

# Role of Vitamin D in Activity and Severity of Inflammatory Bowel Disease in Egyptian Patients

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## Abstract

**Background and aim:** Inflammatory Bowel Diseases (IBD) Comprise Ulcerative Colitis (UC) and Crohn's Disease (CD), which are chronic and recurrent disorders that affect the gastrointestinal tract. Diagnosing IBD requires a combination of clinical findings, inflammatory laboratory markers, imaging findings, and endoscopic biopsies. Vitamin D deficiency is generally higher in patients with CD than UC and usually higher than that of the general population. This study aims to evaluate the role of vitamin D in activity and severity of inflammatory bowel disease in Egyptian patients.

**Methods:** Our study was conducted on 62 IBD (UC and CD) naïve patients and 31 normal persons from the GI endoscopy unit of internal medicine department, Menoufia university hospital during the period between November 2021 and June 2023. All participants were subjected to history taking, clinical examination and routine lab investigations. Serum vitamin D level was also measured.

**Results:** This study showed highly significant difference between studied groups as regard serum vitamin D level with low level of vitamin D in IBD patients. Vitamin D is associated with different IBD activity status.

**Conclusion:** Vitamin D is associated with different IBD activity status and its deficiency is highly prevalent among IBD patients.

**Keywords:** IBD; Ulcerative colitis; Crohn's disease; Vitamin D

**Abbreviations:** IBD: Inflammatory Bowel Disease; UC: Ulcerative Colitis; CD: Crohn's Disease; GI: Gastrointestinal; CBC: Complete Blood Count; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; CDAI: Crohn's Disease Activity Index; ELISA: Enzyme-Linked Immunosorbent Assay; PLT:

Platelets; TLC: Total Leukocyte Count; HB: Hemoglobin

## Introduction

Inflammatory Bowel Diseases (IBD) comprise Ulcerative Colitis (UC) and Crohn's Disease (CD), which are chronic and recurrent disorders that affect the gastrointestinal tract. The etiology of IBD is not yet fully understood, but there are reports of a complex relationship between genetic, immunological and environmental factors, as well as gut microbiota [1-4].

Diagnosing IBD requires a combination of clinical findings, inflammatory laboratory markers, imaging findings, and endoscopic biopsies [5].

Many studies have evaluated the prevalence of vitamin D deficiency and insufficiency in people with IBD. Vitamin D deficiency is generally higher in patients with CD than UC and usually higher than that of the general population [6].

Various studies reported the role of vitamin D in IBD. Vitamin D deficiency may lead to a reduction in bacterial clearance in the colon. This vitamin changes the immune responses by influencing macrophages and T lymphocytes, hence avoiding excessive immune responses, and also repairs the intestinal mucosal barrier [7].

We conducted this study to evaluate the role of vitamin D in activity and severity of inflammatory bowel disease in Egyptian patients.

## Materials and Methods

### Patients and methods

This study was approved by the local institutional ethical committee of Menoufia University, Menoufia University and the

participants gave an informed consent. The study was conducted on 62 IBD (UC and CD) naïve patients and 31 normal persons from the GI endoscopy unit of internal medicine department, Menoufia University hospital during the period between November 2021 and June 2023.

Participants were classified into three groups:

- **Group 1:** Ulcerative colitis patients including 31 participants.
- **Group 2:** Crohn's disease patients including 31 participants.
- **Group 3:** Control group resemble normal persons including 31 participants.

Participants included in the study aged 18 years or older and were naïve IBD patients with no previous treatment.

Exclusion criteria showed age younger than 18 years and patients on IBD medications.

Participants were subjected to the following: History taking (age and gender), complete clinical examination including (temperature, blood pressure measurement, pulse, and body mass index), routine Laboratory investigations including (CBC, AST, ALT, albumin, urea and creatinine), ESR, CRP, fecal calprotectin, serum vitamin D level and serum TNF alpha level.

Ileocolonic biopsies were collected from patients undergoing colonoscopy for histopathological evaluation.

Mayo score and Crohn's Disease Activity Index (CDAI) were used to assess disease activity in patients with ulcerative colitis and Crohn's disease respectively.

Demographic, clinical and laboratory data of the cases were given in below **Figure 1**.

**Details about tools were used in this study**

**Colonscope:** Company manufacturing (Olympus Corporation), country (Japan), city (Tokyo).

**Human vitamin D<sub>3</sub> ELISA kits:** company manufacturing (SunRed Biotechnology Company), country (China), and city (Shanghai).

**Human TNF alpha ELISA kits:** company manufacturing (SunRed Biotechnology Company), country (China), and city (Shanghai).

**Statistical analysis**

Data entry, coding, and analysis were conducted using SPSS (22), IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0 Armonk, NY: IBM Corp. USA. Description of quantitative variables was in the form of mean and Standard Deviation (mean ± SD), description of qualitative variables was by frequency and percentage, chi square test was used to assess the relationship between two qualitative groups, t-test was to assess the relationship between two quantitative groups. P value ≤ 0.05 was set to be statistically significant.

**Results**

This study showed highly significant difference between studied groups as regard serum vitamin D level with low level of vitamin D in IBD patients. Vitamin D is associated with different IBD activity status.

Our study showed highly significant difference between studied groups regarding ESR and CRP with p value <0.001 and <0.001 respectively (**Table 1**).

| Variable  | Quantity | Multiple | Total |
|---|----------|----------|-------|
| Stool frequency   |          |          |       |
| 0 = Normal  |          |          |       |
| 1 = 1-2 stools/day more than normal   |          |          | 2     |
| 2 = 3-4 stools/day more than normal   |          |          | 5     |
| 3 = >4 stools/day more than normal  |          |          |       |
| Rectal bleeding*  |          |          |       |
| 0 = None  |          |          | 7     |
| 1 = Visible blood with stool less than half the time  |          |          |       |
| 2 = Visible blood with stool half of the time or more   |          |          |       |
| 3 = Passing blood alone   |          |          | 20    |
| Mucosal appearance at endoscopy <sup>b</sup>  |          |          |       |
| 0 = Normal or inactive disease  |          |          |       |
| 1 = Mild disease (erythema, decreased vascular pattern, mild friability)  |          |          | 30    |
| 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)   |          |          | 10    |
| 3 = Severe disease (spontaneous bleeding, ulceration)   |          |          |       |
| Physician rating of disease activity  |          |          |       |
| 0 = Normal  |          |          | 6     |
| 1 = Mild  |          |          |       |
| 2 = Moderate  |          |          |       |
| 3 = Severe  |          |          | 1     |
| *A score of 3 for bleeding required patients to have at least 50% of bowel motions accompanied by visible blood and at least one bowel motion with blood alone. |          |          |       |
| <sup>b</sup> The mucosal appearance at endoscopy is not included in the Partial Mayo Score.   |          |          |       |
| From Best et al <sup>22</sup> : CDAI <150 = remission; >450 = severely ill.   |          |          |       |

