

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

28 Jun 2026

### The effects of probiotic supplementation on intestinal permeability, inflammatory factors and clinical status in pediatrics with severe sepsis: a randomized double blind clinical trial

#### Protocol summary

##### Study aim

Determining the effect of probiotic supplementation on intestinal permeability biomarkers, inflammatory factors and clinical status of children with severe sepsis

##### Design

A phase 2 randomized double blind, controlled, parallel clinical trial on 44 patients. Stratified Permuted Block Randomization according to NPO status will be performed.

##### Settings and conduct

The current study will be conducted on children with severe sepsis in a children's medical center. The study subjects will be assigned to two probiotic supplement and placebo groups based on the NPO variable using the Stratified Permuted Block Randomization method. For children in the intervention group, Kidilact probiotic supplement (Kidilact VSL#3) will be prescribed two sachets of 1 gram per day for 7 days, and for the placebo group, a placebo that is completely similar to the probiotic supplement in terms of shape and color. At the beginning and end of the study, 5 ml of venous blood will be taken from the patients to evaluate biochemical indicators, and anthropometric and clinical characteristics will also be collected.

##### Participants/Inclusion and exclusion criteria

Inclusion criteria: Age between 1 and 12 years; Diagnosis of severe sepsis Exclusion criteria: Admission more than 72 hours in the PICU; Ileus, overt gastrointestinal bleeding, anatomic obstruction; Gastrointestinal diseases; Probiotic use one month before entering the study; Use of steroids and other immunosuppressive drugs; Suffering from immunosuppressive diseases; Severe acute malnutrition; Discharged from the hospital; Gastrointestinal and allergic reactions; Disagreement of the patient's parents

##### Intervention groups

Intervention group: Probiotics (Kidilact: including several

probiotic bacteria. Control group: Placebo (Corn starch)

##### Main outcome variables

Serum Zonulin; Serum LPS-Binding Protein; Serum IL-6; Serum IL-10; Serum CRP

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20170202032367N10**

Registration date: **2023-08-15, 1402/05/24**

Registration timing: **prospective**

Last update: **2023-08-15, 1402/05/24**

Update count: **0**

##### Registration date

2023-08-15, 1402/05/24

##### Registrant information

##### Name

Hossien Imani

##### Name of organization / entity

Tehran University of Medical Sciences

##### Country

Iran (Islamic Republic of)

##### Phone

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##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2023-08-23, 1402/06/01

##### Expected recruitment end date

2024-03-20, 1403/01/01

**Actual recruitment start date**

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

The effects of probiotic supplementation on intestinal permeability, inflammatory factors and clinical status in pediatrics with severe sepsis: a randomized double blind clinical trial

**Public title**

Probiotic supplementation and sepsis

**Purpose**

Treatment

**Inclusion/Exclusion criteria****Inclusion criteria:**

Aged 1-12 years old Diagnosis of severe sepsis according to pediatric sepsis consensus conference 2005 criteria in children admitted to PICU

**Exclusion criteria:**

PICU admission more than 72 hours Ileus, overt gastrointestinal bleeding, anatomic obstruction of the gastrointestinal tract (eg, volvulus, intestinal atresia), recent esophageal or gastrointestinal surgery Gastrointestinal diseases such as celiac disease, inflammatory bowel disease (IBD), short bowel syndrome (SBS), irritable bowel syndrome (IBS) Use of feeding routes leading to jejunum such as jejunostomy Probiotic use one month before entering the study Use of steroids and other immunosuppressive drugs Suffering from immunosuppressive diseases such as malignant tumors, acquired immunodeficiency syndrome, etc. Severe acute malnutrition (According to the World Health Organization: Z-Score weight for height/length and BMI less than -3 SD average child growth standards WHO

**Age**

From **1 year** old to **12 years** old

**Gender**

Both

**Phase**

3

**Groups that have been masked**

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

**Sample size**

Target sample size: **44**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

Random allocation will be done by Stratified Permuted Block Randomization method. Stratification is done based on the NPO variable. Eligible people who meet the criteria for entering the study, are selected, and then the two groups are randomly divided into 4 or 6 intervention

blocks at a ratio of 1:1. Then, the list of blocks is divided equally between the two strata. Block randomization (4 or 6 people in each block) is done using the website [www.randomization.com](http://www.randomization.com). In this way, the letters A and B will be spread between the patient codes. Numbers will be assigned to patients according to the order of participants' entry, and patients will be enrolled in the study based on special letters (A and B).

