early enteral feeding group (initiated within 48 hours of hospital admission) had significantly lower incidences of multiple organ dysfunction syndrome (MODS), SIRS, pancreatic infection, and duration of stay in the ICU compared to patients whose enteral feeding commenced on the eighth day of hospital stay. However, there was no observed difference in mortality between the two groups [19]. Our study yielded similar results regarding hospital stay and mortality. However, unlike the study mentioned, we did not observe any significant difference between the groups concerning the development of infected pancreatic necrosis, abscess formation, or organ failure.

Overall mortality rate in our study was 6%, with 8% in the CF group and 4% in the EEF group. Although not statistically significant, these findings align with the study conducted by Manjunath et al, where early enteral feeding was associated with reduced mortality [20]. A meta-analysis by Petrov et al, based on 11 randomized controlled trials, indicated that initiating enteral feeding within the first 48 hours of admission in AP patients led to a significant reduction in the risk of multi-organ failure, pancreatic infectious complications, and mortality compared to parenteral feeding [21]. Interestingly, there were no statistically significant differences observed when enteral nutrition was initiated 48 hours after admission.

Efforts to reduce the length of hospital stay in patients with non-severe AP could significantly reduce the consumption of healthcare resources. As these patients constitute the majority of all AP cases, focusing on shortening their hospital stay could be particularly cost-effective. This underscores the importance of the present study, which aims to explore strategies for optimizing hospital stay duration in non-severe AP cases, thereby contributing to more efficient resource utilization and improved patient care, especially in a resource limited developing country like India.

The strength of our study lies in the well-matched groups. However, there are a few limitations: it did not examine the impact of different etiological factors on subsequent nutritional management; it included only mild to moderate AP cases; and the sample size was small due to it being a single-center study.

Table 3. Clinical outcomes of the patients

Outcome	Group A (CF) (n = 25)	Group B (EEF) (n = 25)	p value
Nausea & vomiting, n (%)	11 (44%)	9 (36%)	0.563
Abdominal distension, n (%)	5 (20%)	3 (12%)	0.440
Infection, n (%)	5 (20%)	3 (12%)	0.440
Organ dysfunction, n (%)	8 (32%)	5 (20%)	0.333
Necrotizing Pancreatitis, n (%)	3 (12%)	1 (4%)	0.297
Duration of hospital stay (days) (mean + SD)	11.21 + 2.96	6.58 + 1.74	<0.05
Mortality, n (%)	2 (8%)	1 (4%)	0.551

Abbreviations: CF: conventional feeding; EEF: early enteral feeding; SD: Standard Deviation.

Conclusion

Early enteral feeding can be safely initiated within 48 hours of hospital admission in patients with mild to moderate AP. This timely nutritional intervention has been proven to reduce both the duration of hospitalization and the financial burden associated with prolonged hospital stay. By facilitating early recovery and minimizing complications, early enteral feeding contributes to providing optimal care for patients with this condition.

Source of support/funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest: Nil

Acknowledgements: None

Ethical approval: The study was passed by the Institutional Review Board of Studies, Department of Surgery, J.N.Medical College, Aligarh Muslim University, Aligarh, India on 03/10/2015 vide no 2427/S/2015.