**Figure 1:** Mayo score and Crohns disease activity index.

**Table 1:** Comparison between the three studied groups according to ESR and CRP.

|                  | Group 1 (n=31) | Group 2 (n=31) | Group 3 (n=31) | F        | P       | Sig. bet. grps. |         |         |
|------------------|----------------|----------------|----------------|----------|---------|-----------------|---------|---------|
|                  |                |                |                |          |         | 1 vs. 2         | 1 vs. 3 | 2 vs. 3 |
| <b>ESR (mms)</b> |                |                |                |          |         |                 |         |         |
| Min.-Max.        | 40.0-80.0      | 44.0-87.0      | 5.0-9.0        | 428.917* | <0.001* | 0.94            | <0.001* | <0.001* |
| Mean ± SD.       | 68.52 ± 10.92  | 67.71 ± 11.19  | 7.16 ± 1.19    |          |         |                 |         |         |

|                    |                  |                   |               |          |         |       |         |         |
|--------------------|------------------|-------------------|---------------|----------|---------|-------|---------|---------|
| Median (IQR)       | 68.0 (59.0-76.0) | 68.0 (59.50-76.0) | 7.0 (6.0-8.0) |          |         |       |         |         |
| <b>CRP (IU/ml)</b> |                  |                   |               |          |         |       |         |         |
| Min.-Max.          | 30.0-70.0        | 30.0-65.0         | 2.0-5.0       | 394.511* | <0.001* | 0.611 | <0.001* | <0.001* |
| Mean ± SD.         | 44.52 ± 7.81     | 46.13 ± 8.53      | 3.97 ± 0.84   |          |         |       |         |         |
| Median (IQR)       | 45.0 (39.0-49.0) | 45.0 (41.0-53.50) | 4.0 (3.0-5.0) |          |         |       |         |         |

**Note:** IQR: Inter Quartile Range.  
 SD: Standard Deviation.  
 F: F for one way ANOVA test; pairwise comparison bet.  
 Each 2 groups was done using Post Hoc Test (Tukey).  
 p: p value for comparing between the studied groups.  
 \*: Statistically significant at  $p \leq 0.05$ .  
 ESR: Erythrocyte Sedimentation Rate.  
 CRP: C Reactive Protein.  
 Group 1: Ulcerative colitis group.  
 Group 2: Crohns disease group.  
 Group 3: Control group.  
 n: number.

In the current study there is no significant difference between ulcerative colitis group and Crohn's disease group as regard ESR and CRP with P value 0.940 and 0.611 respectively (**Table 1**).

This study showed highly significant difference between the 3 studied groups as regard fecal calprotectin with (P value <0.001) (**Table 2**).

**Table 2:** Comparison between the three studied groups according to fecal calprotectin.

| Fecal calprotectin (microgram/milligram) | Group 1 (n=31)      | Group 2 (n=31)      | Group 3 (n=31)   | H       | p       | Sig. bet. grps. |         |         |
|--|---------------------|---------------------|------------------|---------|---------|-----------------|---------|---------|
|  |                     |                     |                  |         |         | 1 vs. 2         | 1 vs. 3 | 2 vs. 3 |
| Min.-Max.                                | 260.0-80.0          | 280.0-870.0         | 30.0-75.0        | 61.425* | <0.001* | 0.836           | <0.001* | <0.001* |
| Mean ± SD.                               | 463.8 ± 153.9       | 479.3 ± 169.8       | 54.29 ± 13.68    |         |         |                 |         |         |
| Median (IQR)                             | 453.0 (350.5-538.0) | 453.0 (350.5-611.5) | 55.0 (45.0-64.0) |         |         |                 |         |         |

**Note:** IQR: Inter quartile range  
 SD: Standard deviation  
 H: H for Kruskal Wallis test, pairwise comparison bet.  
 Each 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test)  
 p: p value for comparing between the studied groups

\*: Statistically significant at  $p \leq 0.05$

Group 1: ulcerative colitis group, group 2: Crohns disease group, group 3: control group, n: number

The present study showed highly significant difference between the 3 studied groups as regard serum vitamin D level with (P value <0.001) (Table 3).

**Table 3:** Comparison between the three studied groups according to serum vitamin D level.

| Vitamin D level (ng/ml) | Group 1 (n=31)   | Group 2 (n=31)   | Group 3 (n=31)   | H       | p       | Sig. bet. grps. |         |         |
|-------------------------|------------------|------------------|------------------|---------|---------|-----------------|---------|---------|
|                         |                  |                  |                  |         |         | 1 vs. 2         | 1 vs. 3 | 2 vs. 3 |
| Min.-Max.               | 4.0-39.0         | 7.0-21.0         | 15.0-153.0       | 58.582* | <0.001* | 0.163           | <0.001* | <0.001* |
| Mean ± SD.              | 12.87 ± 5.79     | 13.48 ± 2.64     | 63.03 ± 40.23    |         |         |                 |         |         |
| Median (IQR)            | 12.0 (11.0-14.0) | 14.0 (12.0-15.0) | 54.0 (37.5-73.5) |         |         |                 |         |         |

**Note:** IQR: Inter quartile range

SD: Standard deviation

H: H for Kruskal Wallis test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test)

p: p value for comparing between the studied groups

\*: Statistically significant at  $p \leq 0.05$

Group 1: ulcerative colitis group, group 2: Crohns disease group, group 3: control group, n: number

In the current study there is highly significant difference between the 3 studied groups as regard serum TNF alpha level with (P value <0.001) (Tables 4-6).

**Table 4:** Comparison between the three studied groups according to serum TNF alpha level.

| TNF alpha level (pg/ml) | Group 1 (n=31)     | Group 2 (n=31)      | Group 3 (n=31)   | H       | p       | Sig. bet. grps. |         |         |
|-------------------------|--------------------|---------------------|------------------|---------|---------|-----------------|---------|---------|
|                         |                    |                     |                  |         |         | 1 vs. 2         | 1 vs. 3 | 2 vs. 3 |
| Min.-Max.               | 52.0-723.0         | 68.0-940.0          | 32.0-81.0        | 54.601* | <0.001* | 0.665           | <0.001* | <0.001* |
| Mean ± SD.              | 256.1 ± 176.4      | 290.5 ± 210.0       | 61.55 ± 13.30    |         |         |                 |         |         |
| Median (IQR)            | 222.0 (95.5-375.0) | 261.0 (119.0-376.5) | 60.0 (53.5-71.5) |         |         |                 |         |         |

**Note:** IQR: Inter quartile range

SD: Standard deviation

H: H for Kruskal Wallis test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test)

p: p value for comparing between the studied groups.

\*: Statistically significant at  $p \leq 0.05$

TNF: tumor necrosis factor

Group 1: ulcerative colitis group, group 2: Crohns disease group, group 3: control group, n: number

**Table 5:** Relation between clinical activity and severity with serum TNF alpha level and serum vitamin D level in ulcerative colitis group.

|  | Clinical activity and severity |                               |                            | H     | p     |
|--|--------------------------------|-------------------------------|----------------------------|-------|-------|
|  | Mild<br>(n=14)<br>(45.2%)      | Moderate<br>(n=13)<br>(41.9%) | Severe<br>(n=4)<br>(12.9%) |       |       |
| <b>TNF alpha level (pg/mg)</b>   |                                |                               |                            |       |       |
| Min.-Max.  | 52.0-613.0                     | 76.0-723.0                    | 78.0-371.0                 | 0.722 | 0.697 |
| Mean ± SD.   | 270.6 ± 182.2                  | 260.2 ± 188.7                 | 191.5 ± 135.8              |       |       |
| Median   | 246                            | 206                           | 158.5                      |       |       |
| <b>Vitamin D level (ng/mg)</b>   |                                |                               |                            |       |       |
| Min.-Max.  | 7.0-39.0                       | 4.0-15.0                      | 10.0-13.0                  | 0.885 | 0.642 |
| Mean ± SD.   | 14.43 ± 7.95                   | 11.62 ± 3.12                  | 11.50 ± 1.29               |       |       |
| Median   | 12                             | 13                            | 11.5                       |       |       |
| <p><b>Note:</b> SD: Standard deviation<br/>                     H: H for Kruskal Wallis test<br/>                     p: p value for comparing between different category<br/>                     TNF: tumor necrosis factor<br/>                     SD: standard deviation, n: number</p> |                                |                               |                            |       |       |