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

Blinding of patients: due to the fact that in this study, the patients are children under 12 years old and usually do not have optimal GCS, people in each group do not know the type of intervention. In order to blind the researcher, the probiotic supplements and placebo will be delivered to the supervisor by the bio-fermentation company. Probiotic and placebo supplements are similar in appearance and packaging.

**Placebo**

Used

**Assignment**

Parallel

**Other design features****Secondary Ids**

empty

**Ethics committees****1****Ethics committee****Name of ethics committee**

Children's Medical Center-Tehran University of Medical sciences

**Street address**

Children's Medical Center, Dr Gharib St, Keshavarz Blvd, Tehran, Iran

**City**

Tehran

**Province**

Tehran

**Postal code**

1419733151

**Approval date**

2023-08-09, 1402/05/18

**Ethics committee reference number**

IR.TUMS.CHMC.REC.1402.084

**Health conditions studied****1****Description of health condition studied**

Severe sepsis

**ICD-10 code**

R65.2

**ICD-10 code description**

Severe sepsis

## Primary outcomes

### 1

#### **Description**

Serum Zonulin

#### **Timepoint**

Measurement of the serum level of zonulin in the initial study (before the start of the intervention) and 7 days after the start of probiotic consumption

#### **Method of measurement**

ELISA

### 2

#### **Description**

Serum LPS-Binding Protein

#### **Timepoint**

Measurement of the serum level of lipopolysaccharide binding protein (LBP) in the initial study (before the start of the intervention) and 7 days after the start of probiotic consumption

#### **Method of measurement**

ELISA

### 3

#### **Description**

Serum IL-6

#### **Timepoint**

Measurement of the serum level of Interleukin 6 (IL-6) in the initial study (before the start of the intervention) and 7 days after the start of probiotic consumption

#### **Method of measurement**

ELISA

### 4

#### **Description**

Serum IL-10

#### **Timepoint**

Measurement of the serum level of Interleukin 10 (IL-10) in the initial study (before the start of the intervention) and 7 days after the start of probiotic consumption

#### **Method of measurement**

ELISA

### 5

#### **Description**

Serum CRP

#### **Timepoint**

Measurement of the serum level of C-reactive protein (CRP) in the initial study (before the start of the intervention) and 7 days after the start of probiotic consumption

#### **Method of measurement**

ELISA

## Secondary outcomes

### 1

#### **Description**

Duration of starting nutrition

#### **Timepoint**

The effect of probiotic supplementation on the length of starting nutrition duration of the study (7 days)

#### **Method of measurement**

Questionnaire forms

### 2

#### **Description**

The number of days to reach the nutritional goal

#### **Timepoint**

The effect of probiotic supplementation on the number of days to reach the nutritional goal duration of the study (7 days)

#### **Method of measurement**

Questionnaire forms

### 3

#### **Description**

Nutrition intolerance

#### **Timepoint**

The effect of probiotic supplementation on nutrition intolerance duration of the study (7 days)

#### **Method of measurement**

Questionnaire forms

### 4

#### **Description**

Need to vasoactive agents

#### **Timepoint**

The effect of probiotic supplementation on need to vasoactive agents duration of the study (7 days)

#### **Method of measurement**

Questionnaire forms

### 5

#### **Description**

The length of vasoactive use

#### **Timepoint**

The effect of probiotic supplementation on the length of vasoactive use duration of the study (7 days)

#### **Method of measurement**

Questionnaire forms

### 6

#### **Description**

Vasoactive inotropic score

#### **Timepoint**

The effect of probiotic supplementation on vasoactive inotropic score duration of the study (7 days)

#### **Method of measurement**

Calculation

### 7

#### **Description**

Need to mechanical ventilation

**Timepoint**

The effect of probiotic supplementation on need to mechanical ventilation duration of the study (7 days)

**Method of measurement**

Questionnaire forms

**8**

**Description**

The length of using mechanical ventilation

**Timepoint**

The effect of probiotic supplementation on the length of using mechanical ventilation duration of the study (7 days)

