

# Intrahepatic Cholestasis of Pregnancy Associated Vitamin D deficiency

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## Abstract:

Here, we investigated the serum vitamin D level in pregnant women with ICP. Serum level of 25(OH)D, from 125 pregnant women with ICP and 95 healthy women with uncomplicated pregnancies were measured. Serum 25(OH)D level in pregnant women with ICP and healthy pregnant women were significantly different ( $17.25 \pm 7.02$  ng/ml,  $23.36 \pm 4.64$  ng/ml, respectively). ICP patients had a higher rate of vitamin D deficiency and insufficiency relative to control group ( $P$  all  $< 0.001$ ). Serum 25(OH)D level in pregnant women with severe ICP was lower than in those with mild ICP. Importantly, low 25(OH)D serum level are associated with high level of total bile acid (TBA) in pregnant women with ICP ( $r = -0.276$ ,  $P < 0.001$ ). These findings suggest the potential role of vitamin D in the pathogenesis of ICP.

**Keywords:** Vitamin D, ICP, Pathogenesis, TBA.

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## I. INTRODUCTION

ICP is associated with unexplained pruritus and increase of serum TBA and liver transaminases concentrations, and closely linked to adverse pregnancy outcomes, including premature delivery, fetal distress and intrauterine death [1]. The incidence of this disease ranges from 0.1% to 10% due to ethnicity and geographic location. The exact etiology of ICP remained unclear; however, hormonal, genetic, nutritional and environmental factors were considered to be one of the contributing factors in the pathogenesis of ICP. Vitamin D status may modulate the risk of pregnancy complications including gestational diabetes, ICP and periodontal disease [2].

Vitamin D is not merely a key nutrient which serves a role in normal Ca homeostasis but also has a potentially important role in the prevention of many disease. However, it is a known fact that vitamin D deficiency is a prominent feature of various chronic liver diseases

regardless of the etiology [3]. Although low serum levels of vitamin D levels have been previously described from the European women with ICP [4], there are not any relevant publications focused on vitamin D in Chinese women with ICP. The incidence of this disease ranges from 0.1% to 10% due to ethnicity and geographic location. The exact etiology of ICP remained unclear, however, nutritional factors were considered to be one of the contributing factors in the pathogenesis of the disease in China.

Aiming to provide more information about the pathogenesis of ICP, we investigated the possible association of ICP with vitamin D deficiency in a Chinese population, which may provide a new therapeutic strategies for treating ICP.

As shown in Fig 1, serum 25(OH)D level was  $17.25 \pm 7.02$  ng/ml in ICP pregnant women compared with  $23.36 \pm 4.64$  ng/ml in pregnant controls ( $p < 0.001$ ). Of the pregnant women with ICP, 90 (74.4%) women had vitamin D deficiency, 24 (19.8%) women had vitamin D insufficiency and 7 (5.8%) women had normal values of vitamin D. This high proportion of vitamin D insufficiency in ICP patients was likely to be due to inadequate physical activity and insufficient sunlight, for most of the ICP patients spent more hours lying indoors compare with the days before pregnancy. In pregnant controls, 26 (27.4%) women had vitamin D deficiency, 59 (62.1%) women had vitamin D insufficiency and 10 women (10.5%) had normal values of vitamin D. It was likely to be due to inadequate physical activity and insufficient sunlight, for most of the ICP patients spent more hours lying indoors compare with the days before pregnancy. The findings in this study were consistent with related researches' results[4].

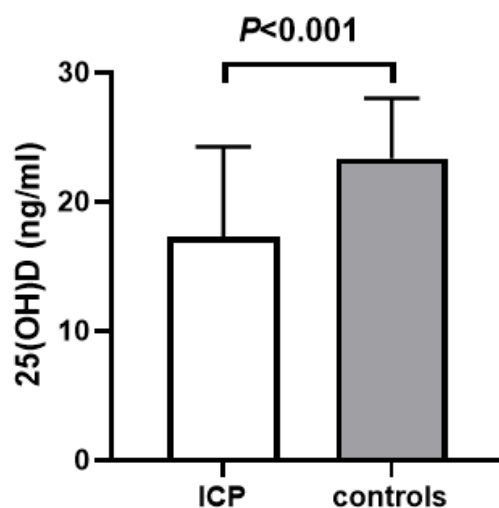


Fig 1: Serum 25(OH)D levels in pregnant controls and pregnant women with ICP

As shown in Fig 2A., the result showed that serum 25(OH)D level in pregnant women with severe ICP was lower than in those with mild ICP. Since total bile acids (TBA) is an important marker for assessment of the severity of ICP. If serum TBA level was higher than 40  $\mu\text{mol/L}$  in ICP patients, it was often suggested a serious liver injury. A significant negative correlation between serum 25(OH)D level and TBA level was found in the pregnant women with ICP, as shown in Fig 2B. Although this specific mechanism of the association had not been clarified, previous study demonstrated that vitamin D could decrease human cholesterol 7 $\alpha$ -Hydroxylase (hCYP7A1) expression, a gene which encodes a key enzyme involved in TBA synthesis, thus producing feedback repression of bile acid synthesis in vivo. However, this probable causal relationship needed to be further confirmed by later experiments.