**Table 6:** Relation between clinical activity and severity with serum TNF alpha level and serum vitamin D level in Crohns disease group.

|                                | Clinical activity and severity |                               |                           | H     | p    |
|--------------------------------|--------------------------------|-------------------------------|---------------------------|-------|------|
|                                | Mild<br>(n=9)<br>(29%)         | Moderate<br>(n=19)<br>(61.3%) | Severe<br>(n=3)<br>(9.7%) |       |      |
| <b>TNF alpha level (pg/mg)</b> |                                |                               |                           |       |      |
| Min.-Max.                      | 68.0-377.0                     | 77.0-940.0                    | 90.0-238.0                | 3.322 | 0.19 |
| Mean ± SD.                     | 204.3 ± 116.6                  | 350.4 ± 238.5                 | 169.3 ± 74.57             |       |      |

|  |              |              |              |       |       |
|--|--------------|--------------|--------------|-------|-------|
| Median   | 195          | 323          | 180          |       |       |
| <b>Vitamin D level (ng/mg)</b>   |              |              |              |       |       |
| Min.-Max.  | 11.0-16.0    | 7.0-17.0     | 15.0-21.0    | 5.829 | 0.054 |
| Mean ± SD.   | 13.44 ± 1.67 | 12.89 ± 2.54 | 17.33 ± 3.21 |       |       |
| Median   | 13           | 14           | 16           |       |       |
| <p><b>Note:</b> SD: Standard deviation<br/>                 H: H for Kruskal Wallis test<br/>                 p: p value for comparing between different category<br/>                 TNF: tumor necrosis factor<br/>                 SD: Standard Deviation, n: number</p> |              |              |              |       |       |

Our study showed no significant difference between studied groups regarding sociodemographic data including age and gender with p value (0.842) (0.827) respectively (**Tables 7 and 8**).

**Table 7:** Comparison between the three studied groups according to demographic data.

|                                 | Group 1 (n=31)    |      | Group 2 (n=31)     |      | Group 3 (n=31)     |      | Test of sig.              | P     |
|---------------------------------|-------------------|------|--------------------|------|--------------------|------|---------------------------|-------|
|                                 | No.               | %    | No.                | %    | No.                | %    |                           |       |
| <b>Gender</b>                   |                   |      |                    |      |                    |      |                           |       |
| Male                            | 14                | 45.2 | 16                 | 51.6 | 20                 | 64.5 | χ <sup>2</sup> =<br>0.344 | 0.842 |
| Female                          | 17                | 54.8 | 15                 | 48.4 | 11                 | 35.5 |                           |       |
| <b>Age (years)</b>              |                   |      |                    |      |                    |      |                           |       |
| Min.-Max.                       | 18.0-55.0         |      | 19.0-50.0          |      | 20.0-54.0          |      | F=0.190                   | 0.827 |
| Mean ± SD.                      | 34.84 ± 10.67     |      | 33.35 ± 9.34       |      | 33.71 ± 9.64       |      |                           |       |
| Median (IQR)                    | 36.0 (26.50-42.0) |      | 35.0 (26.50-39.50) |      | 35.0 (26.50-40.50) |      |                           |       |
| <b>Residence</b>                |                   |      |                    |      |                    |      |                           |       |
| Urban                           | 15                | 48.4 | 17                 | 54.8 | 12                 | 38.7 | χ <sup>2</sup> =0.087     | 0.958 |
| Rural                           | 16                | 51.6 | 14                 | 45.2 | 19                 | 61.3 |                           |       |
| <b>Special habits (smoking)</b> |                   |      |                    |      |                    |      |                           |       |
| Yes                             | 10                | 32.3 | 15                 | 48.4 | 8                  | 25.8 | χ <sup>2</sup> =1.824     | 0.402 |
| No                              | 21                | 67.7 | 16                 | 51.6 | 23                 | 74.2 |                           |       |

| <b>Consanguinity</b>   |    |      |    |      |    |      |                 |                        |
|--|----|------|----|------|----|------|-----------------|------------------------|
| Yes  | 5  | 16.1 | 7  | 22.6 | 2  | 6.5  | $\chi^2=3.205$  | MC <sub>p</sub> =0.237 |
| No   | 26 | 83.9 | 24 | 77.4 | 29 | 93.5 |                 |                        |
| <b>Family history</b>  |    |      |    |      |    |      |                 |                        |
| Yes  | 4  | 12.9 | 6  | 19.4 | 2  | 6.5  | $\chi^2= 4.798$ | 0.091                  |
| No   | 27 | 87.1 | 25 | 80   | 29 | 93.5 |                 |                        |
| <p><b>Note:</b> IQR: Inter quartile range<br/>                     SD: Standard deviation<br/> <math>\chi^2</math>: Chi square test<br/>                     MC: Monte Carlo<br/>                     F: F for One way ANOVA test<br/>                     F: F for One way ANOVA test<br/>                     Group 1: Ulcerative colitis patients, Group 2: Crohn's disease patients, Group 3: Control, n: number</p> |    |      |    |      |    |      |                 |                        |

**Table 8:** Comparison between the three studied groups according to vital signs.

|  |                    | <b>Group 1<br/>(n=31)</b> | <b>Group 2<br/>(n=31)</b> | <b>Group 3<br/>(n=31)</b> | <b>F</b> | <b>P</b> |
|--|--------------------|---------------------------|---------------------------|---------------------------|----------|----------|
| <b>Systolic blood pressure (mmHg)</b>  |                    |                           |                           |                           |          |          |
| Min.-Max.                              |                    | 93.0-156.0                | 90.0-160.0                | 90.0-145.0                | 0.005    | 0.995    |
| Mean ± SD.                             |                    | 110.8 ± 16.16             | 116.9 ± 19.0              | 117.2 ± 18.76             |          |          |
| Median (IQR)                           |                    | 119.0 (105.0-124. 50)     | 119.0 (99.50-126. 50)     | 119.0 (100.0-126.0)       |          |          |
| <b>Diastolic blood pressure (mmHg)</b> |                    |                           |                           |                           |          |          |
| Min.-Max.                              |                    | 60.0-950.0                | 60.0-100.0                | 60.0-90.0                 | 0.052    | 0.95     |
| Mean ± SD.                             |                    | 73.35 ± 9.67              | 73.84 ± 10.20             | 74.16 ± 9.90              |          |          |
| Median (IQR)                           |                    | 74.0 (67.50-80.0)         | 75.0 (65.0-80.0)          | 75.0 (67.50-80.0)         |          |          |
| <b>Temperature(°C)</b>                 |                    |                           |                           |                           |          |          |
| Min.-Max.                              | 37.40-39.0         |                           | 37.60-40.0                | 37.0-38.0                 | 1.311    | 0.275    |
| Mean ± SD.                             | 38.16 ± 0.49       |                           | 38.18 ± 0.52              | 36.87 ± 0.31              |          |          |
| Median (IQR)                           | 38.0 (37.85-38.55) |                           | 38.0 (37.80-38.65)        | 37.90 (37.70-38.40)       |          |          |
| <b>Pulse (bpm)</b>                     |                    |                           |                           |                           |          |          |
| Min. – Max.                            | 80.0-115.0         |                           | 77.0-112.0                | 79.0-110.0                | 2.019    | 0.139    |

|              |                   |  |                  |                  |  |  |
|--------------|-------------------|--|------------------|------------------|--|--|
| Mean ± SD.   | 96.74 ± 9.06      |  | 94.94 ± 8.40     | 92.26 ± 9.04     |  |  |
| Median (IQR) | 99.0 (89.0–100.0) |  | 95.0 (89.0-99.0) | 90.0 (88.0-99.0) |  |  |

**Note:** IQR: Inter quartile range

SD: Standard deviation

F: F for One way ANOVA test

p: p value for comparing between the studied groups

Group 1: Ulcerative colitis patients, Group 2: Crohn's disease patients, Group 3: Control, n: number

Also, there was no significant difference in this study as regard body mass index with p value (0.712) (**Table 9**).

