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An Insight On The Effects Of Lactobacillus Plantarum 299v (*L. Plantarum 299v*) Probiotic Supplementation Added To Oral Iron Replacement Therapy On Serum Iron Status Markers In Patients With Newly Diagnosed Iron Deficiency Anaemia : A Single-Centre Study From West Bengal

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Abstract
Anemia remains a widespread health issue globally, especially in impoverished regions where the rates are high. The condition is multifactorial, with iron deficiency being the most common. Current treatments mainly involve taking iron supplements or using drugs that stimulate red blood cell production. However, these options may not work well for everyone. Emerging research suggests that probiotics, prebiotics, and synbiotics—agents that modify the microbiome—could be valuable in treating anemia. They might help improve how the body absorbs iron and boost blood health by changing gut bacteria. These approaches could serve as alternatives or additions to traditional therapies. This study was designed to explore the impact of adding Lactobacillus plantarum 299v (*L. plantarum 299v*) probiotic to oral iron therapy on serum iron markers in patients newly diagnosed with iron deficiency anemia.

Introduction
Iron deficiency anaemia (IDA) represents one of the most widespread micronutrient deficiencies and poses a significant global health issue [1-3]. It affects millions of people, especially in developing countries. The health effects of IDA are serious and include symptoms like extreme tiredness, difficulty breathing, and problems with body temperature regulation. It can also impair brain function and weaken the immune system. IDA is linked to worse outcomes for people with chronic kidney disease and heart failure [4, 5]. The causes of iron deficiency anemia are varied. They include poor iron intake through diet, increased needs during growth or pregnancy, and ongoing blood loss caused by gastrointestinal issues or heavy periods. Certain groups, such as young children, pregnant women, and vegetarians, are at higher risk because of their unique nutritional needs or dietary choices. Combating this problem requires a broad approach. Improving diet habits, adding iron to foods, and raising awareness about iron's importance are key parts of the plan. Because of its impact on global health, preventing and treating iron deficiency and IDA is crucial. Common strategies include dietary changes, food fortification, and iron supplements [6, 7]. Oral iron supplements, like ferrous sulfate, gluconate, and fumarate, are the most accessible and affordable options for treatment [1, 6, 7].

The gut microbiota helps the body absorb more dietary iron by lowering the levels of compounds that bind iron in the intestines and by converting in a form that the body can easily absorb [1, 8]. Because gut bacteria influence iron balance, probiotics have been proposed as a way to boost iron absorption and reduce deficiency. They help turn ferric iron into a more available form, improve iron uptake by intestinal cells, and promote an anti-inflammatory immune response.

Lactic acid bacteria can improve iron absorption by lowering the pH in the intestines and they activate enzymes that break down plant compounds that block iron, change microbiota metabolism, and help reduce inflammation [8, 9].. This suggests that using probiotic bacteria may be a useful tool in preventing and treating iron deficiency anemia [8, 9]. The probiotic strain *Lactobacillus plantarum* 299v (*L. plantarum 299v)* can survive stomach acids and colonize the gut. It has been shown to reduce bloating and abdominal pain in patients with irritable bowel syndrome. It also increases iron absorption and makes dietary iron more available in patients with iron deficiency anemia [9, 10].

This study aimed to assess whether adding *L. plantarum 299v* probiotic supplementation to oral iron replacement therapy (OIRT) would improve iron levels in patients newly diagnosed with iron deficiency anemia.

Materials and methods
A total of 148 patients with newly diagnosed IDA who were planned to receive routine oral iron supplements were included in this prospective 3-month follow-up study. Patients were randomly assigned via simple randomisation method (computer-generated sequence) to receive either oral iron supplementation alone (74 patients, OIRT-only group) or oral

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iron supplementation plus probiotic support (74 patients, OIRT-Pb group). Adult (aged > 18 years) treatment-naïve patients diagnosed with newly diagnosed IDA without previous oral iron supplementation were included in the study, while those with irritable bowel syndrome, previous oral iron supplementation therapy or intolerance to oral iron supplementation and those with a known chronic disease (i.e. inflammatory bowel disease and celiac disease) or untreated active menometrorrhagia and haemorrhoid were excluded from the study. Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study.