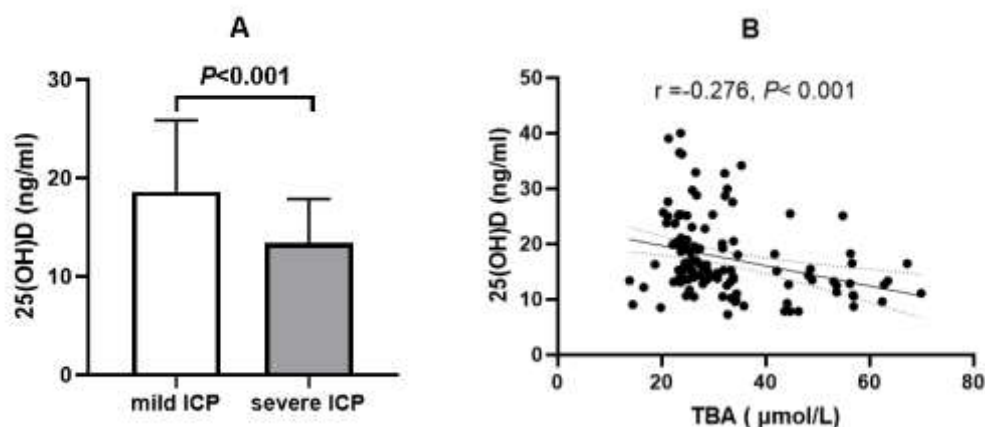


Fig 2: The correlation between serum 25(OH)D levels with ICP severity.

Previous results showed that the influence of geographic latitude was quite important to vitamin D levels. Difference in the regional distribution of ICP women may lead to significantly different prevalence of vitamin D deficiency. In order to exclude the possible effects of seasonal factors on serum level of vitamin D, we analyzed serum 25(OH)D level for the pregnant women with ICP in winter/spring and summer/autumn. As shown in Fig 3, serum 25(OH)D level was similar across seasons suggesting that seasonal fluctuation had limited influence on serum 25(OH)D level of ICP.

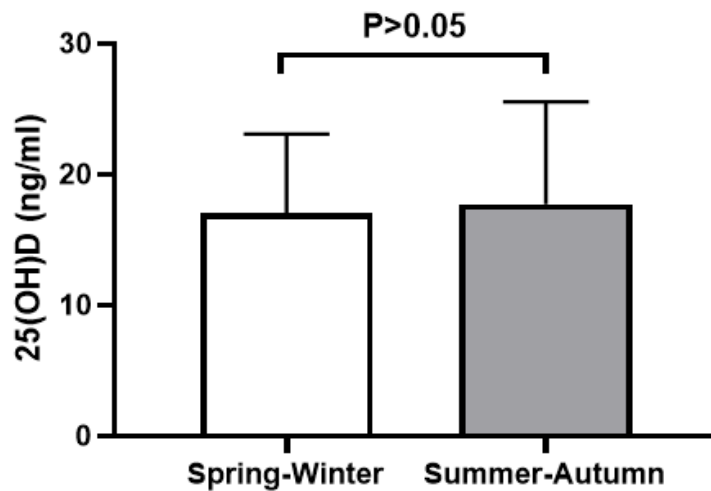


Fig 3: The effects of season on serum 25(OH)D levels in ICP pregnant women.

## II. MATERIALS AND METHODS

This study was conducted between January 2019 and January 2021 at the Department of Gynecology, Anhui No.2 Provincial People’s Hospital. ICP was diagnosed in accordance with recognized criteria. Patients were subdivided into two groups: mild ICP and severe ICP. They were also excluded if they had liver dysfunction of any kind. The baseline characteristics of all subjects are shown in TABLE I.

TABLE I. Subject characteristics

	Control	ICP
Age, years	25.23± 5.43	26.92 ± 4.37
Gestational week at assessment	36.26±3.42	36.73±1.49
Weight, kg	74.63±11.7	75.92±10.47
BMI at assessment, kg/m <sup>2</sup>	27.5±5.91	28.55±3.88
ALT, U/L	10.46 ± 4.27	76.54 ± 54.95
AST, U/L	16.63 ± 4.62	98.75 ± 70.54
TBA, μmol/L	4.27± 3.18	36.69±6.71

### 2.1 Materials and Methodology

Serum 25(OH) D was quantified by Roche Cobas e601 (Roche Diagnostics, Mannheim, Germany).

### **III. CONCLUSION**

Above all, this study had indicated that vitamin D deficiency was clearly associated with ICP, and we could infer that vitamin D deficiency may have an essential role in the pathogenesis of ICP.

### **ACKNOWLEDGEMENTS**

This research was supported by Provincial Natural Science Research Project of Anhui Colleges (Grant No. KJ2020ZD68)

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