**Table 9:** Comparison between the three studied groups according to anthropometric measurement.

|   | Group 1<br>(n=31)   | Group 2<br>(n=31)   | Group 3<br>(n=31)   | F     | P     |
|---|---------------------|---------------------|---------------------|-------|-------|
| <b>Weight (kg)</b>                        |                     |                     |                     |       |       |
| Min.-Max.                                 | 60.0-93.0           | 67.0-100.0          | 60.0-107.0          | 0.399 | 0.672 |
| Mean ± SD.                                | 76.48 ± 8.46        | 78.58 ± 9.94        | 77.90 ± 9.85        |       |       |
| Median (IQR)                              | 77.0 (71.0-83.0)    | 78.0 (71.50-87.50)  | 77.0 (71.0-86.50)   |       |       |
| <b>Height (cm)</b>                        |                     |                     |                     |       |       |
| Min.-Max.                                 | 162.0-183.0         | 166.0-187.0         | 160.0-185.0         | 0.056 | 0.946 |
| Mean ± SD.                                | 174.1 ± 5.32        | 174.5 ± 5.13        | 174.2 ± 5.09        |       |       |
| Median (IQR)                              | 173.0 (169.0-180.0) | 174.0 (170.0-180.0) | 173.0 (170.0-180.0) |       |       |
| <b>Body mass index (kg/m<sup>2</sup>)</b> |                     |                     |                     |       |       |
| Min.-Max.                                 | 19.0-31.20          | 20.30-30.50         | 22.30-31.80         | 0.341 | 0.712 |
| Mean ± SD.                                | 25.25 ± 3.11        | 25.84 ± 2.93        | 25.71 ± 2.94        |       |       |
| Median (IQR)                              | 25.60 (23.15-27.50) | 25.0 (23.70-28.0)   | 24.80 (23.70-28.0)  |       |       |

**Note:** IQR: Inter quartile range

SD: Standard deviation

F: F for One way ANOVA test

p: p value for comparing between the studied groups

Group 1: Ulcerative colitis patients, Group 2: Crohn's disease patients, Group 3: Control, n: number

The present study showed highly significant difference between studied groups regarding Number of bowel motions per 24 h with p value <0.001 (**Table 10**).

**Table 10:** Comparison between the three studied groups according to number of bowel motions per 24 h.

| Number of bowel | Group 1<br>(n=31) | Group 2<br>(n=31) | Group 3<br>(n=31) | H | p | Sig. bet. grps. |         |         |
|-----------------|-------------------|-------------------|-------------------|---|---|-----------------|---------|---------|
|                 |                   |                   |                   |   |   | 1 vs. 2         | 1 vs. 3 | 2 vs. 3 |
|                 |                   |                   |                   |   |   |                 |         |         |



|                         |                 |               |               |         |         |         |        |       |
|-------------------------|-----------------|---------------|---------------|---------|---------|---------|--------|-------|
| <b>motions per 24 h</b> |                 |               |               |         |         |         |        |       |
| Min.-Max.               | 4.0-12.0        | 3.0-8.0       | 4.0-7.0       | 13.140* | <0.001* | <0.001* | 0.009* | 0.386 |
| Mean ± SD.              | 8.03 ± 2,3      | 5.23 ± 1.23   | 5.52 ± 1.09   |         |         |         |        |       |
| Median (IQR)            | 7.0 (5.50-7.50) | 5.0 (4.0-6.0) | 6.0 (5.0-6.0) |         |         |         |        |       |

**Note:** IQR: Inter quartile range  
 SD: Standard deviation  
 H: H for Kruskal Wallis test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test)  
 p: p value for comparing between the studied groups  
 \*: Statistically significant at  $p \leq 0.05$   
 Group 1: Ulcerative colitis patients, Group 2: Crohn's disease patients, Group 3: Control, n: number

Also there was highly significant difference between studied groups regarding presence of rectal bleeding with p value <0.001 (Tables 11-13 and Figures 2-5).

**Table 11:** Comparison between the three studied groups according to rectal bleeding.

| Rectal bleeding    | Group 1 (n=31) |      | Group 2 (n=31) |      | Group 3 (n=31) |      | $\chi^2$ | p       | Sig. bet. grps.            |         |                            |
|--------------------|----------------|------|----------------|------|----------------|------|----------|---------|----------------------------|---------|----------------------------|
|                    | No.            | %    | No.            | %    | No.            | %    |          |         | 1 vs. 2                    | 1 vs. 3 | 2 vs. 3                    |
| No blood           | 0              | 0    | 6              | 19.4 | 24             | 77.4 | 70.639*  | <0.001* | MC <sub>p</sub><br><0.001* | <0.001* | MC <sub>p</sub><br><0.001* |
| Trace              | 7              | 22.6 | 16             | 51.6 | 7              | 22.6 |          |         |                            |         |                            |
| Occasionally frank | 14             | 45.2 | 9              | 29   | 0              | 0    |          |         |                            |         |                            |
| Usually frank      | 10             | 32.3 | 0              | 0    | 0              | 0    |          |         |                            |         |                            |

**Note:**  $\chi^2$ : Chi square test  
 MC: Monte Carlo  
 p: p value for comparing between the studied groups  
 \*: Statistically significant at  $p \leq 0.05$   
 Group 1: Ulcerative colitis patients, Group 2: Crohn's disease patients, Group 3: Control, n: number

**Table 12:** Comparison between the three studied groups according to general wellbeing.

| General wellbeing (average daily rates in the past 7 days) | Group 1 (n=31) |      | Group 2 (n=31) |      | Group 3 (n=31) |     | $\chi^2$ | p       | Sig. bet. grps. |         |             |
|--|----------------|------|----------------|------|----------------|-----|----------|---------|-----------------|---------|-------------|
|  |                |      |                |      |                |     |          |         | 1 vs. 2         | 1 vs. 3 | 2 vs. 3     |
|  | No.            | %    | No.            | %    | No.            | %   |          |         |                 |         |             |
| Generally well   | 7              | 22.6 | 11             | 35.5 | 31             | 100 | 49.102*  | <0.001* | 0.065           | <0.001* | MCp <0.001* |
| Slightly under par   | 12             | 38.7 | 16             | 51.6 | 0              | 0   |          |         |                 |         |             |
| Poor   | 12             | 38.7 | 4              | 12.9 | 0              | 0   |          |         |                 |         |             |

**Note:**  $\chi^2$ : Chi square test

MC: Monte Carlo

p: p value for comparing between the studied groups

\*: Statistically significant at  $p \leq 0.05$

Group 1: Ulcerative colitis patients, Group 2: Crohn's disease patients, Group 3: Control, n: number

**Table 13:** Comparison between the three studied groups according to extra intestinal Manifestations and complications.