All patients received oral iron supplementation with ferrous ascorbate (equivalent to 100 mg elemental iron) preparation (100 mg, once daily) for 3 months, while those in the OIRT-Pro group also received daily (10B CFU) *L. plantarum 299v* probiotic supplementation. Serum Hb levels (g/dl) and serum iron status markers including ferritin (ng/ml), iron (µg/dl), total iron-binding capacity (TIBC, µg/dl) and transferrin saturation (TSat%) were recorded at baseline and at 3rd month of oral iron supplementation.

Results

After three months of therapy, the OIRT-Pb group showed significantly higher serum iron levels ($P < 0.001$) and transferrin saturation(TSat) ($P < 0.001$) compared to the OIRT-only group. Additionally, their ferritin levels increased more from the baseline ($P < 0.001$). The TIBC levels at this point were notably lower in the OIRT-Pb group ($P < 0.001$) and had decreased more from their initial values ($P < 0.001$).

Parameter	**OIRT**	**OIRT-PB**	**p-value**
Serum Iron - Baseline	48	44	0.08
Serum Iron - After 3 months	61	70	<0.001

Parameter	**OIRT**	**OIRT-PB**	**p-value**
TSat% - Baseline	12.7	11.8	0.02
TSat% - After 3 months	14.6	19.7	<0.001

Parameter	**OIRT**	**OIRT-PB**	**p-value**
Serum Ferritin - Baseline	10	8	<0.001
Serum Ferritin - After 3 month	18	19	<0.001

Parameter	**OIRT**	**OIRT-PB**	**p-value**
TIBC - Baseline	407	405	0.9
TIBC - After 3 months	395	370	<0.001

Discussion

To the best of our knowledge, this appears to be the first study to explore whether adding the probiotic L. plantarum 299v to oral iron supplements can boost iron levels in patients recently diagnosed with iron deficiency anaemia in this part of West Bengal.

Research shows that probiotics influence various aspects of human health, especially iron metabolism [11, 12]. Iron is vital for many bodily functions, and a deficiency can cause anaemia and other health issues [11-13]. Insufficient iron levels shift the balance of gut bacteria and increase the risk of intestinal infections. Recent studies reveal that some probiotics, like Lactobacillus acidophilus and Bifidobacterium longum, can improve iron absorption and help manage anaemia [11-13]. Several studies involving pregnant women suggest that L. plantarum 299v may slow the decline in maternal blood and iron levels during pregnancy, both in women without anemia and those at risk for IDA [14, 15]. Animal studies have found that prebiotics can boost iron absorption in young rats with iron deficiency. This may happen

through changes in protein expression and the gut microbiome [16]. A randomized controlled trial using iron stable isotopes in Kenyan infants found that prebiotics increased iron absorption, reduced the negative effects of iron on gut bacteria, and lowered inflammation [17]. Lactobacillus fermentum produces a compound called p-hydroxyphenyl-lactic acid. This compound converts ferric iron into ferrous iron, making it easier for the intestines to absorb [18]. Multi-species probiotics have also shown promise in raising iron availability. They improve absorption in the duodenum, the first section of the small intestine [18].

The study's main limitation is that probiotics and iron supplements were given in just one dose. This limitation impedes the investigation of whether the results observed in the study are dose-dependent.

Conclusion

In summary, our study on iron deficiency anemia patients showed that adding L. plantarum probiotic supplements along with oral iron supplementation led to greater improvements in serum iron levels than using iron alone. This suggests that combining the *L. plantarum 299v* probiotic with iron could be a better treatment for iron deficiency anemia, especially since gastrointestinal side effects and poor compliance often limit iron therapy. Because gut bacteria influence how well the body absorbs iron, more research is needed on how different probiotic strains and iron preparations affect iron status. Future studies should focus on diverse populations to better understand long-term effects and optimize treatment strategies for iron deficiency anemia.

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