The Effect of Administering the Probiotic Lactiplantibacillus Plantarum DAD-13 on Procalcitonin Levels, C-Reactive Protein, and Interleukin-6 in Sepsis Patients in the ICU of H. Adam Malik Hospital, Medan

NCT Number: Pending

Document Date: July 9, 2025

Study Protocol

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Background and Rationale: Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Dysbiosis and disruption of intestinal barrier function are critical components of sepsis pathophysiology. Probiotics may modulate inflammatory responses and restore gut microbiota balance. L. plantarum DAD-13, an Indonesian probiotic strain, has demonstrated immunomodulatory potential in preclinical studies. This study aims to evaluate the effect of L. plantarum DAD-13 on inflammatory markers and gastrointestinal outcomes in ICU patients with sepsis.

Study Objectives: Primary Objective:

- To assess the effect of L. plantarum DAD-13 on Procalcitonin (PCT), C-Reactive Protein (CRP), and Interleukin-6 (IL-6) levels.

Secondary Objective:

- To assess changes in defecation frequency and stool consistency.

Study Design:

- Type: Prospective, randomized, double-blind, placebo-controlled trial
- Sample size: 30 patients (15 per group)
- Duration: 4-day intervention period

Eligibility Criteria: Inclusion:

- Age 18–65 years
- Diagnosed with sepsis
- Admitted to ICU
- Receiving enteral nutrition

Exclusion:

- Known gastrointestinal disease
- Immunocompromised status
- Probiotic allergy
- Use of other probiotic products

Intervention:

- Experimental Group: 2 capsules/day of L. plantarum DAD-13 (Vipilac®)
- Control Group: 2 capsules/day of placebo (maltodextrin)
- Duration: 4 days

Endpoints:

- Primary: Change in serum PCT, CRP, and IL-6 from baseline to day 4
- Secondary: Frequency and consistency of defecation

Data Collection and Monitoring:

- Biomarkers (PCT, CRP, IL-6) measured at T0 (day 1) and T1 (day 4)
- Stool data collected daily
- Double-blind protocol maintained throughout study

Ethics: Approved by the Health Research Ethics Committee of Universitas Sumatera Utara. Informed consent obtained from all participants or legal representatives.

Statistical Analysis Plan (SAP)

Study Population:

- Intent-to-Treat (ITT): All randomized participants
- Per-Protocol (PP): Participants who completed the 4-day intervention

Descriptive Analysis:

- Means and standard deviations (SD) for continuous variables
- Frequencies and percentages for categorical variables

Comparative Analysis:

- Within-group (T0 vs T1): Wilcoxon Signed Rank Test (non-parametric)
- Between-group: Mann-Whitney U Test for biomarkers, Chi-square for defecation frequency/consistency
- Significance level: $p < 0.05$

Missing Data:

- Data imputed using last observation carried forward (LOCF) method for missing T1 values

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Informed Consent Form (ICF)

Study Title: The Effect of Administering the Probiotic Lactiplantibacillus plantarum DAD-13 on PCT, CRP, and IL-6 in Sepsis Patients

Investigator: Andriamuri Primaputra Lubis, MD **Institution:** H. Adam Malik Hospital, Universitas Sumatera Utara **Contact:** andriamuri@usu.ac.id, 08126078194

Purpose: You are invited to participate in a clinical study evaluating the effects of a probiotic on inflammation and gut function in sepsis patients. Participation is voluntary.

Procedures:

- You will receive either probiotic capsules or placebo for 4 days
- Blood samples will be taken twice (day 1 and day 4)
- Stool consistency and frequency will be recorded

Risks and Benefits:

- Risks: Mild gastrointestinal discomfort, rare allergic reaction
- Benefits: Possible improvement in inflammation and gut function

Confidentiality: All data will be anonymized. Your name will not appear in any publication.

Voluntary Participation: You may withdraw from the study at any time without affecting your medical care.

Consent: By signing this form, you agree to participate in this study.

Participant Name: _____ Date: _____ Signature: _____

Witness Name: _____ Signature: _____