Dear Editor, and Reviewers

Thanks very much for your comments on our Manuscript ID: ijms-2612415, Tittle: Genotype Prevalence of Lactose Intolerance, Vitamin D Deficiency, and Vitamin D Receptor in a Chilean Inflammatory Bowel Disease Cohort: Insights from an Observational Study. Thanks again for the time and effort dedicated to improving our manuscript.

Regarding English language, we attached the certificated that this article was edited by MDPI, previously to submitted for first time. In addition, MDPI give guarantee to edit and correct again the English. **They mentioned "Please note that this manuscript did not require an extensive level of editing, as the language in both the previously edited and newly edited sections were of a high standard and did not require much intervention"**. **In this case, the language in your manuscript is clear, consistent, grammatically correct, and suitable for submission.**

We checked and added more references relevant to the contents of the manuscript.

We include the suggestions of the reviewers as is explained below.

All the text changes were highlighted in yellow.

We could not address only one comments from the reviewer 1, we explained the reason below, and add this commentary in the discussion.
We hope the new version meets your expectations.

Yours
sincerely,
The authors

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Reviewer 2.

**1.The article is well written. The introduction section is quiet short and might be improved.**

Thanks, for your feedback and commentary. We improve the introduction according to your suggestions.

Lines 46 to 146

Inflammatory Bowel Disease (IBD) is a complex syndrome where several factors may influence the clinical course. Dietary issues such as low vitamin D levels are relevant because they relate to IBD severity, risk, and quality of life. Moreover, food intolerance, such as lactose intolerance (LI), might induce symptoms that can mimic an IBD flare. Despite these potentially relevant links with IBD, these conditions often go unnoticed because of a lack of awareness on the part of the clinicians, who may miss asking relevant questions.

LI corresponds to a clinical syndrome…. .

. …Importantly, IBD patients with LI/LNP may favor vitamin D deficiency by avoiding lactose product consumption, a main source of vitamin D. This issue could be relevant in IBD since several studies have linked low vitamin D levels with disease outcomes. Epidemiological studies have shown that vitamin D deficiency (VDD) is highly prevalent among IBD patients, and low levels of vitamin D correlate not only with a higher osteoporosis risk but also with more severe disease and higher disease activity (hospitalization, surgery risk, Clostridioides difficile infection, and anti-TNF $\alpha$ response) [16]–[25]. Deficiencies in vitamin D have been associated with increased susceptibility to immune-mediated diseases, infections, and cancer [26]–[29].

…These mechanisms might influence IBD development and progression [30][31]. Interestingly, it has been reported that there is an association between IBD and SNPs related to VDD and the VDR [31]–[35]. SNPs associated with vitamin D levels in IBD have been reported previously[36]. A New Zealand study analyzed the relevance of serum vitamin D levels and genotypes to CD status. They found that serum vitamin D levels were significantly lower in CD than in health, and two allele variants, rs731236-A (VDR) and rs732594-A (SCUBE3), showed a significant association with serum vitamin D in CD [32]. A meta-analysis of several studies evaluated the impact of VDR gene polymorphisms on the risk of UC and CD. Four VDR polymorphisms (rs731236; TaqI, rs1544410; BsmI, rs2228570; FokI, and rs17879735; ApaI) were examined. This meta-analysis reveals that carrying the TaqI tt genotype increases CD risk in Europeans, while the ApaI "a" allele decreases CD risk in all carriers. The FokI polymorphism confers susceptibility to UC in Asians [37]. Despite a handful of clinical studies showing that lower vitamin D levels have been associated with IBD clinical relapse, current data have failed to establish a conclusive genetic association between VDD and VDR SNPs with IBD [38]. Thus, studies to explore this link are needed.

Our study aimed to evaluate the prevalence of LCT-13910-CC (LNP) in Chilean patients with IBD, as well as the genotypes associated with VDD and VDR. We found that 61% of Chilean IBD patients have a genetic predisposition to lactose malabsorption, and a significant proportion have SNPs associated with low vitamin D levels and VDR SNPs. Screening for lactose intolerance and VDD is important in this population to prevent negative IBD outcomes and an increased risk of osteoporosis. The consideration of lactose intolerance is important for symptomatic Chilean IBD patients with inactive disease. The prevalence of the CC genotype of LCT-13910 in the Latin American population suggests that lactose intolerance may affect Latin American IBD patients.

**2. The material and methods section are very detailed and there is no need to change anything.**

Thanks for your commentary, we appreciate it.

**3. The results are clearly demonstarted and the discussion is rigorous. I recommend to decsribe patients more detailed (medications, treatment, were they on special diet, how were they diagnosed, etc.)**

Thanks for your commentary. We added more detailed information about patients. Lines 153-165.

Within this cohort of IBD patients, it was observed that 36% exhibited extraintestinal manifestations, over 50% had a history of IBD-related hospitalization, and only 15% had undergone bowel resection surgery. Additionally, more than 50% of the patients received thiopurine treatment, while only 17% underwent anti-TNF therapy. Based on the Montreal Classification, 35% of UC cases were classified as extensive colitis, 31% as left colitis, and 25% as proctitis, and information regarding the classification was unavailable for 9% of cases. In the CD group, only 4% received a diagnosis before age 17. The most common extension of CD was colonic (L2) involvement, accounting for 46% of cases, followed by ileocolonic (L3) extension. Upper digestive tract involvement (L4) was observed in only 5% of CD cases, while 54% exhibited perianal involvement. The predominant CD phenotype was structuring (B2), observed in 37% of cases, followed by 33% exhibiting an inflammatory phenotype (B1).

The IBD diagnosis was supported by clinical, endoscopic, histologic, and imaging findings according to clinical guidelines and International Disease Classification criteria [65]–[67]. It is mentioned in the Methods