| Extra intestinal Manifestations and complications | Group 1 (n=31) |      | Group 2 (n=31) |      | Group 3 (n=31) |     | $\chi^2$ | P           | Sig. bet. grps. |             |             |
|---|----------------|------|----------------|------|----------------|-----|----------|-------------|-----------------|-------------|-------------|
|   |                |      |                |      |                |     |          |             | 1 vs. 2         | 1 vs. 3     | 2 vs. 3     |
|   | No.            | %    | No.            | %    | No.            | %   |          |             |                 |             |             |
| <b>Local</b>                                      |                |      |                |      |                |     |          |             |                 |             |             |
| None  | 20             | 64.5 | 11             | 35.5 | 31             | 100 | 29.129*  | <0.001*     | 0.022*          | <0.001*     | <0.001*     |
| Skin tag  | 11             | 35.5 | 20             | 64.5 | 0              | 0   |          |             |                 |             |             |
| <b>Systemic</b>                                   |                |      |                |      |                |     |          |             |                 |             |             |
| None  | 13             | 41.9 | 0              | 0    | 31             | 100 | 77.527*  | MCp <0.001* | MCp <0.001*     | MCp <0.001* | MCp <0.001* |
| Stomatitis  | 12             | 38.7 | 14             | 45.2 | 0              | 0   |          |             |                 |             |             |
| Arthralgia  | 5              | 16.1 | 15             | 48.4 | 0              | 0   |          |             |                 |             |             |
| Arthritis \iritis \erythema nodosum               | 1              | 3.2  | 2              | 6.5  | 0              | 0   |          |             |                 |             |             |

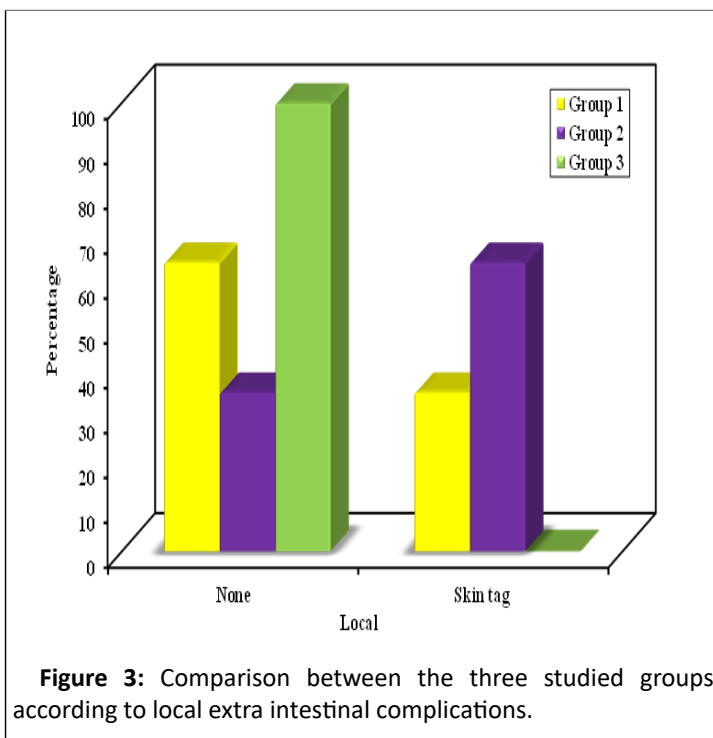
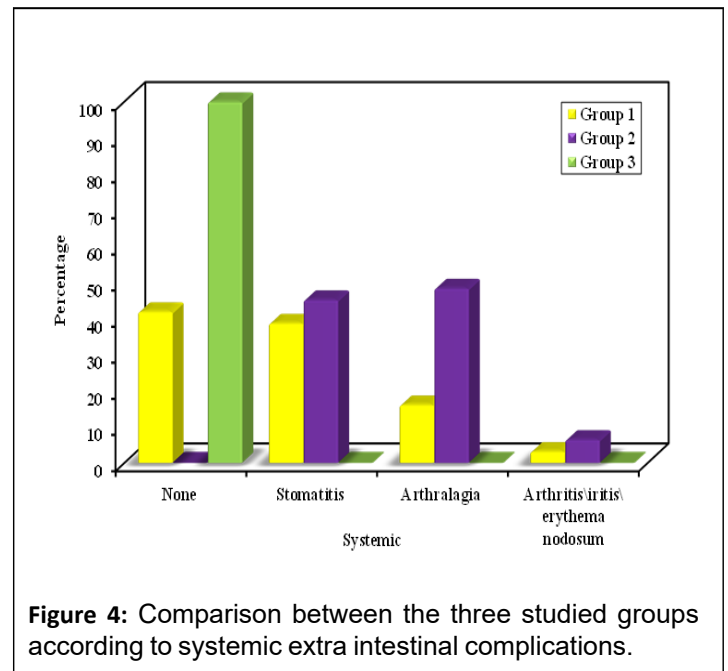
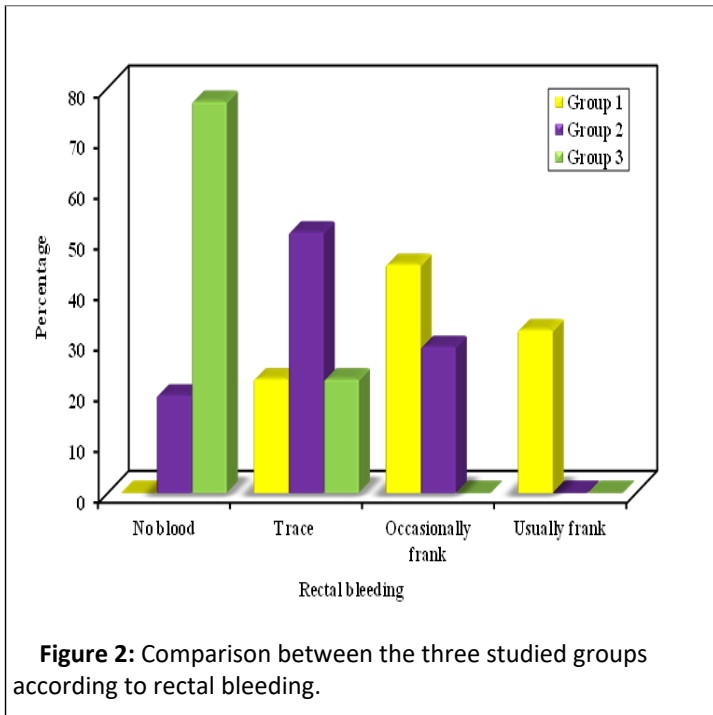
**Note:**  $\chi^2$ : Chi square test

MC: Monte Carlo

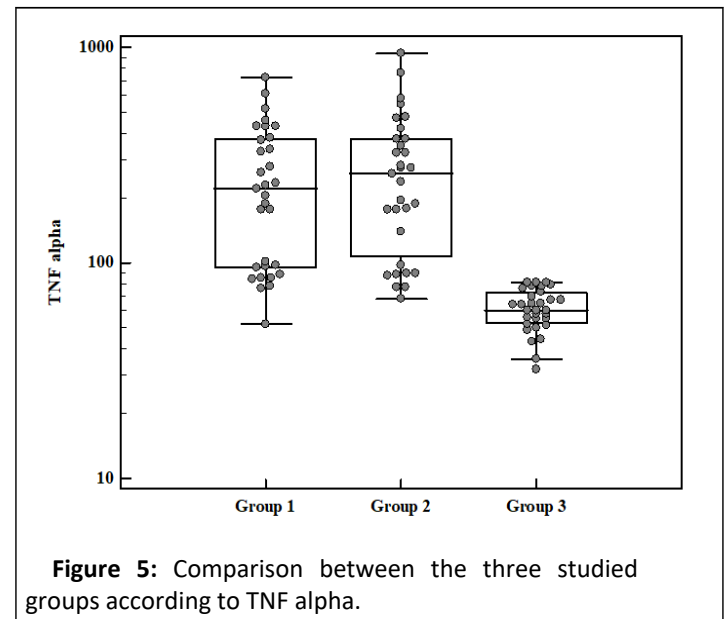
p: p value for comparing between the studied groups

\*: Statistically significant at  $p \leq 0.05$

Group 1: Ulcerative colitis patients, Group 2: Crohn's disease patients, Group 3: Control, n: number



This study showed highly significant difference between studied groups as regard PLT, TLC and HB with (P value <0.001) (Tables 14-16).



