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CLINICAL, BIOCHEMICAL AND MICROBIOLOGICAL CORRELATES OF CHRONIC PANCREATITIS: OXIDATIVE STRESS AND GUT MICROBIOTA AS KEY PATHOGENIC LINKS

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Abstract. Chronic pancreatitis (CP) is a long-standing inflammatory disease characterized by progressive fibrosis and loss of pancreatic function. The interplay between oxidative stress and gut microbiota imbalance plays a pivotal role in sustaining inflammation and tissue injury. This study evaluated biochemical and microbiological parameters in patients with chronic pancreatitis and assessed the therapeutic impact of combined probiotic and antioxidant treatment.

Keywords: chronic pancreatitis, oxidative stress, cytokines, microbiota, antioxidant therapy, probiotics

Introduction. Chronic pancreatitis remains a global health problem, affecting up to 12 per 100,000 individuals annually [3]. The disease leads to recurrent abdominal pain, malabsorption, diabetes, and a significant decline in quality of life. Traditional therapeutic approaches focus mainly on symptomatic relief, yet recent evidence highlights oxidative stress and gut dysbiosis as interdependent drivers of inflammation and fibrotic progression [1,2,4].

Oxidative stress, manifested by excessive production of reactive oxygen species (ROS), damages pancreatic acinar cells, triggers cytokine release, and promotes apoptosis [4,7]. Simultaneously, gut microbiota imbalance reduces intestinal barrier integrity, facilitating bacterial translocation and systemic immune activation [8,9]. The relationship between these mechanisms suggests that targeting both redox imbalance and microbial dysbiosis may yield substantial therapeutic benefits.

The current study aimed to: assess oxidative and inflammatory biomarkers in CP; evaluate intestinal microbiota composition; determine clinical and biochemical effects of antioxidant and probiotic therapy.

Materials and Methods. The study included 84 patients with chronic pancreatitis (mean age 46.3 ± 2.8 years) and 30 healthy controls. Diagnosis was confirmed via

ultrasound and CT imaging according to the Revised Cambridge Classification [6]. Blood samples were analyzed for malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPO), and inflammatory cytokines IL-6 and TNF-α using ELISA kits [4]. Fecal samples were examined for *Lactobacillus spp.*, *Bifidobacterium spp.*, *E. coli*, and *Clostridium spp.* using culture and qPCR techniques [1,8].

Patients were randomized into two subgroups:

- Group A (n=42): standard therapy (enzyme replacement + analgesics + diet);
- Group B (n=42): same regimen + antioxidant (vitamin E 400 mg/day) + probiotic (*Lactobacillus rhamnosus GG*, 10^9 CFU/day) for 21 days [2,5].

Statistical analysis: SPSS v25.0; significance $p<0.05$.

Results.

Table 1.

Clinical, biochemical, and inflammatory indicators in patients with chronic pancreatitis (mean ± SD)

Parameter	Control (n=30)	CP before treatment (n=84)	Group A after therapy (n=42)	Group B after therapy (n=42)	p-value (vs control)
Pain intensity (VAS, points)	0	7.8 ± 1.1	5.2 ± 0.9	3.1 ± 0.8	<0.001
MDA (μmol/L)	1.7 ± 0.2	6.1 ± 0.5	4.8 ± 0.4	3.2 ± 0.4	<0.001
SOD (U/mL)	18.4 ± 1.6	9.8 ± 1.1	12.2 ± 1.3	14.6 ± 1.3	<0.01
GPO (U/mL)	22.1 ± 2.2	12.7 ± 1.8	15.9 ± 1.9	18.5 ± 2.0	<0.01
IL-6 (pg/mL)	15.3 ± 1.7	68.5 ± 6.8	49.4 ± 5.1	31.4 ± 4.2	<0.001
TNF-α (pg/mL)	12.8 ± 1.5	55.7 ± 5.3	42.6 ± 4.1	28.9 ± 3.7	<0.001