**Method of measurement**

Questionnaire forms

**9**

**Description**

Antibiotics use

**Timepoint**

The effect of probiotic supplementation on antibiotics use duration of the study (7 days)

**Method of measurement**

Questionnaire forms

**10**

**Description**

The length of antibiotic use

**Timepoint**

The effect of probiotic supplementation on the length of antibiotic use duration of the study (7 days)

**Method of measurement**

Questionnaire forms

**11**

**Description**

Treatment-related infection incidence

**Timepoint**

The effect of probiotic supplementation on treatment-related infection incidence duration of the study (7 days)

**Method of measurement**

Questionnaire forms

**12**

**Description**

Type of treatment-related infection

**Timepoint**

The effect of probiotic supplementation on type of treatment-related infection duration of the study (7 days)

**Method of measurement**

Questionnaire forms

**13**

**Description**

Change in incidence of Multiple Organ Dysfunction Syndrome (MODS)

**Timepoint**

The effect of probiotic supplementation on change in incidence of Multiple Organ Dysfunction Syndrome (MODS) duration of the study (7 days)

**Method of measurement**

Calculation

**14**

**Description**

The length of PICU stay

**Timepoint**

The effect of probiotic supplementation on the length of PICU stay duration of the study (7 days)

**Method of measurement**

Questionnaire forms

**15**

**Description**

Mortality

**Timepoint**

The effect of probiotic supplementation on mortality duration of the study (7 days)

**Method of measurement**

Questionnaire forms

**Intervention groups**

**1**

**Description**

Intervention group: Probiotic (KidiLact ZistTakhmir Company); Lactobacillus rhamnosus, Lactobacillus rotrilactobacillus Acidophilus, Lactobacillus bulgarico, Lactobacillus caseibifidobacterium infantis, Bifidobacterium brohbifidobacterium, Bifidobacterium bifidombifidobacterium, Lactistreptococcus thermophilus, 109 CFU per sachet, 1 gram, twice a day; Probiotics will be given in doses of one sachet twice a day with an interval of 12 hours for 7 days orally or through enteral feeding through a Nasogastric or Orogastic tube depending on the clinical condition of the patients. became. To prepare the supplement, mix the contents of one sachet in 5 ml of sterile water and use immediately.

**Category**

Treatment - Drugs

**2**

**Description**

Control group: placebo (corn starch); Placebo was given in doses of one 1 gram sachet twice a day with an interval of 12 hours for 7 days orally or through enteral feeding through Nasogastric or Orogastic tube depending on the clinical condition of the patients. will be. To prepare, mix the contents of one sachet in 5 ml of sterile water and use immediately.

**Category**

Placebo

## Recruitment centers

1

### Recruitment center

**Name of recruitment center**

Children's medical center

**Full name of responsible person**

Masoud Mohammadpour

**Street address**

Children's Medical Center, Dr Gharib St, Keshavarz Blvd, Tehran, Iran

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cmcpr@tums.ac.ir

## Sponsors / Funding sources

1

### Sponsor

**Name of organization / entity**

Tehran University of Medical Sciences

**Full name of responsible person**

Hossein Imani

**Street address**

School of Nutritional Sciences & Dietetics, Tehran University of Medical Sciences, No: 44 Hojjat-dost Alley, Naderi St.

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**Grant name****Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

Tehran University of Medical Sciences

**Proportion provided by this source**

100

**Public or private sector**

Public

**Domestic or foreign origin**

Domestic

**Category of foreign source of funding**

empty

**Country of origin**

## Type of organization providing the funding

Academic

## Person responsible for general inquiries

### Contact

**Name of organization / entity**

Tehran University of Medical Sciences

**Full name of responsible person**

Maryam Safabakhsh

**Position**

PhD student

**Latest degree**

Master

**Other areas of specialty/work**

Nutrition

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## Person responsible for scientific inquiries

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## Person responsible for updating data

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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**

No - There is not a plan to make this available

**Justification/reason for indecision/not sharing IPD**

There is no more information

**Study Protocol**

No - There is not a plan to make this available

**Statistical Analysis Plan**

No - There is not a plan to make this available

**Informed Consent Form**

No - There is not a plan to make this available

**Clinical Study Report**

No - There is not a plan to make this available

**Analytic Code**

No - There is not a plan to make this available

**Data Dictionary**

No - There is not a plan to make this available