**Table 14:** Comparison between the three studied groups according to CBC.

|                  | Group 1<br>(n=31) | Group 2<br>(n=31) | Group 3<br>(n=31) | F        | p       | Sig. bet. grps. |         |         |
|------------------|-------------------|-------------------|-------------------|----------|---------|-----------------|---------|---------|
|                  |                   |                   |                   |          |         | 1 vs. 2         | 1 vs. 3 | 2 vs. 3 |
| <b>Hb (g/dl)</b> |                   |                   |                   |          |         |                 |         |         |
| Min.-Max.        | 9.0-10.5          | 9.0-12.0          | 12.0-15.0         | 145.949* | <0.001* | 0.913           | <0.001* | <0.001* |
| Mean ± SD.       | 9.39 ± 0.71       | 10.32 ± 0.71      | 13.18 ± 0.83      |          |         |                 |         |         |

|   |                     |                      |                    |         |         |       |         |         |
|---|---------------------|----------------------|--------------------|---------|---------|-------|---------|---------|
| Median (IQR)  | 10.30 (10.0-11.0)   | 10.0 (10.0-11.0)     | 13.0 (12.50-14.0)  |         |         |       |         |         |
| <b>PLT(10<sup>3</sup>/ul)</b>   |                     |                      |                    |         |         |       |         |         |
| Min.-Max.   | 145.0-22.0          | 145.0-254.0          | 177.0-467.0        | 44.391* | <0.001* | 0.989 | <0.001* | <0.001* |
| Mean ± SD.  | 179.2 ± 18.81       | 177.6 ± 23.39        | 265.3 ± 66.12      |         |         |       |         |         |
| Median (IQR)  | 178.0 (170.0-194.5) | 178.0 (158.0-190.50) | 254.0 (230.5-82.5) |         |         |       |         |         |
| <b>TLC (10<sup>3</sup>/ul)</b>  |                     |                      |                    |         |         |       |         |         |
| Min. – Max.   | 7.0-18.50           | 7.0-16.50            | 7.0-11.0           | 8.014*  | 0.001*  | 0.626 | 0.001*  | 0.013*  |
| Mean ± SD.  | 11.66 ± 2.59        | 11.13 ± 2.69         | 9.46 ± 1.11        |         |         |       |         |         |
| Median (IQR)  | 11.0 (10.0-14.0)    | 10.0 (9.25-13.0)     | 10.0 (9.0-10.0)    |         |         |       |         |         |
| <b>HCT (%)</b>  |                     |                      |                    |         |         |       |         |         |
| Min.-Max.   | 19.0-36.0           | 19.0-46.0            | 30.0-47.0          | 14.140* | <0.001* | 0.336 | <0.001* | 0.001*  |
| Mean ± SD.  | 30.45 ± 5.51        | 32.55 ± 6.64         | 38.06 ± 5.22       |         |         |       |         |         |
| Median (IQR)  | 33.0 (26.50-34.0)   | 34.0 (30.0-35.0)     | 38.0 (34.0-43.0)   |         |         |       |         |         |
| <p><b>Note:</b> IQR: Inter Quartile Range<br/>                 SD: Standard deviation<br/>                 F: F for One way ANOVA test, pairwise comparison bet.<br/>                 Each 2 groups was done using Post Hoc Test<br/>                 p: p value for comparing between the studied groups (Tukey)<br/>                 *: Statistically significant at p ≤ 0.05<br/>                 Group 1: Ulcerative colitis patients, Group 2: Crohn's disease patients, Group 3: Control, n: number<br/>                 Hb: Hemoglobin; PLT: Platelets; TLC: Total Leukocytic Count; HCT: Hematocrit</p> |                     |                      |                    |         |         |       |         |         |

**Table 15:** Comparison between the three studied groups according to liver function tests and kidney function tests.

|                    | Group 1 (n=31)   | Group 2 (n=31)   | Group 3 (n=31)  | Test of sig. | p       | Sig. bet. grps. |         |         |
|--------------------|------------------|------------------|-----------------|--------------|---------|-----------------|---------|---------|
|                    |                  |                  |                 |              |         | 1 vs. 2         | 1 vs. 3 | 2 vs. 3 |
| <b>Alb (gm/dl)</b> |                  |                  |                 |              |         |                 |         |         |
| Min.-Max.          | 3.1-3.5          | 3.30-3.8         | 3.60-4.50       | F=7.954*     | <0.001* | 0.867           | 0.006*  | <0.001* |
| Mean ± SD.         | 3.0 ± 0.22       | 3.5 ± 0.25       | 3.96 ± 0.20     |              |         |                 |         |         |
| Median (IQR)       | 3.70 (3.65-3.90) | 3.70 (3.50-3.95) | 3.90 (3.90-4.0) |              |         |                 |         |         |

| <b>AST (UI )</b>   |                   |                   |                    |           |         |       |         |         |
|--|-------------------|-------------------|--------------------|-----------|---------|-------|---------|---------|
| Min. – Max.  | 20-100.0          | 22.0-98.0         | 19.0-9.0           | F=27.600* | <0.001* | 0.959 | <0.001* | <0.001* |
| Mean ± SD.   | 63.90 ± 23.15     | 62.55 ± 23.55     | 31.68 ± 5.36       |           |         |       |         |         |
| Median (IQR)   | 67.0 (48.50-79.0) | 66.0 (46.0-78.50) | 33.0 (30.0-35.0)   |           |         |       |         |         |
| <b>ALT (UI )</b>   |                   |                   |                    |           |         |       |         |         |
| Min.-Max.  | 24.0-98.0         | 34.0-97.0         | 19.0-39.0          | H=40.538* | <0.001* | 0.774 | 0.774   | 0.774   |
| Mean ± SD.   | 63.97 ± 25.67     | 63.45 ± 19.36     | 30.90 ± 5.83       |           |         |       |         |         |
| Median (IQR)   | 76.0 (44.0-82.0)  | 65.0 (46.0-81.50) | 33.0 (25.50-34.50) |           |         |       |         |         |
| <b>Urea (mg/dl)</b>  |                   |                   |                    |           |         |       |         |         |
| Min.-Max.  | 46.0-100.0        | 21.0-100.0        | 19.0-39.0          | 57.730*   | <0.001* | 0.925 | 0.774   | 0.774   |
| Mean ± SD.   | 76.74 ± 18.99     | 78.32 ± 19.77     | 31.13 ± 5.40       |           |         |       |         |         |
| Median (IQR)   | 88.0 (57.50-92.0) | 87.0 (67.0-96.0)  | 31.0 (30.0-34.50)  |           |         |       |         |         |
| <b>Creatinine (mg/dl)</b>  |                   |                   |                    |           |         |       |         |         |
| Min.-Max.  | 1.0-2.2           | 1.0-2.0           | 0.70-1.20          | 45.280*   | <0.001* | 0.629 | 0.774   | 0.774   |
| Mean ± SD.   | 1.29 ± 0.25       | 1.30 ± 0.21       | 0.97 ± 0.12        |           |         |       |         |         |
| Median (IQR)   | 1.20 (1.20-1.30)  | 1.30 (1.20-1.40)  | 1.0 (0.90-1.0)     |           |         |       |         |         |
| <p><b>Note:</b> IQR: Inter Quartile Range<br/>                     SD: Standard deviation<br/>                     H: H for Kruskal Wallis test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test)<br/>                     F: F for One way ANOVA test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey)<br/>                     p: p value for comparing between the studied groups<br/>                     *: Statistically significant at p ≤ 0.05<br/>                     Group 1: Ulcerative colitis patients, Group 2: Crohn's disease patients, Group 3: Control, n: number<br/>                     Alb: Albumin; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase</p> |                   |                   |                    |           |         |       |         |         |