Duration of hospitalization (days)	—	13.8 ± 2.2	12.1 ± 1.9	9.5 ± 1.8	<0.05

At baseline, CP patients demonstrated significant elevation in oxidative (MDA) and inflammatory (IL-6, TNF-α) markers. Antioxidant enzyme levels (SOD, GPO) were nearly halved, reflecting an exhausted redox system. After 21 days, Group B (combination therapy) exhibited faster pain relief, a 47% decrease in MDA, and normalization of cytokine levels. Hospital stay duration was reduced by 4.3 days compared with Group A, confirming the additive benefit of combined therapy [1,2,4,5].

Table 2.

Quantitative composition of intestinal microbiota in chronic pancreatitis (log_{10} CFU/g)

Microorganism	Control	CP before treatment	Group A after therapy	Group B after therapy	% Change (Group B)
Lactobacillus spp.	7.8 ± 0.4	5.6 ± 0.5	6.3 ± 0.4	7.1 ± 0.3	+26%
Bifidobacterium spp.	8.2 ± 0.3	6.1 ± 0.6	6.9 ± 0.4	7.6 ± 0.4	+24%
E. coli (hemolytic)	3.2 ± 0.3	5.4 ± 0.4	4.8 ± 0.3	3.9 ± 0.3	−28%
Clostridium spp.	3.8 ± 0.2	6.3 ± 0.5	5.5 ± 0.4	4.2 ± 0.3	−33%
Enterococcus spp.	4.1 ± 0.3	6.0 ± 0.5	5.2 ± 0.4	4.4 ± 0.3	−27%

The baseline microbiota of CP patients showed severe dysbiosis, characterized by a depletion of beneficial *Lactobacillus* and *Bifidobacterium* and proliferation of pathogenic *E. coli*, *Clostridium*, and *Enterococcus* species. This imbalance was associated with elevated inflammatory biomarkers (IL-6, TNF-α). After therapy, only minor microbiota recovery occurred in Group A, while Group B

achieved a near-normal bacterial spectrum, accompanied by a marked reduction in oxidative markers. These findings indicate a bidirectional link between intestinal microbiota normalization and systemic oxidative homeostasis [1,2,8,9].

The correlation analysis demonstrated a moderate positive relationship between IL-6 concentration and VAS pain score ($r = 0.62$, $p < 0.01$), confirming that systemic inflammation intensifies pain severity. Conversely, increased *Bifidobacterium* counts correlated with reduced CRP and MDA levels ($r = –0.58$, $p < 0.05$).

Discussion. The obtained data strongly support the hypothesis that oxidative stress and intestinal dysbiosis are mutually reinforcing mechanisms in chronic pancreatitis. Elevated lipid peroxidation products (MDA) damage pancreatic acinar cells and promote cytokine cascades [4,7,10]. Restoration of microbial balance, primarily through the reintroduction of *Lactobacillus* and *Bifidobacterium*, reduces intestinal permeability and systemic immune activation [1,8].

The combined use of vitamin E and probiotics significantly enhanced redox recovery and clinical outcomes compared with standard therapy. These effects align with previous international studies reporting antioxidant–microbial synergy in controlling pancreatic inflammation [2,5,8,9]. Clinically, patients reported improved appetite, decreased bloating, normalization of stool, and reduced pain episodes — all of which corresponded with biochemical improvements.

The results confirm that personalized therapy, targeting both oxidative and microbial mechanisms, can provide superior disease control and improve long-term prognosis [5,6].

Conclusion. Chronic pancreatitis is accompanied by deep disturbances in oxidative and microbial homeostasis. Elevated levels of MDA, IL-6, and TNF-α indicate sustained inflammation and can serve as biomarkers of disease activity. Combined probiotic and antioxidant therapy restores antioxidant enzyme activity, improves gut microbiota composition, and shortens recovery time. Correction of oxidative stress and dysbiosis should be considered an integral component of modern treatment algorithms for chronic pancreatitis.

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