Disclaimers: None

References

- Banks PA, Freeman ML; Practice Parameters Committee of the American College of Gastroenterology. Practice guidelines in acute pancreatitis. *Am J Gastroenterol*. 2006; 101(10): 2379-400. doi: 10.1111/j.1572-0241.2006.00856.x.
- Yadav D, Lowenfels AB. Trends in the epidemiology of the first attack of acute pancreatitis: a systematic review. *Pancreas*. 2006; 33(4): 323-30. doi: 10.1097/01.mpa.0000236733.31617.52.
- Pandolfi SJ, Saluja AK, Imrie CW, Banks PA. Acute pancreatitis: bench to the bedside. *Gastroenterology*. 2007; 132(3): 1127-51. doi: 10.1053/j.gastro.2007.01.055.
- Spanier BW, Dijkgraaf MG, Bruno MJ. Epidemiology, aetiology and outcome of acute and chronic pancreatitis: An update. *Best Pract Res Clin Gastroenterol*. 2008; 22(1): 45-63. doi: 10.1016/j.bpg.2007.10.007.
- Beger HG, Rau B, Mayer J, Pralle U. Natural course of acute pancreatitis. *World J Surg*. 1997; 21(2): 130-5. doi: 10.1007/s002689900204.
- Van Santvoort HC, Bakker OJ, Bollen TL, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. *Gastroenterol*. 2011; 141(4): 1254-63. doi: 10.1053/j.gastro.2011.06.073.
- Forsmark CE, Baillie J. AGA Institute technical review on acute pancreatitis. *Rev Gastroenterol Mex*. 2007; 72(3): 257-85. doi: 10.1053/j.gastro.2007.03.065.
- Ioannidis O, Lavrentieva A, Botsios D. Nutrition support in acute pancreatitis. *JOP*. 2008; 9(4): 375-90.
- Talukdar R, Vege SS. Recent developments in acute pancreatitis. *Clin Gastroenterol Hepatol*. 2009; 7(11): S3-9. doi: 10.1016/j.cgh.2009.07.037.
- Al-Omran M, Groof A, Wilke D. Enteral versus parenteral nutrition for acute pancreatitis. *Cochrane Database Syst Rev*. 2003; (1): CD002837. doi: 10.1002/14651858.CD002837.
- McClave SA, Greene LM, Snider HL, et al. Comparison of the safety of early enteral vs parenteral nutrition in mild acute pancreatitis. *J Parenter Enteral Nutr*. 1997; 21(1): 14-20. doi: 10.1177/014860719702100114.
- Faghih M, Fan C, Singh VK. New advances in the treatment of acute pancreatitis. *Curr Treat Options Gastroenterol*. 2019; 17(1): 146-60. doi: 10.1007/s11938-019-00223-8.
- Li JY, Yu T, Chen GC, et al. Enteral nutrition within 48 hours of admission improves clinical outcomes of acute pancreatitis by reducing complications: a meta-analysis. *PLoS One*. 2013; 8(6): e64926. doi: 10.1371/journal.pone.0064926.
- Qi D, Yu B, Huang J, Peng M. Meta-analysis of early enteral nutrition provided within 24 hours of admission on clinical outcomes in acute pancreatitis. *J Parenter Enteral Nutr*. 2018; 42(7): 1139-47. doi: 10.1002/jpen.1139.
- Feng P, He C, Liao G, Chen Y. Early enteral nutrition versus delayed enteral nutrition in acute pancreatitis: A PRISMA-compliant systematic review and meta-analysis. *Medicine (Baltimore)*. 2017; 96(46): e8648. doi: 10.1097/MD.00000000000008648.
- Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013; 62(1): 102-11. doi: 10.1136/gutjnl-2012-302779.
- Foitzik T, Mithöfer K, Ferraro MJ, et al. Time course of bacterial infection of the pancreas and its relation to disease severity in a rodent model of acute necrotizing pancreatitis. *Ann Surg*. 1994; 220(2): 193-8. doi: 10.1097/00000658-199408000-00011.
- Gupta R, Patel K, Calder PC, et al. A randomised clinical trial to assess the effect of total enteral and total parenteral nutritional support on metabolic, inflammatory and oxidative markers in patients with predicted severe acute pancreatitis (APACHE II > or =6). *Pancreatol*. 2003; 3(5): 406-13. doi: 10.1159/000073657.
- Sun JK, Mu XW, Li WQ, et al. Effects of early enteral nutrition on immune function of severe acute pancreatitis patients. *World J Gastroenterol*. 2013; 19(6): 917-22. doi: 10.3748/wjg.v19.i6.917.
- Manjunath BD, Abhishek G. Early versus delayed enteral feeding in acute pancreatitis. *Int Surg J*. 2018; 5(3): 942-45. doi: 10.18203/2349-2902.isj20180808.
- Petrov MS, Pylypchuk RD, Uchugina AF. A systematic review on the timing of artificial nutrition in acute pancreatitis. *Br J Nutr*. 2009; 101(6): 787-93. doi: 10.1017/S0007114508123443.