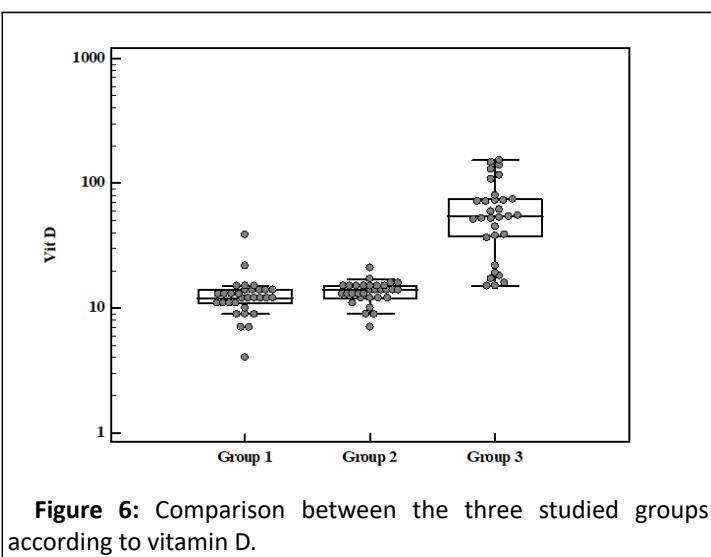
**Table 16:** Comparison between the three studied groups according to mean platelet volume and platelet distribution width.

|  | Group 1<br>(n=31) | Group 2<br>(n=31) | Group 3<br>(n=31) | Test of sig. | p | Sig. bet. grps. |         |         |
|--|-------------------|-------------------|-------------------|--------------|---|-----------------|---------|---------|
|  |                   |                   |                   |              |   | 1 vs. 2         | 1 vs. 3 | 2 vs. 3 |
|  |                   |                   |                   |              |   |                 |         |         |

| Mean platelet volume (femto liters)  |                  |                   |                   |           |         |       |         |         |
|--|------------------|-------------------|-------------------|-----------|---------|-------|---------|---------|
| Min.-Max.  | 5.0-9.5          | 5.3-9.0           | 8.0-11.0          | F=70.524* | <0.001* | 0.767 | <0.001* | <0.001* |
| Mean ± SD.   | 6.68 ± 1.04      | 6.50 ± 1.02       | 9.35 ± 1.11       |           |         |       |         |         |
| Median (IQR)   | 7.0 (6.0-7.0)    | 6.0 (5.70-7.0)    | 9.0 (8.0-10.0)    |           |         |       |         |         |
| Platelet distribution width (%)  |                  |                   |                   |           |         |       |         |         |
| Min.-Max.  | 18.0-40.0        | 19.0-41.0         | 20.0-50.0         | H=13.030* | <0.001* | 0.573 | 0.005*  | <0.001* |
| Mean ± SD.   | 29.16 ± 5.61     | 28.26 ± 5.93      | 35.58 ± 8.74      |           |         |       |         |         |
| Median (IQR)   | 30.0 (23.0-34.0) | 28.0 (23.0-33.50) | 34.0 (29.0-44.50) |           |         |       |         |         |
| <p><b>Note:</b> IQR: Inter Quartile Range<br/>                     SD: Standard deviation<br/>                     H: H for Kruskal Wallis test, Pairwise comparison bet.<br/>                     Each 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test) bet.<br/>                     Each 2 groups was done using Post Hoc Test (Tukey)<br/>                     F: F for One way ANOVA test, Pairwise comparison<br/>                     p: p value for comparing between the studied groups<br/>                     *: Statistically significant at <math>p \leq 0.05</math><br/>                     Group 1: Ulcerative colitis patients, Group 2: Crohn's disease patients, Group 3: Control, n: number</p> |                  |                   |                   |           |         |       |         |         |

## Discussion

This study showed highly significant difference between studied groups as regard serum vitamin D level with low level of vitamin D in IBD patients. Vitamin D is associated with different IBD activity status (**Figure 6**).



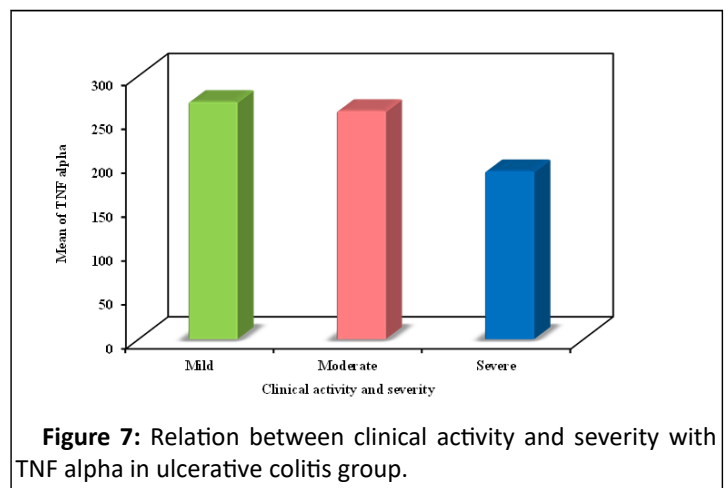
In our study, there was no significant difference between the studied groups as regard age (P value=0.827).

As our study, Huang, et al., [8] showed no significant difference between studied groups as regard age p value 0.099.

The present study showed no significant difference between studied groups as regard gender with (P value=0.842).

Our study agreed with Huang et al., [8] that showed no significant difference between studied groups as regard gender with (P value 0.715) (**Figure 7**).

Law, et al., [9] showed no significant difference between ulcerative colitis group and control group as regard age and gender with P value 1.00 and 0.087 respectively.



In our study, there was no significant difference between the studied groups as regard body mass index (P value=0.712).

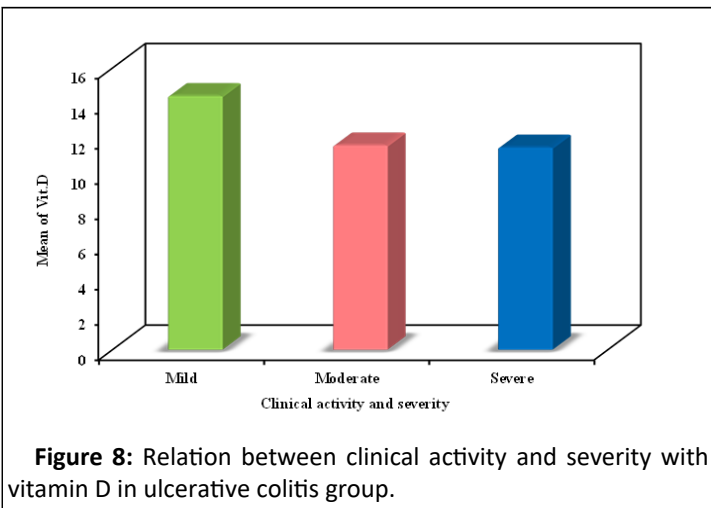
As our study, Huang, et al., [8] showed no significant difference between studied groups as regard body mass index p value 0.115.

In the current study there is no significant difference between ulcerative colitis group and Crohn's disease group as regard ESR and CRP with P value 0.940 and 0.611 respectively.

Against our study KIM, et al., [10] showed significant differences between ulcerative colitis group and Crohn's disease group as regard ESR with P value 0.005.

The present study showed highly significant difference between ulcerative colitis group and Crohn's disease group compared to control group as regard ESR with P value <0.001 (Figure 8).

This study agreed with Mak, et al., [11] that showed that ESR was highly significantly higher in ulcerative colitis and crohn's disease group than control group (P value <0.001).



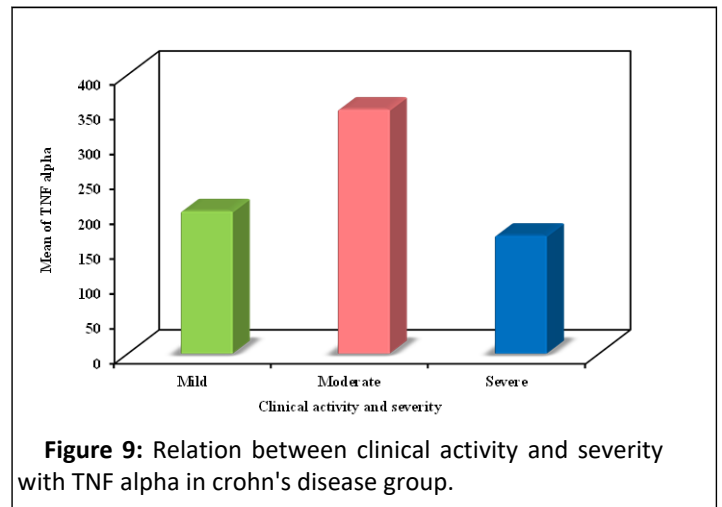
**Figure 8:** Relation between clinical activity and severity with vitamin D in ulcerative colitis group.

Against our study KIM, et al., [10] showed highly significant differences between ulcerative colitis group and Crohn's disease group as regard CRP with P value <0.001.

The present study showed that CRP (C-Reactive Protein) levels were significantly higher in ulcerative colitis group and crohn's disease group compared to control (Figure 9).

This is agreed with Chen, et al., [12] who conducted a retrospective study that involved 876 IBD patients (275 patients with UC and 601 patients with CD) and reported that CRP levels in active IBD patients were significantly higher.

Our study showed no significant difference between ulcerative colitis group and Crohn's disease group as regard serum albumin with P value 0.867.



**Figure 9:** Relation between clinical activity and severity with TNF alpha in crohn's disease group.

Against our study KIM et al., [10] Showed highly significant differences between ulcerative colitis group and Crohn's disease group as regard albumin with P value <0.001.

This study showed highly significant difference between the 3 studied groups as serum vitamin D level with (P value <0.001) with mean serum vitamin D level was (12.87 ± 5.79) (ng/ml) in ulcerative colitis group and (13.48 ± 2.64) (ng/ml) in Crohn's disease group and (63.03 ± 40.23) (ng/ml) in control group.

Huang, et al., showed significant difference between the 3 studied groups as regard serum vitamin D level with (P value 0.005) with mean vitamin D level was (36.6 ± 9.7) (ng/ml) in ulcerative colitis group and (46.4 ± 9.4) (ng/ml) in Crohn's disease group and (89.9 ± 10.9) (ng/ml) in control group.

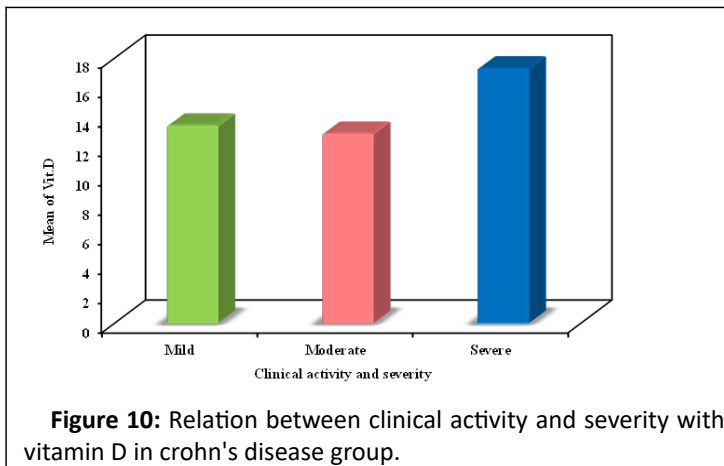
In the current study there is no significant difference between ulcerative colitis group and Crohn's disease group as regard serum vitamin D level with (P value 0.163).

With our study KIM, et al., [10] showed no significant differences between ulcerative colitis group and Crohn's disease group as regard serum vitamin D level with P value 0.611.

Our study showed highly significant difference between ulcerative colitis group and control group as regard serum vitamin D level with P value <0.001.

As our study, Law, et al., [9] showed highly significant difference between ulcerative colitis group and control group as regard serum vitamin D level with P value <0.001.

In the current study there is no significant difference between serum vitamin D level and disease activity in ulcerative colitis group and Crohn's disease group with P value 0.642 and 0.054 respectively (Figure 10).



**Figure 10:** Relation between clinical activity and severity with vitamin D in crohn's disease group.

Against our study KIM, et al., [10] showed highly significant difference between vitamin D deficiency and activity of inflammatory bowel disease with P value <0.001.

Against our study Wu, et al., [13] showed highly significant difference between vitamin D deficiency and activity of inflammatory bowel disease with P value <0.001.

Meckel, et al., [14] showed that vitamin D levels inversely correlated with mucosal inflammation and disease activity.

Ye, et al., [15] showed that vitamin D levels were inversely correlated with endoscopic, clinic and laboratory disease activity.

Our study showed highly significant difference between the 3 studied groups as serum TNF alpha level with (P value <0.001) with mean serum TNF alpha level was ( $256.1 \pm 176.4$ ) (pg/ml) in ulcerative colitis group and ( $290.5 \pm 210.0$ ) (pg/ml) in Crohn's disease group and ( $61.55 \pm 13.30$ ) (pg/ml) in control group.

As our study, Huang, et al., [8] showed highly significant difference between the 3 studied groups as regard serum TNF alpha level with (P value <0.001) with mean serum TNF alpha level was ( $364 \pm 90.7$ ) (pg/ml) in ulcerative colitis group and ( $283.0 \pm 160.1$ ) (pg/ml) in Crohn's disease group and ( $49.6 \pm 10.6$ ) (pg/ml) in control group.

In the current study there is highly significant difference between ulcerative colitis group and Crohn's disease group compared to control group as regard fecal calprotectin with P value <0.001.

As our study Lin, et al., [16] reported that fecal calprotectin was highly significantly higher in ulcerative colitis and crohn's disease group than control group (P value <0.001).

## Conclusion

Vitamin D is associated with different IBD activity status and its deficiency is highly prevalent among IBD patients with low levels of vitamin D in IBD patients.

## Ethics Approval and Consent to Participate

The study was approved by the local institutional ethical committee of Menoufia University and informed consents were taken from the participants recruited to the study.

## The Ethical Committee Approval Number

11/2021 INTM 36

## Availability of Data and Materials

The authors confirm that the data supporting the findings of this study are available within the article.

## Competing Interests

The authors declared no potential competing interests with respect to the research, authorship, and/or publication of this article.

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